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DTT

Diabetes Technology & Therapeutics

ATTD 2015 Invited Speakers

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CSII IN TYPE 2 DIABETES: EVOLUTION OR REVOLUTION?

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The use of external pumps in patients with type 2 diabetes is a much more recent practice than for type 1 diabetes. In only a few countries, continuous subcutaneous insulin infusion (CSII) using an external pump is an alternative in type 2 diabetes that is reimbursed by health authorities. Very few randomized controlled studies have looked at the comparative effectiveness of CSII versus multiple daily injections (MDI) and until recently their results were controversial. Recent data from the randomized, open-label, controlled OPT2MISE trial have changed the approach of insulin intensification when multiple daily injections fail to reach the glycaemic targets. The study has demonstrated that pump therapy is beneficial for a group of patients who fail to respond to MDI after active insulin titration. Observational long term studies have also suggested the durability of pump efficacy in type 2 diabetes cohorts and have emphasized that complete autonomy with the device is not a prerequisite for obtaining the anti-hyperglycemic effect of pump therapy in these older populations. Careful selection of the good candidate is of paramount importance since it guarantees the anti-hyperglycemic action and the safety of pump therapy, as observed in randomized and real-life studies. This demonstration of the safety and efficacy of pump therapy offers a realistic treatment alternative for type 2 diabetes and opens to patients a new way for thriving with technology and devices aimed to prevent them from diabetes complications.

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THE IMPACT OF NEW TECHNOLOGY IN TYPE 2 DIABETES

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Recent evidence from clinical trials indicates that technology applied to type 2 diabetes (T2D) can indeed be very useful to improve metabolic control in affected patients. The first study using CSII and published by Weng in the Lancet in 2008 demonstrated that the use of CSII may induce clinical remission and protect residual beta cell function. In a recent study published in 2014 in the Lancet it was shown that in patients with poorly controlled T2D despite using multiple daily insulin injections, pump treatment can be considered as a safe and valuable treatment option.

Intensive glucose monitoring in T2D is also useful to improve metabolic control. In the PRISMA study published in Diabetes Care in 2013 we aimed to evaluate the added value of intensive self-monitoring of blood glucose (SMBG), structured in timing and frequency, in noninsulin-treated patients with T2D. The use of structured SMBG improves glycemic control and provides guidance in prescribing diabetes medications in patients with relatively well-controlled noninsulin-treated T2D.

Barriers to use technology in T2D include older age in some patients and lack of proper patient education regarding the advantage of using technology in disease management. Diabetes technology is therefore an example of personalized medicine, which should be designed according to patient features and therapeutic target. This is particularly true for the new patch pumps, closed-loop insulin delivery systems and applications in nanomedicine.

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LATE COMPLICATIONS OF BARIATRIC SURGERY

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THREE DIMENSIONAL AND FUNCTIONAL QUANTIFICATION OF OBESITY

Background: The quantification of obesity has been limited by the unreliability of the Body Mass Index (BMI = Kg/M2) and the expense and X-ray exposures CT and DEXA scans. White light scanning, a technology that constructs a three dimensional avatar of the human body, permits, for the first time, the calculation of body surface area, volume and shape to relate these measures to the manifestations of the metabolic syndrome. The scans are safe and can be carried out with a patient, dressed in underclothes, in less than a minute.

Methodology: Patients were scanned before and after bariatric surgery 1) to determine the accuracy of the methodology vs. body measurements by RN's, 2) to follow weight loss and body shape, 3) to assess the three dimensional shape of the lost fat, 4) to determine whether the surgery changed the shape of patients from ''apple'' to ''pear'' and 5) to identify whether the shapes of the patients could be correlated with expressions of the metabolic syndrome.

Results: White light scanning 1) measures body circumference levels more accurately than nurses with tape 2) documents loss of adiposity following bariatric surgery in three dimensions

3) allows three dimensional representation of lost fat (Fig. 1), 4) documents that the body shape, i.e. ''apple'' vs. ''pear'' is not changed by bariatric surgery and 5) predicts the presence or absence of diabetes ($p < 0.07$), hypertension ($p < 0.0007$) and dyslipidemia ($p < 0.07$).

Conclusions: White light scanning offers a new, inexpensive, rapid and safe technology to assess body shape, volume and surface area and to examine correlations between the relationships of fat distribution to the development of the metabolic syndrome.

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PSYCHOLOGICAL MEASURES USED IN DIABETES TECHNOLOGIES RESEARCH

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Quality of life (QoL) is widely recognized as an important health outcome in diabetes, where the burden of self-management is demanding. Optimal diabetes management goes beyond glycaemic control, with broader psychological factors having an important role to play. As such, psychosocial assessment is crucial. The devil is, of course, in the detail. What should we measure, how can we measure it, what will it tell us and how will that inform the regulatory approvals process and best clinical practice? These are all questions that will be addressed in my talk.

In order to develop diabetes devices that are inclusive, accessible, effective, safe, and integrated into routine diabetes care with acceptance from people with diabetes requires a clearer view of outcomes other than glucose and key questions remain unanswered. Regulatory and commissioning bodies such as NICE and FDA expect psychosocial evaluation and outcomes to support the implementation of devices into routine care. Comparability across clinical trials is crucial in this regard. Transparent, robust, evidence-based and theory driven psychological assessment is required alongside engineering and biomedical evaluation. These issues will be addressed.

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REPORTING OF GLUCOSE CONTROL METRICS

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After one decade on intense clinical research on glycemic control in critically ill patients hospitalized in an Intensive Care Unit, several issues are still unanswered, including the optimal blood glucose target range in various categories of patients and the presence of causality between dysglycaemia and poor outcome. New technological developments, including intravascular or interstitial continuous glucoe monitoring and closed-loop systems for insulin titration require an evalaution of their reliability and clinical usefulness.

The answers to these issues will need an accurate and uniform definition of the performance of glucose control, implying the use of standard metrics.

This talk will describe the available indices of hyperglycaemia, hypoglycaemia and glycaemic variability that were used and validated in ICU patients. The adoption of uniform metrics will hopefully improve the quality of care, and will allow the estimation of the magnitude of outcome improvement when

blood glucose can be maintained within a narrow range. Quite importantly, different therapeutic interventions will be unequivocally comparable, using a single metrics.

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GLUCOSE CONTROL IN THE ICU USING CONTINUOUS GLUCOSE MONITORING: WHAT LEVEL OF MEASUREMENT ERROR IS ACCEPTABLE?

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Safe and efficacious glucose control in the intensive care unit (ICU) depends on accuracy and frequency of blood glucose measurements. Accuracy standards to determine adequate devices are subject of ongoing debate. At present, majority of glucose measurements in ICU are carried out intermittently using YSI, arterial blood gas analysers or point of care devices. Emerging continuous glucose monitors (CGM) offer potential benefits by providing frequent measurements, trending information, threshold and predictive alarms. These potential benefits need to be evaluated and documented. In this study we utilized a validated virtual population of the critically ill to contrast the outcomes from three established insulin titrating protocols informed by either continuous or intermittent glucose measurements. Results showed similar efficacy of CGM-informed and BG-informed protocols but lower risk of hypoglycaemia using CGM with MARD up to 10%. Type of protocol had a larger effect on glucose outcomes than the measurement method.

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PERIOPERATIVE GLUCOSE CONTROL IN CARDIAC SURGERY PATIENTS: ANOTHER POSSIBILITY TO IMPROVE THE OUTCOMES?

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During the last two decades, the treatment of hyperglycemia in critically ill patients has become one of the most discussed topics in the intensive medicine field. The initial data suggesting significant benefit of normalization of blood glucose levels in all critically ill patients using intensive intravenous insulin therapy have been challenged or even neglected by some later studies. At the moment, the need for glucose control in critically ill patients is generally accepted yet the target glucose values are still the subject of ongoing debates. Current data suggest that certain subgroups of critically ill, in particular the cardiac surgery patients, may benefit from tight glucose control while this may not be generally true for other groups of critically ill patients. We have recently demonstrated that even short-term perioperative tight glucose control in cardiac surgery patients significantly reduced their morbidity suggesting the patophysiological importance of this parameter. The morbidity reduction in our study was primarily driven by improved morbidity in patients without previous history of diabetes while much less benefit could be seen in diabetics. Since increased risk of hypoglycemia appears to be the major obstacle of tight glucose control, the novel technological approaches including continuous glucose

monitoring and its combination with computer-based algorithms may help to overcome some this hurdle. Additionally, a combination of insulin with other glucose lowering medications such as intravenously administered glucagon like peptide-1 agonists may improve glucose control without increasing the risk of hypoglycemia or other significant side effects. The benefits of these approaches need to be further tested not only in cardiac surgery patients but also in other subgroups of critically ill.

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MARKET ACCESS OF ANTIDIABETICS IN GERMANY: ASSESSMENT OF ANTIDIABETICS BY THE FEDERAL JOINT COMMITTEE (G-BA)

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Diabetes affects several million people in Germany and is a major contributor to the ever increasing spending in healthcare. This talk will give an overview of the reimbursement of antidiabetic drugs, blood glucose measurement devices and treatment appliances in Germany and which rules and regulations apply to them. Furthermore a brief introduction will be given to the structure and function of the G-BA, Germany's highest decision-making body in the statutory health insurance system. The early benefit assessment according to the AMNOG law (introduced in 2011) will also be presented as well as experiences with the assessment of new antidiabetic drugs since 2011, assessment criteria and some results of the G-BA assessment of new drugs. Thus far, the G-BA determined a minor additional benefit over the appropriate comparator in 4 out of 14 assessments, because a reduction of non-severe hypoglycemias was shown. As long-term data regarding mortality, cardiovascular morbidity and safety were not available, several resolutions of the G-BA were time-limited.

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DIADVISOR

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The key goal of diabetes treatment is to maintain blood glucose (BG) at near to normal level. This is a demanding and difficult task for the individual patient and requires extensive support from Health Care Providers. The objective of the DIAdvisor Project, funded by a FP7 EC Grant, was to provide a medical device technology that minimises the diabetes-related burden to patients and to healthcare systems by increased patient empowerment. From a data base gathering information on glucose levels, insulin doses, food intakes, physical activity in a large series of patients with Type 1 or Type 2 diabetes treated by various insulin regimens, algorithms were developed aiming at prediction of glucose evolution at various horizons. Besides, a controller was connected to the prediction algorithms in order to deliver online advices to the patients aiming at the reduction of out-of-range glucose excursions. A wearable tablet platform was developed to collect continuous glucose monitoring inputs, compute predicted glucose evolution and deliver advices when needed, also serving as patient interface with the system so that insulin doses and food intakes could be introduced by the patient. After two iterations tested in patients, the DIAdvisor device was shown to be able to predict accurately BG at 20-min horizon and to deliver safe advices to patients with insulin-treated (basal-bolus regimen) diabetes. A final multicentre clinical study has demonstrated that DIAdvisor use can help patients with Type 1 diabetes under basal-bolus insulin regimen to keep BG in target range and reduce hypoglycemia. These results support the development of this device and its further evaluation on longer term in outpatient conditions.

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HYPOGLYCEMIA REDUCTION WITH CLOSED-LOOP SYSTEMS BY AGE

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RANDOMIZED TRIALS OF A HOME SYSTEM TO REDUCE HYPOGLYCEMIA USING A PREDICTIVE LOW GLUCOSE SUSPEND (PLGS) ALGORITHM IN DIFFERENT AGED SUBJECTS WITH TYPE 1 DIABETES

The effects of temporarily (up to 3 hrs/night) suspending pump insulin delivery when hypoglycemia was predicted by an algorithm based on CGM glucose levels was previously described for 1,912 home-study nights in 45 people, ages 15–45 yrs with T1D (Diabetes Care 37, 1885, 2014). These studies are now extended to evaluate 1,524 home-study nights in 36 subjects 4–10 yrs old and in 1,896 study-nights in 45 subjects 11–14 yrs old.

Median time below 70 mg/dl was reduced significantly on intervention nights versus control nights in both the 11–14 year olds (54% reduction) and the 4–10 year olds (50% reduction), comparable to the reduction previously reported in 15–45 year olds. The percent of nights with a pump suspension decreased with the age of the participants (76%, 70%, 65% respectively for 15–45, 11–14, and 4–10 year olds). Hypoglycemia reduction came at the cost of increased mean sensor glucose overnight between 7 and 8 mg/dl for each age group on intervention nights versus control nights. However, in all three age groups, there was no increase in morning serum ketones ≥ 0.6 mmol/L following intervention nights compared with control nights.

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PATCH PUMPS VS. DURABLE PUMPS IN CHILDREN WITH TYPE 1 DIABETES

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Insulin pumps (CSII) are the most physiologic means currently available for insulin delivery. Today's pumps are available as durable pumps (with external tubing) and disposable (without external tubing, e.g., OmniPod) versions. In German pediatric diabetology, the change from a conventional twice daily regimen of former years, to multiple dose injections and more recently, insulin pumps, has been associated with a continuous improvement of glycaemic control. The durable pumps are attached to the body using an infusion set. The current second-generation OmniPod is the only patch pump available for type 1 diabetes in Germany and is attached directly to the body. A small catheter is inserted subcutaneously from the underside of the patch pump by pressing a button on the remote control. This serves as the patch pump's infusion set. Durable pumps can be detached from the site for activities. Currently available patch pumps remain on the body for 3 days and are waterproof. According to the German/Austrian pediatric DPV-registry approximately 48% of the 25,000 children with type 1 diabetes are currently using CSII with 1214 cumulative patients using the Omipod (R. Holl, Ulm, personal communication). Today, basal rates can be titrated in small increments as needed particularly for children. There is controversy regarding the clinical relevance of the accuracy of insulin delivery between different pump models and patch pumps vs. durable pumps. We have therefore undertaken a 12 week cohort study of 30 consecutive type 1 diabetes patients switching to Omnipod (age: 7 to 17 years, baseline HbA1c: 6.2–8.9%, 15 previously using pens, 15 using durable pumps) to assess the effects of patch pump therapy on glycemic control and treatment satisfaction. The results will become available at ATTD 2015.

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APPROACHES TO BEHAVIORAL INTERVENTIONS TO ENCOURAGE CGM USE IN PEDIATRIC PATIENTS

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Modern intensive insulin therapy uses advanced therapeutics and diabetes technologies, including insulin analogs, pumps with bolus calculators, and continuous glucose monitors (CGM). Intensive therapy aims to achieve target levels of glycemic control. Yet, the majority of pediatric patients fail to achieve the A1c target of <7.5%, with only 1 out of 4 youth with type 1 diabetes succeeding.

Adults utilizing CGM generally achieve a greater proportion of glucose values in range (70–150 mg/dL; 3.8–8.3 mM), hemoglobin A1c reduction of 0.5%, and either reduced occurrence of severe hypoglycemia or no increase in severe hypoglycemia compared to standard therapy. Pediatric patients do not achieve the same benefits. The age of the pediatric patient predicts use of CGM and CGM use, in turn, predicts glycemic benefits. For patients who consistently use CGM, hemoglobin A1c can improve by at least 0.5% without increased risk of severe hypoglycemia. However, the school age child, the adolescent, and the young adult continue to demonstrate significant challenges in sustaining CGM use.

In the JDRF CGM study, only 30% of patients ages 15–24 and 50% of patients ages 8–14 utilized CGM consistently. A recent study has demonstrated that self-efficacy related to CGM predicts CGM use and improved A1c. Therefore, there are opportunities to increase CGM use in pediatric patients by assessing self-efficacy and supporting pediatric patients and families with low confidence related to CGM use. Newer CGM devices have increased accuracy yet they continue to require care with insertion, calibration, responding to alerts/alarms, and ongoing blood glucose monitoring. Therefore, it is important to recognize and overcome behavioral barriers to CGM implementation so that pediatric patients can achieve the CGM benefits related to improved glycemic control without severe hypoglycemia.

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WHAT SHOULD BE THE GLYCEMIC GOALS IN PREGNANCY COMPLICATED BY DIABETES?

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The association between diabetes during pregnancy and the risk of adverse maternal and fetal outcome is well established. Maternal complications include spontaneous abortions, preterm deliveries, pre-eclampsia, nephropathy, cesarean section and among others birth trauma. The main fetal and neonatal complications are congenital anomalies, deviant fetal growth, birth related trauma, metabolic abnormalities and still birth. Moreover, evolving evidence indicate that diabetes, among other components of the metabolic syndrome, is a significant risk factor for childhood and adult obesity, cardiovascular disease, and diabetes, due to in utero programming mechanisms including altered organ development, cellular signalling responses, and epigenetic modifications of gene expression.

Not only that improving glycemic control reduces the risk for adverse outcome in pre-gestational diabetes, but also ingestational diabetes mellitus (GDM), treatment and achieving desired level of glycemic status effectively diminishes the risk for complications. Yet, several issues should be addressed when discussing the relation between glycemic control and adverse pregnancy outcome. First, how is good glycemic control defined? What is the glucose threshold that should be reached in order to diminish the risk for adverse outcome? Second, is maintaining glycemic control according to the recommendations and guidelines can truly abolish the increased risk for complications as compared to the general population? Finally, how glucose status should be monitored during pregnancy in regards to the methods used, diurnal occasions and frequencies?

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FASTER-ACTING INSULIN ASPART IMPROVES POSTPRANDIAL GLYCAEMIA VERSUS INSULIN ASPART IN PATIENTS WITH TYPE 1 DIABETES MELLITUS

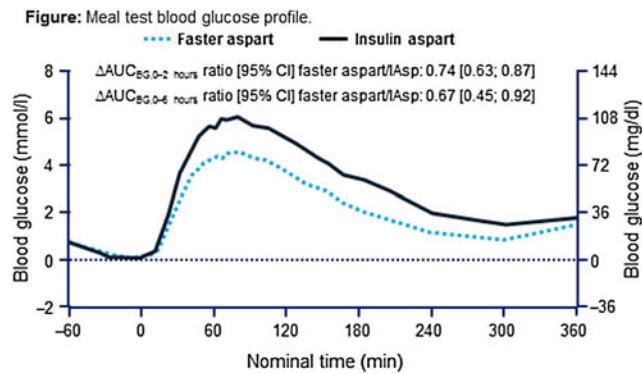*T. Heise[1], H. Haahr[2], L. Jensen[2], L. Erichsen[3], M. Hompesch[4]*

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Background: Faster-acting insulin aspart (faster aspart) is insulin aspart (IAsp) in a new formulation containing excipients nicotinamide and arginine, resulting in faster initial absorption after s.c. injection.

Figure: Meal test blood glucose profile.

········ Faster aspart —— Insulin aspart

$\Delta AUC_{BG,0-2\ hours}$ ratio [95% CI] faster aspart/IAsp: 0.74 [0.63; 0.87]
$\Delta AUC_{BG,0-6\ hours}$ ratio [95% CI] faster aspart/IAsp: 0.67 [0.45; 0.92]

Methods: Thirty six patients with T1D (mean ± standard deviation age: 38.6 ± 12.5 years; HbA_{1c}: 7.8 ± 0.81%) received a single dose (0.2 U/kg s.c.) of faster aspart or IAsp immediately (≤ 2 minutes) before a standardised liquid meal test (600 kcal) in a randomised, crossover design.

Results: Compared with IAsp, faster aspart had a faster onset of appearance (time from drug administration until first time serum insulin aspart concentration was > 30 pmol/l; median difference [95% confidence interval (CI)]: -6.6 minutes $[-8.0; -5.0]$) and greater exposure during the first 2 hours, with the largest difference in the first 15 minutes, whereas overall pharmacokinetic exposure was similar between the two insulins (mean ratio [95% CI] $AUC_{0-15\ minutes}$: 3.14 [2.59;3.80]; $AUC_{0-30\ minutes}$: 1.93 [1.64;2.26]); $AUC_{0-1\ hour}$: 1.30 [1.15;1.46]; $AUC_{0-2\ hours}$: 1.13 [1.03;1.24]; $AUC_{0-10\ hours}$: 0.99 [0.93;1.06]). Faster absorption led to a greater reduction in postprandial blood glucose (BG) with faster aspart versus IAsp, with lower post-meal AUC_{BG} over 2 and 6 hours (26% and 33% reduction, respectively; Figure), and by lower BG values 1 and 2 hours postprandially (mean difference [95%CI] $BG_{1\ hour}$: -1.24 mmol/l $[-2.01; -0.46]$; $BG_{2\ hours}$: -1.45 mmol/l $[-2.49; -0.42]$). No safety/tolerability issues were identified, including no injection site reactions.

Conclusions: Faster aspart was absorbed faster, with an increased early exposure, leading to improved postprandial glycaemic control versus insulin aspart.

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INTRODUCTION

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The availability of a system allowing a closed-loop insulin treatment of diabetes, also called artificial pancreas (AP), has been a dream for many patients with Type 1 diabetes since the first bedside versions have been developed in the 1970s concomitantly in Europe and North America. The development of wearable, miniaturized, safe and reliable insulin pumps from the 1980s and the emergence of ambulatory continuous glucose monitoring (CGM) systems from 1999 have made feasible the concept of an AP system usable in free-life. The third needed component is a controller which computes insulin delivery rate from CGM data so that blood glucose can be kept in a safe near-normal range. The two challenges to address were (i) the development of algorithms for the controller with the main hurdle being related to the delays of insulin action when infused subcutaneously and (ii) the avail-

ability of a wearable platform allowing wireless connections to the CGM and to the insulin pump, also serving as patient interface with the device system. Initiated by the JDRF-sponsored Artificial Pancreas Initiative, prolonged by the EC-funded AP at Home Project, further deployed by NIH- and Hemsley Trust-granted research, tight collaborations between European and US teams working on AP occurred. In the present session, the main achievements from 5 research studies performed in 2014 on both and/or each sides of the Atlantic Ocean will be presented. All of them use the wearable DiAs (for Diabetes Assistant) AP system whose elaboration has been coordinated by the Diabetes Technology Centre at UVA. The presentations of DiAs and the recent study results will demonstrate how current AP investigations pave the way toward a new paradigm for the care of Type 1 diabetes.

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STUDY 3 (JDRF-3)

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I will present the results of two trials: the completed AP@home transitional and the ongoing JDRF3 Europe.

The AP@home transitional trial has been performed in Montpellier (August 2013), Padova (September 2013) and Amsterdam (October 2013). 13 patients with type 1 diabetes were involved in this non-randomized 42-hours trial aimed to preliminary test safety and efficacy of Modular Model Predictive Control (MMPC) in outpatient conditions, in view of the larger final AP@home trial. The study included two dinner & overnight periods, the first day spent under CSII driven by the patient and the second day spent with the pump driven by MMPC. Results showed statistically significant improvement of both time-in-target and time-in-hypo in closed-loop with respect to open-loop, suggesting that this AP prototype is safe and effective. This trial opened the door for sustained home use, performed in the recently completed AP@home final trial.

The JDRF3 is a trial performed in six centers in Europe and USA under the coordination of the JAEB center for Health Research, (Tampa, Florida). I will focus on the European data, collected in Montpellier, Padova and Tel-Aviv. This non-randomized clinical trial first tests for a 3-week period the glycemic control achieved by the patient with Sensor Augment Pump (SAP) therapy. During the last of the 3-week period, SAP is delivered by the patient through the DiAs system. Then, the patients undergo a second 3-week period where closed-loop control is active during the night, while throughout the day the patient is still in charge to handle her/his glycemia through standard SAP. Finally, the patients undergo a third 3-week period, where closed-loop control is active throughout the whole day. Preliminary results of the patients that completed the study will be presented.

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CONCLUSION

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Since the initiation of the JDRF Artificial Pancreas Consortium, research initiatives got under way supported by the National Institutes of Health (NIH), the European Commission

(AP@Home), and the Helmsley Charitable Trust (HCT). Following a successful multi-center international study of control-to-range in the hospital, our next logical step was transition to outpatient trials, which we initiated by introducing in 2011 the first smart phone running closed-loop control – the Diabetes Assistant (DiAs).

In this presentation we summarize the timeline of our 2014–2015 studies. To date, DiAs has received 8 Investigational Device Exemptions from FDA, as well as regulatory approvals in 3 European countries and in Israel. Five-night NIH trials were done at the University of Virginia (UVA), Padova, Mount Sinai Medical School in New York, and the Mayo Clinic. One-week 24/7 HCT summer camp studies in children were completed at Stanford and at UVA. The latest AP@Home trials in Italy, France, and Holland included 2 months of overnight DiAs use at home. A 1-month JDRF study combining overnight and 24/7 control was concluded in the U.S. (UVA, Stanford, UCSB), Europe (Montpellier and Padova) and Israel, and now continues with 6 months of 24/7 DiAs home use at several of these centers. On the horizon are long-term NIH trials aiming to reverse hypoglycemia unawareness via closed-loop control and testing patient preferences to different closed-loop modalities.

Thus, in the past year our collaborative research grew to encompass 4 countries East of the Atlantic and 4 U.S. states. Four multi-center trials were completed, or are under way, confirming the viability of closed-loop control at home. More long-term studies are planned for 2015, transforming the development of the artificial pancreas into an unprecedented global effort.

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TECHNOLOGY-ENABLED INTERVENTIONS: THE FUTURE IS NOW

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Individuals with, or at risk for, diabetes must manage their everyday lives and their behaviors if they are going to remain healthy, and slow the rate of adding additional conditions or complications. There are decades of research-proven approaches which have been shown to effectively help patients adopt and sustain health promoting behaviors. When trying to impact outcomes for a population of patients, key challenges for success are to (1) engage enough of the population to take positive action, (2) provide an effective approach to those who engage which can promote sustainable behavior changes and improved outcomes, and (3) at a price and logistical burden that is acceptable to whomever is paying for the services and supports. This presentation will describe technology-enabled interventions which have been able to meet these 3 goals. Core principles for success will be presented and examples of effective approaches will be demonstrated.

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INHALED INSULIN RELOADED: IMPACT OF AFREZZA

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Pulmonary delivery of insulin is the only alternative route of insulin administration (ARIA) available to patients with diabetes, ever. This is not too surprising when one considers the major advantages of pulmonary delivery compared to other non-invasive delivery routes: (i) the lung does not contain peptidases that break down insulin before it can be absorbed (i.e. no need to modify and encapsulate the insulin), (ii) the lung has a very large surface area for absorption and (iii) the lung is naturally permeable to insulin (i.e. no need for absorption enhancers). High patient preference and favourable pharmacokinetic and pharmacodynamic properties compared to injectable insulins seemed to guarantee the success of the pulmonary delivery route. The first approved inhaled insulin product, Exubera (Nektar Therapeutics / Pfizer Inc) was however pulled from the market in October 2007, one year after its market introduction, due to disappointing sales and high production costs. Consequently, most other inhaled insulin developments at the time were stopped. Only recently a second inhaled insulin product, Afrezza (MannKind / Sanofi), was approved by the FDA. Afrezza is a drug/device combination with promising properties: The time-action profile is more rapid than any other currently marketed rapid-acting insulin analogue and the inhalation device is more efficient than any other previous development, resulting in a relative bioavailability of 30%. Based on the available clinical data, the strengths and limitations of Afrezza will be discussed in detail. As Afrezza may start a renewed interest in inhaled insulin, the presentation will conclude with an overview of other inhaled insulin products in development.

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ORAL INSULIN: WHAT IS GOING ON?

L. Plum-Morschel[1]

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Despite great demand for an an insulin pill and numerous attempts over the last nine decades to develop an orally available insulin formulation, still no insulin for oral dosing is commercially available. This presentation will discuss the obstacles hampering such a development and will provide an overview on the most recent approaches toward an oral insulin formulation with a clear focus on data from clinical-experimental and clinical studies.

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IMPLANTABLE INSULIN PUMPS

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The treatment using implantable pumps for insulin delivery into the peritoneal cavity has been developed in a few European countries for the last twenty five years and more particularly in France under the impulse of the EVADIAC study group (EVAluation dans le DIabète du traitement par implants ACtifs, EVAluation in DIabetes of the treatment through ACtive implants). This group gathering all the French implantation centers has allowed the performance of studies that addressed a large population of diabetic patients, but also a unique shared experience and vigilance of this therapy.

Randomized and observational studies have shown both the safety and the effectiveness of implanted pumps that combines

near-normal glycemic control with improved diabetes stability and a reduced occurrence of severe hypoglycaemia compared to reference subcutaneous insulin therapy in patients with Type 1 diabetes.

This treatment using implantable pumps has been recommended by our EVADIAC group, as a beneficial option for patients with Type 1 diabetes failing to reach HbA1c target and/ or presenting high blood glucose variability including frequent severe hypoglycemia in spite of well conducted continuous subcutaneous insulin infusion. Moreover patients with unreliable subcutaneous insulin absorption or showing sustained uncontrolled diabetes resulting in recurrent or prolonged hospital stays have been shown to be dramatically improved by implanted insulin pumps therapy.

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CONTINUOUS SUBCUTANEOUS INSULIN INFUSION (CSII) SETS - REDUCED FLOW INTERRUPTIONS WITH A NOVEL INVESTIGATIONAL CATHETER INFUSION SET

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Background: Effective CSII requires infusion sets to consistently deliver insulin. A novel investigational infusion set has been developed to reduce flow interruptions including sub-alarm 'silent' occlusions. With a pressure-measuring method that reliably reflects fluid flow; we compared the investigational set with the Medtronic Quick-set®. The primary objective was to characterize infusion pressure profiles during insulin diluent infusion.

Method: This was an exploratory study in 25 healthy subjects. Each received 4 diluent basal/bolus infusions (2 with each set, one inserted manually, the other with mechanical inserter). After insertion, diluent was infused at 0.01 mL/hour (= 1.0 U/hour) via insulin pump for 2 hours, followed by a 10 U bolus. The set was then clamped and remained on subject for 30 minutes. A flow interruption/silent occlusion was defined as continuous pressure rise ≥30 minutes.

Results: Demographics: female 48%, mean(SD) age 39.1(14.9) years, BMI 28.7(5.8) kg/m^2. Ninety-five infusions were evaluable; 7 Quick-sets had occlusion alerts vs. 0 investigational sets. Flow interruptions/silent occlusions with Quick-sets vs investigational sets occurred in 21 vs 5, respectively (see Table). The average percent of time with interruptions with Quick-sets were approximately 16% (manual/inserter data combined) and 3% with investigational set (see Figure).

Percent time of interruption by device/insertion method (N=95)
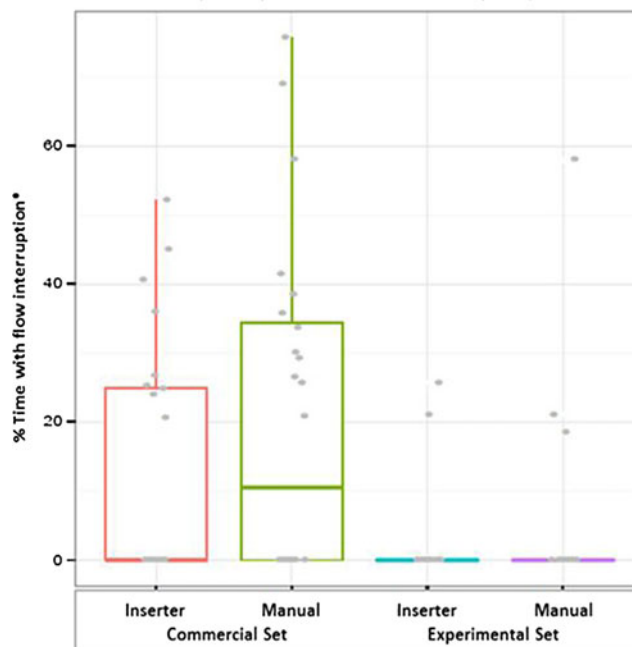
*continuous pressure rise for ≥30 minutes

Conclusion: In this exploratory study, compared to Medtronic Quick-set®, the new investigational set had fewer flow interruptions/silent occlusions, fewer occlusion alarms and less time with interrupted flow. Fewer flow interruptions may benefit CSII patients by providing more consistent insulin flow and reducing hyperglycemic episodes caused by infusion set failures.

Sets with flow interruptions and occlusion alerts by device and insertion method (N=95)

Infusion set	Insertion method	Pressure interruption#		Occlusion alerts ("no delivery")	
		Number	Percent	Number	Percent
Quick-set®	Inserter	9 / 25	36%	2 / 25	8%
	Manual	12 / 24	50%	5 / 24	21%
Investigational set	Inserter	2 / 24	8.3%	0 / 24	0%
	Manual	3 / 22	13.6%	0 / 22	0%

*continuous pressure rise for ≥30 minutes

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A DIABETES EDUCATION PROGRAM INCORPORATING SUPERVISED EXERCISE IMPROVES ACUTE BLOOD GLUCOSE MANAGEMENT IN INDIVIDUALS WITH TYPE 1 DIABETES

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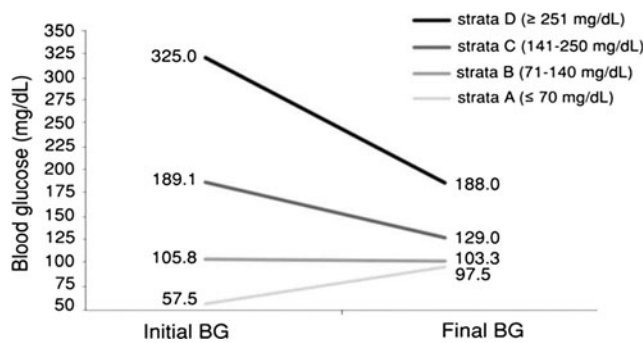
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This study was designed to examine both acute and long-term improvements in glycemic control in T1DM individuals who undertook supervised exercise and received other diabetes management strategies during participation in an interdisciplinary diabetes education program.

Methods: 39 individuals with T1DM attended 20 program meetings 1–3 times per week during a 4-month period. Subjects (16 males/23 females) ranged in age from 7 to 58 years (mean age, 23 ± 12; mean diabetes diagnosis, 8 ± 7 years). Data collected during the first 20 sequential meetings included: 1) initial capillary blood glucose(IBG) self-monitoring; 2) nutritional and insulin recalls, with recommended adjustments when necessary; 3) 50 min of exercise; 4) 30 min of educational activities; and 5) final self-monitoring of blood glucose (FBG). BG values were categorized into strata based on glycemic goals and analyzed for acute and chronic improvements in meeting targets.

Results: In data from 780 paired BG measures collected at each program meeting, IBG averaged 182.38 ± 93.83 mg/dL and FBG values were significantly lower (131.43 ± 68.70 mg/dL, $p < 0.001$). Normoglycemic BG strata (71–140 mg/dL) shifted from 33.3% to 47.2%. Most IBG values were between 141–250 mg/dL and 44.2% of those finished in normoglycemic range. Among the 27.9%(n=218) with hypoglycemia or severe hyperglycemia in their IBG, only 7.7%(n=60) of FBG values remained into one of these strata by the end of the meeting. Long-term effect of the program on BG values were not significant($p > 0.11$).

Conclusions: Diabetes education that includes supervised exercise appeared to be beneficial to acute blood glucose management in individuals of all ages with T1DM.

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SIMPLE CSII IS HIGHLY COST-EFFECTIVE

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Objective: Continuous subcutaneous insulin infusion (CSII) in people with type 2 diabetes (T2DM) has proven to improve glycemic control (HbA1c) and reduce insulin dosage compared to multiple daily injections (MDI). However, CSII has not been widely adopted in T2DM due to costs, complexity and training requirements. New devices that provide simple CSII reduce complexity and training requirements. This analysis assessed the cost effectiveness in Germany of simple infusion (SII) compared to MDI in people with T2DM not in glycemic control.

Methods: The UKPDS Outcomes Model was used to project long-term cost-effectiveness over 40 years, based on results of recently published studies and costs for Germany. Costs and outcomes were discounted at 3%. Cost-effectiveness was pre-defined in relation to per capita gross domestic product (GDP) with Incremental Cost Effectiveness Ratios (ICERs) below 1X, respectively 3X GDP per capita per life year gained, defined as highly 'cost-effective', respectively 'cost-effective'.

Results: Our analysis showed 0.2 life year gained on average and annual discounted savings on complication costs and insulin reductions of 1.187€. Based on projected costs and life expectancy, a simple CSII device will be highly cost-effective in Germany at a price of €11.7 per day. This implied an ICER at 0.66 times per capita GDP per life year gained. The estimate was very robust to sensitivity analyses on both reductions in HbA1c and dose effects.

Conclusions: For people with T2DM not in glycemic control on MDI, simple CSII is highly cost-effective at a daily cost in Germany of €11.7 or less.

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PUMP BREAKDOWN OR MALFUNCTIONS IN A LARGE COHORT OF ITALIAN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES USING INSULIN PUMP THERAPY

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Background and Aim: Pump breakdown and/or malfunctions, and consequent replacement have not been often investigated. We evaluated pump replacement in children and adolescents, with type 1 diabetes (T1D), using insulin pump therapy.

Methods: Data have been collected for all patients with less than 18 years, starting insulin pump therapy before December 31th, 2013. For each patient age, disease duration, date of insulin pump therapy initiation, insulin pump model, breakdown/malfunction/pump replacement yes/no and reason have been considered for the calendar year 2013.

Results: Data have been returned by 38 pediatric Centers belonging to the Diabetes Study Group of the Italian Society of Pediatric Endocrinology and Diabetology (ISPED). A total of 1611 out of 11.959 (13.5%) children and adolescents with T1D were using an insulin pump: 29.5% Animas VIBE™,13.7%

Minimed Medtronic 715/515™, 31.3% Medtronic VEO™, 23.2% Accu-Check Spirit Combo™, and 2.3% other types. In 2013, insulin pump has been replaced in 24.2% of patients: for pump breakdown/malfunctions in 53.8%, accidental damage by users in 20.2%, 'physiologyc' replacement after warranty end in 26%. Animas Vibe™ and Medtronic VEO™ seem to be the most replaced pumps (32.6% and 25.1%, respectively), and sensor-users seem to replace pump more often than no-sensor-users (23.3% vs 15.3%, p < 0.0002). No severe hypoglycemia or DKA, nor pump discontinuation have been recorded due to pump replacement.

Conclusions: Insulin pump breakdown/malfunction and consequent replacement in a large cohort of pediatric Italian patients with T1D are not as frequent as previously reported and seem to be more frequent in higher technological model.

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OPT2MISE STUDY: THE IMPACT OF INSULIN PUMP THERAPY ON TREATMENT SATISFACTION AND RESOURCE UTILIZATION IN PATIENTS WITH TYPE 2 DIABETES

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Objective: to assess the effect of insulin pump (CSII) versus multiple daily injection (MDI) on treatment satisfaction (TS) and on medical resource utilization, in sub-optimally controlled type 2 patients (T2D) participating in the OpT2mise study.

Methods: T2D, with HbA1c ≥ 8 were randomly assigned to CSII or continuing MDI. TS was measured with Diabetes-Treatment-Satisfaction-Questionnaire, status (DTSQs) and change (DTSQc). Data on medical resource use (diabetes-related hospitalizations, insulin usage and number of glucose testing strips) were collected.

Results: Subjects assigned to CSII achieved significantly greater HbA1c reduction than MDI arm (−1.1 ± 1.2% vs. − 0.4 ± 1.1%, p < 0.001). Mean DTSQs score increased significantly in the CSII arm after 6 months, with no change in the MDI arm with significant improvements in treatment convenience, flexibility, understanding of diabetes, willingness to recommend the treatment, satisfaction to continue treatment, and perceived frequency of hyperglycemia (P < 0.001). There was no difference in the perceived frequency of hypoglycemia. Greater HbA1c decrease at 6-month was significantly associated with improved satisfaction, in the CSII arm only (P < 0.05). Results were consistent in both DTSQs and DTSQc.

Mean total daily insulin dose (TDD) significantly declined from baseline to end of study in the CSII arm (112.1 ± 54 to 96.9 ± 55.8, P < 0.001). Mean TDD increased in the MDI arm over the same period (106.1 ± 49.2 to 121.7 ± 68.2, P < 0.05). Both groups had statistically significant decline in daily strip use

over the study. No significant difference in the number or length of stay of diabetes-related hospitalizations.

Conclusion: CSII therapy, in sub-optimally controlled T2D, provides improved outcomes with greater TS.

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INSULIN PUMP THERAPY IN CHILDREN WITH TYPE 1 DIABETES AND MALFUNCTIONS: OBSERVATIONAL PROSPECTIVE COHORT STUDY

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Background and Aim: It is well established that insulin pump therapy has several advantages when compared to multiple daily insulin injections. However, we do not know whether the improvement in technology has been accompanied by a higher or lower frequency of pump breakdowns or malfunctions, and if so whether this has an impact on metabolic control in children with type 1 diabetes.

Methods: The study involved paediatric patients affected by type 1 diabetes for >6 months, using an insulin pump since >6 months. The study lasted 1 year, during which patients were asked for pump malfunction or breakdown and infusion set problems. Moreover, HbA1c was analysed every 3 months for each patient.

Results: Data were analysed for 59 patients, mean age 14.7 ± 5.5 yrs., with type 1 diabetes since 8.59 ± 5.41 yrs., using an insulin pump since 4.2 ± 3.0 yrs. (range 0.5–11 yrs.), regarding malfunctions, only 12 patients (20.3%) didn't have any problem while 47 (79.7%) had at least one major or minor problem with pump (20.3%), infusion set (32.2%) or both (27.2%). Main malfunctions reported were damage, breakdown, keypad problems, blockage, and delivery failure. Interestingly, patients who had pump's malfunctions, experienced an increase in average HbA1c (p = 0.04) (Figure).

Conclusions: Insulin pump and infusion set's problems are frequent and pump's malfunctions can compromise the achievement of a good glycemic control. However, some strategies can be used to reduce the problems' recurrence (i.e., careful selection of children for insulin pump therapy, education of patients and families and prompt identification and solution of malfunctions).
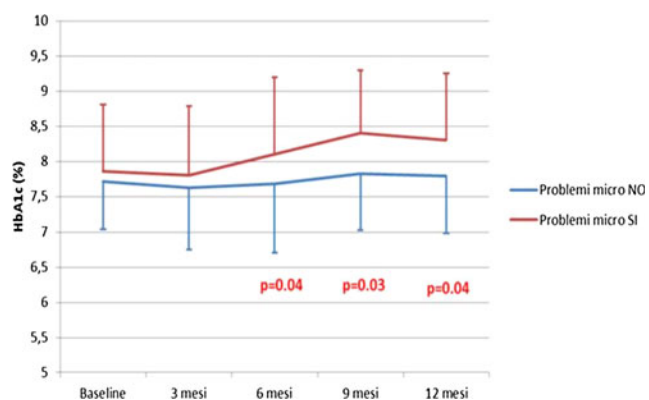
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HUMAN FACTORS AND HYBRID CLOSED-LOOP: EXPERIENCES OF PARTICIPANTS AND REMOTE MONITORS

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Background: Refinement of hybrid closed loop (HCL) is a research priority. This pilot study examined human factors during implementation of a proportional-integral-derivative algorithm with insulin feedback (PID-IFB) in a real-world setting. Eight adults with T1D wore a study insulin pump and Enlite2 sensor for a 3–7 day baseline and then initiated a Medtronic HCL system for five days. Overnights were spent in a hotel to facilitate research staff oversight. Each participant had a remote monitor (RM; spouse, partner or friend) with access to system data.

Methods: Participants and RMs completed a human factors assessment to evaluate attitudes, preferences and experiences related to HCL in a pre/post fashion. In addition, focus groups were completed at each site to obtain qualitative feedback.

Results: Participants were 27.8 ± 5.8 years of age with 17.7 ± 5.7 years T1D duration; mean A1c was $6.7\% \pm 0.6$. Survey responses in tables 1 and 2 show positive experiences for participants and RMs. Medium to large effect sizes were found with more positive response to diabetes devices, less worry about hypoglycemia, and less diabetes distress.

Themes extracted from focus groups are displayed in Table 3.

Conclusion: Examination of human factors assists in documenting the safety and feasibility of HCL. Participants experienced less worry about hypoglycemia and better response to diabetes devices. Likewise, the RMs were less worried about hypoglycemia, less distressed overall about diabetes, and felt more positive about diabetes devices. Even with increased oversight and technologic challenges, survey and focus group responses suggest a mostly favorable response to HCL.

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WAVY BASAL RATE PROFILES IN INSULIN PUMP THERAPY ASSOCIATE WITH INCREASED RISK FOR ACUTE COMPLICATIONS IN TYPE 1 DIABETES—CROSS-SECTIONAL ANALYSIS FROM THE DPV REGISTRY

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Table 1. Participants

	Pre Score	Post Score	Pre-Post comparison p value	Pre-Post comparison effect size (cohen's d)
Diabetes Distress Scale	1.75±0.46	1.58±0.42	0.27	0.39
Diabetes Technology Questionnaire	100.63±24.43	118.38±21.81	0.03	0.77
Hypoglycemia Fear Survey-Worry Scale	17.13±11.84	11.38±6.93	0.12	0.59
Hypoglycemia Confidence Scale	28.88±2.95	28.25±3.45	0.62	0.20

Table 2. Remote Monitors

	Pre Score	Post Score	Pre-Post comparison p value	Pre-Post comparison effect size (cohen's d)
Diabetes Distress Scale	1.64±0.53	1.33±0.25	>0.05	0.75
Diabetes Technology Questionnaire	119.88±24.53	134.29±14.22	0.04	0.72
Hypoglycemia Fear Survey-Worry Scale	18.75±12.71	12.38±9.72	0.02	0.56
Hypoglycemia Confidence Scale	28.38±4.27	28.13±3.87	0.71	0.06

Table 3. Focus Group themes

Group	Positive Feedback	Negative Feedback	Future Directions
Participant	-Devices were described as comfortable and reasonably user friendly -Described more leniency with nutrition choices and taking more liberties with food while retaining glucose control - Viewed benefits of HCL in improving management for patients with poorer control -Considered HCL more advantageous for overnight applications	-Would prefer more consolidated system with integrated functionality and fewer separate devices -Discouraged by frequent disruption in closed-loop secondary to sensor failure or connectivity issues -Experienced the HCL more as a "pump upgrade" than a novel system -Experience with HCL was less of a 'holiday' from diabetes management, and still required substantive involvement	-Eager for market-ready device with flexible patient control to suspend HCL when needed and apply more aggressive correction boluses -Eagerly await more advanced systems with greater patient autonomy, ease of burden
Remote Monitors	-Felt more connected with access to partner's diabetes management data -Described system as well-suited for parental monitoring or for those in poor control - Saw the potential for substantial improvement in HCL approach, and envisioned future where diabetes will be managed via smartphone, "just like any other app"	-Expressed concern about intrusion on their partner's diabetes -Shared ideas for enhancing usability features, such as improved screen interface and maneuverability -Suggested differential alerts based on severity of situation to better distinguish between low and high yield problems requiring eventual or urgent response	-Endorsed high potential for technology advancements to diminish patient burden -Expressed concern that these advancements will be inherently more expensive, and could amplify disparities in quality of care

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Background: Traditionally, basal rate profiles in continuous subcutaneous insulin infusion (CSII) therapy are individually adapted to answer expected insulin requirements. Whether this approach is indeed superior to a more constant basal rate profile has not been assessed so far. This study analysed the associations between wavy BR profiles with acute and chronic complications in type 1 diabetes mellitus (T1DM).

Patients and Methods: BR profiles of 3118 female and 2427 male patients from the ''Diabetes-Patienten-Verlaufsdokumentation'' (DPV) registry from Germany and Austria were analysed. Acute and chronic complications were recorded 6 months prior and after the most recently documented basal rate. The ''wavy index'' (WI) was calculated as variation of BR intervals in percent, describing the excursions of the BR profile.

Results: WI was correlated positively with age (r = .23; $p < 0.001$), male gender (r = .06; $p < 0.001$) duration of disease (r = .07; $p < 0.001$), body mass index (r = .06; $p < 0.001$), severe hypoglycaemia requiring outside assistance (r = .06; $p < 0.001$), hypoglycaemic coma (r = .05; $p = 0.002$), but negatively with total daily insulin (r = −.22; $p < 0.001$) and total daily basal insulin doses (r = −.27; $p < 0.001$). Logistic regression analysis adjusted for age, gender, duration of disease and total daily basal insulin revealed correlations of WI to severe hypoglycaemia requiring outside assistance ($\beta = 0.013$; $p < 0.001$) and diabetic ketoacidosis ($\beta = 0.013$; $p = 0.017$) in the whole population.

Conclusion: In this study, CSII profiles with higher variability were associated with increased risks of acute complications in adults with T1DM.

Funding: This study was supported by the BMBF-Kompetenznetz Diabetes mellitus, FKZ 01GI1106 and the Austrian Science Fund ZFP 266730.

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PAQ, A SIMPLE 3-DAY INSULIN DELIVERY DEVICE, IMPROVES GLYCEMIC CONTROL

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Background: PaQ® is a patch on device which provides preset basal rates and on demand bolus insulin. This pilot study assessed glycemic control and safety in people with type 2 diabetes mellitus (T2DM) using PaQ.

Design and Methods: Eight participants with T2DM with HbA1$_C$ ≥ 7.0% and ≤11.0% on an established regimen of basal-bolus insulin or premix 30/70 therapy ± OADs and/or glucagon like peptide −1 (GLP-1) agonist were enrolled in this single center, single arm evaluation. The study was comprised of three periods; baseline (insulin injections), transition and PaQ treatment (12-weeks). Endpoints included; HbA1c, self-monitored blood glucose, total daily dose of insulin (TDD) and body weight. Safety was assessed using; site examination, hypoglycemic episodes and adverse device effects (ADEs). Ethics Committe and Competent Authority approval and consent to participate was obtained.

Results: Eight subjects enrolled, age 63 ± 5.6, 87% male, BMI 32.7 ± 6.6, diabetes duration 22.2 ± 8.8 years and HbA1c 8.9 ± 1. Preliminary results showed a reduction in HbA1c of 1.8 ± 0.9% from baseline after 12 weeks of PaQ use. All patients transitioned to PaQ with 75% using the first basal rate chosen. TDD and weight at end of study was similar to baseline. No severe hypoglycemic events or serious ADEs occurred.

Conclusions: Preliminary data show people with T2DM using the PaQ device were safely transitioned from injections to PaQ and achieved improved glycemic control than their baseline injectable insulin regimen.

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EFFECT OF GARLIC (ALLIUM SATIVUM L.) ON BIOCHEMICAL PARAMETERS AND HISTOPATHOLOGY OF PANCREAS IN ALLOXAN-INDUCED DIABETIC RATS

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Garlic (*Allium sativum*) has played an important dietary, as well as medicinal, role for centuries. Even today the use of garlic is widespread and growing. The present study investigated the effect of raw garlic homogenate on biochemical parameters, enzyme activities and on pancreas tissue in alloxan-induced diabetic rats. Diabetes mellitus was induced in 21 out of 28 adult male albino rats, using intraperitoneal injection of 150 mg/kg BW alloxan. The diabetic rats were divided into three groups, two of which were administered orally by raw garlic homogenate (250 and 500 mg/kg once daily for 21 days). The control rats (positive and negative) receiving distiller water.

Oral administrations of the garlic extract significantly decreased serum glucose, total cholesterol, triglycerides, total lipids, urea, creatinine, Aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), and alkaline phosphatase (AlP) levels, while increased serum α amylase activity in alloxan-diabetic rats in dose–dependent fashion. Concurrent histological studies of the pancreas of these animals showed comparable preventive effect of the raw garlic homogenate which were earlier, necrosed by alloxan.

It is concluded that this plant must be considered as excellent candidate for future studies on diabetes mellitus.

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INTRANASAL GLUCAGON FOR TREATMENT OF INSULIN-INDUCED HYPOGLYCEMIA IN ADULTS WITH TYPE 1 DIABETES: A RANDOMIZED, CROSS-OVER NON-INFERIORITY STUDY

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Objectives: Treatment of severe hypoglycemia in type 1 diabetes (T1D) is problematic with currently available intramuscular (IM) glucagon due to the need to reconstitute the preparations prior to injection. A novel easy-to-administer, dry-powder formulation of glucagon administered intranasally (IN) was compared with IM for treatment of insulin-induced hypoglycemia.

Methods: A randomized cross-over trial was conducted at 8 T1D Exchange clinics in 75 adults (mean age 33-years, T1D duration 18-years). Insulin was administered intravenously (at 1.0–2.0 mU/kg/min) to induce hypoglycemia. Five minutes after stopping insulin, glucagon (3 mg IN at one visit and 1 mg IM of glucagon at another visit) was given. The primary outcome was an increase in plasma glucose to ≥ 70 mg/dL or an increase of ≥ 20 mg/dL from the glucose nadir within 30-min after receiving glucagon.

Results: Nadir glucose concentrations were 44 ± 8 and 47 ± 8 mg/dL at the IN and IM visits, respectively. Success criteria were met in all but one (98.7%) IN visits and in all 75 IM visits (unadjusted difference 1.3%, 1-sided 97.5% CI 4.0%). In the unsuccessful case, plasma glucose increased from 47 to 65 mg/dL at 30-min and normoglycemia was achieved by 40-min without other intervention. Mean time to success was 17-min and 14-min, IN and IM, respectively (P < 0.001). Nausea (with or without vomiting) occurred with 34% and 38% of visits, respectively.

Conclusions: IN glucagon provides an effective means to correct insulin-induced hypoglycemia in T1D that is non-inferior to IM glucagon. Given its far greater ease of administration, IN glucagon should be considered a viable alternative to commercially available IM glucagon preparations.

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SAROGLITAZAR, A UNIQUE DRUG, POTENTIALLY REVERSES BIOCHEMICAL MANIFESTATIONS OF METABOLIC SYNDROME

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Aims: To study the efficacy of Saroglitazar on biochemical reversibility of Metabolic Syndrome with pre-diabetes & diabetes as an add-on therapy.

Introduction: Metabolic Syndrome (MetS) is a precursor to the development of diabetes & associated cardiovascular morbidity & mortality. Till now no single drug was available which has the potential to reverse this. Saroglitazar, a dual PPAR-α & γ agonist has been approved for treating diabetic dyslipidemia in India.

Materials & Methods: 118 persons (70 men & 48 women)mean age 48.05 years with all 3 biochemical features of MetS were included who were on statin for diabetic or pre-diabetic dyslipidemia. Their general physical & systemic examinations, BMI, WHR, drug history, physical activity were recorded. Baseline anti-diabetic & antihypertensive drugs were continued except for rescue phase. Subjects were counseled for diet & exercise. Fasting lipids (Total Cholestrol TC, Triglycerides, HDLC, LDLC), FPG, HbA1c, LFT, RFT, urine microalbuminuria & EKG were done at baseline, 1,4 & 12 weeks of study. All subjects received 4 mg of Saroglitazar once daily after collecting the baseline biochemical & clinical data. They were advised for regular fasting & postprandial HMBG.

Results & Conclusion: Our study showed a drastic reduction in serum triglycerides (-62%) & significant reductions in FPG (p = 0.012) & HbA1c (p = 0.006). The HDL-C also increased significantly (p = 0.004). Changes in PPG, LDL-C & TC were not significant. No hypoglycemia or any SAE were observed. Saroglitazar effectively attempts to reverse all 3 biochemical markers of MetS. There was also improvement in other 2 biochemical manifestations of MetS, reduces FPG, HbA1c & raises HDL-C. We recommend large global studies on saroglitazar effectiveness in preventing diabetes, severe dyslipidemia & cardiovascular protection.

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CONTINUOUS EXENATIDE INFUSION IMPROVED PERIOPERATIVE GLUCOSE CONTROL AND REDUCED GLYCAEMIC VARIABILITY IN CARDIAC SURGERY PATIENTS: THE EXECUTIVE TRIAL

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	FPG (mg/dl)	PP (mg/dl)	HbA1c (%)	Triglycerides (mg/dl)	HDLC (mg/dl)	LDLC (mg/dl)	Total Cholesterol (mg/dl)
p-value	0.012	ns	0.006	0.04	0.004	ns	ns
SD	28.690	47.94	1.6	50.47	5.56	33.13	23.92
Mean value	V1-146	V1-190	V1-7.7	V1-312	V1-36.87	V1-121.7	V1-214.4
	V12-134.8	V12-183	V12-7.1	V12-132	V12-43.69	V12-117.21	V12-209.8

V1 = baseline visit, V12 = visit at 12 weeks

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Background: Reduction of operation-related hyperglycaemia has been shown to improve postoperative outcomes, though this effect is often blunted by increased number of hypoglycaemic episodes. To intensify perioperative glucose control while minimizing the risk of hypoglycaemia we performed a randomized control trial with the GLP-1 receptor agonist exenatide as add-on to standard perioperative insulin therapy in subjects undergoing elective cardiac surgery.

Methods: Thirty eight subjects with decreased left ventricular systolic function (ejection fraction $\leq 50\%$) scheduled for elective CABG (coronary artery by-pass grafting) were randomized to receive either exenatide or placebo in a continuous 72-hour i.v. infusion on top of standard perioperative insulin therapy. Parameters of glucose control and glycaemic variability together with indices of cardiac function assessed by transthoracic echocardiography were collected as primary endpoints.

Results: Compared to placebo group subjects receiving exenatide showed improved perioperative glucose control (average glycaemia 6.1 ± 2.5 vs. 6.8 ± 2.8 mmol/l, $p < 0.001$; time in target range of 4.5–6.5 mmol/l 55.0 ± 3.4 vs. $38.6 \pm 3.3\%$, $p = 0.001$) without an increased risk of hypoglycaemia (2 episodes of hypoglycaemia ≤ 3.3 mmol/l in exenatide vs. 4 episodes in placebo group). Exenatide infusion also reduced glycaemic variability (SD 1.4 ± 0.5 vs. 2.0 ± 0.6, $p < 0.01$; MAGE 2.5 ± 1.1 vs. 3.3 ± 0.9, $p < 0.01$), while no significant difference in postoperative echocardiographic parameters was found between the groups.

Conclusion: Perioperative administration of i.v. exenatide in subjects undergoing elective CABG improved glucose control and decreased glycaemic variability without increasing the risk of hypoglycaemia, while it did not affect parameters of cardiac function.

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LIRAGLUTIDE: AN EFFECTIVE ADJUNCTIVE TREATMENT FOR TYPE 1 DIABETES WITH OPEN-LOOP AND CLOSED-LOOP INSULIN DELIVERY

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Fully automated closed-loop (CL) systems can attain targeted glycemic control in the overnight period; however, exaggerated postprandial glycemic excursions remain. We previously demonstrated that pre-meal injection of pramlintide, used as an adjunctive therapy to CL control, mitigated postprandial hyperglycemia in an insulin-sparing manner. In type 2 diabetes, treatment with liraglutide suppresses exaggerated plasma glucagon responses to mixed meal feeding and lowers weight and A1c levels, while only requiring once daily administration. We hypothesized that these actions would make this GLP1 receptor agonist an effective adjunct to open-loop (OL) and CL treatment of type 1 diabetes (T1D).

Seven subjects with T1D (age 23 ± 3.6 y, diabetes duration 11 ± 9 y, A1c $7.4 \pm 1.1\%$) signed IRB approved consent forms

Meal Stimulated Glycemic excursions (mg/dL)	CL	CL + Lira	p-value
Breakfast	113±46	81±58	0.22
Lunch	93±56	84±53	0.31
Dinner	122±40	82±46	0.21
All meals	109±47	82±50	0.04
Insulin Delivery (units)	**CL**	**CL +Lira**	**p-value**
Breakfast	7.2±3.3	5.1±3.6	0.03
Lunch	5.4±2.8	4.3±2.8	0.22
Dinner	7.4±2.9	4.5±2.3	0.05
All meals	19.9±7.4	13.8±8.6	0.08

and underwent two 24-hour CL admissions using the Medtronic ePID proportional-integrative-derivative-based controller with insulin feedback: CL-alone (CL), and following a 3-week outpatient liraglutide dose escalation and insulin titration phase, CL + liraglutide (CL + Lira). Meal content was identical for both CL conditions and no meal-announcement was provided.

During the outpatient OL dose titration phase, median weight loss was 2.8 kg (IQ range: 1.1–4.1) ($p = 0.02$ vs. baseline) and total daily insulin dose (TDD) was reduced by $\sim 25\%$ ($p = 0.02$ vs. baseline). As shown in the table, postprandial hyperglycemia was decreased even in the face of significantly reduced insulin delivery during breakfast and dinner on CL therapy.

These preliminary data support our hypothesis that liraglutide will be an effective adjunct to both OL and CL treatment of T1D. Assessment of additional subjects will allow for further validation of this preliminary CL data.

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FERULIC ACID AND ATORVASTATIN, A NOVEL COMBINATION TO COMBAT METABOLIC SYNDROME AND INSULIN RESISTANCE IN MOUSE MODEL

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Metabolic syndromes have deadly and costly outcome if remained untreated. High fat diet (HFD) is one of causal factors of metabolic syndrome including insulin resistance and non alcoholic steatohepatitis (NASH). The current study presents a unique efficacy of ferulic acid (FA), atorvastatin (AS) and their combined treatment against high fat diet induced oxidative stress leading to prevention of a range of metabolic syndromes. The HFD mice showed increased body weight, insulin resistance index, plasma and hepatic lipid profile, histological features of NASH with decreased phosphorylation of AMPK-α. They exhibited increased oxidative damage in liver, lipid peroxidation with compromise in the antioxidant defense, increased apoptosis. The ROS induced apoptotic pathway was shown by increased depolarization of the mitochondrial membrane, increased expressions of Cdc42, p-SAPK/JNK and Bax-Bcl2 ratio. There was relevant decrease in the phosphorylation status of the survival proteins like PI3K and Akt, synergistic to the decreased nuclear translocation of Nrf2. The findings also confirmed ROS mediated increased nuclear translocation of NF-κB and simultaneous up-regulation of its downstream proinflammatory genes. Supplementation with FA or AS and unique combination of FA and AS in the diet significantly counteracted the HFD- induced inflammation and apoptotic effects. The results showed for the first time

that FA, AS and their combination treatment ameliorated the HFD induced oxidative damage to the liver and its apoptosis through the ROS mediated pathway. This unique yet low cost combinatorial therapy will remain very effective against a wide range of metabolic syndrome.

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SUSTAINED GLYCEMIC CONTROL AND LESS HYPOGLYCEMIA WITH NEW INSULIN GLARGINE 300 U/ML VS 100 U/ML: 1-YEAR RESULTS IN T2DM WITH BASAL + MEALTIME INSULIN (EDITION 1)

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Background and aims: EDITION 1 studied the efficacy and safety of new insulin glargine 300 U/mL (Gla-300) versus glargine 100 U/mL (Gla-100) in people with T2DM using basal plus mealtime insulin.

Figure: Glycemic control over 12 months in EDITION 1 study. (A) HbA$_{1c}$ (B) FPG

HbA$_{1c}$ [%] mean

	0	3	6	9	12
Gla-100	8.15	7.26	7.27	7.40	7.42
Gla-300	8.15	7.29	7.24	7.32	7.24

FPG [mg/dL] mean

	0	3	6	9	12
Gla-100	160.6	128.1	129.6	138.5	134.1
Gla-300	158.3	135.6	129.7	134.7	126.8

Materials and methods: In EDITION 1, people (N = 807) with elevated HbA$_{1c}$ were randomized to titrate Gla-300 or Gla-100 once daily in the evening for 6 months while continuing mealtime insulin. In a 6-month open-label extension, participants continued Gla-300 or Gla-100; 89% and 88% completed 12 months' treatment.

Results: Improved glycemic control was maintained over 12 months in both groups (LS mean difference Gla-300 vs Gla-100: -0.17 [95% CI: -0.30, -0.05] % for HbA$_{1c}$ and -6.1 [-12.5, 0.2] mg/dL for FPG) (Figure). Basal insulin doses were higher with Gla-300 than Gla-100 after 12 months (1.03 [SD 0.40] vs 0.90 [0.25] U/kg). During 12 months of treatment, a lower percentage of participants had ≥ 1 nocturnal confirmed (≤ 70 mg/dL [≤ 3.9 mmol/L]) or severe hypoglycemic event with Gla-300 than Gla-100 (54.5% vs 64.7%; RR 0.84 [0.75, 0.94]). These percentages were more similar at any time of day (24 h; 85.9% with Gla-300 vs 91.5% with Gla-100; RR 0.94 [95% CI: 0.89, 0.99]). Severe hypoglycemia was reported by 6.7% of Gla-300- and 7.5% of Gla-100-treated participants. Type and rate of adverse events were comparable between treatment groups.

Conclusion: In conclusion, over 1 year of treatment in people with T2DM using basal and mealtime insulin, Gla-300 provided sustained glycemic control with a lower incidence of nocturnal hypoglycemia compared with Gla-100.

Study sponsored by Sanofi (NCT01499082)

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NEW INSULIN GLARGINE 300 U/ML: GLYCEMIC CONTROL AND HYPOGLYCEMIA IN A META-ANALYSIS OF EDITION CLINICAL TRIALS IN PEOPLE WITH T2DM

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Background and aims: The EDITION 1, 2 and 3 studies compared the efficacy and safety of new insulin glargine 300 U/mL (Gla-300) with insulin glargine 100 U/mL (Gla-100) in people with type 2 diabetes mellitus on basal and mealtime insulin, basal insulin and OADs, and no prior insulin, respectively. A meta-analysis of these studies was conducted to study efficacy and safety.

Materials and methods: Meta-analysis of these three studies enabled glycemic control and hypoglycemia to be examined over 6 months in a large, heterogeneous type 2 diabetes mellitus population (Gla-300, N = 1247; Gla-100, N = 1249).

Results: Mean change in HbA$_{1c}$ was comparable for Gla-300 and Gla-100 (LS mean change [SE]: -1.02 [0.03] % for both groups; Table 1). Gla-300 was associated with reduced risk of experiencing hypoglycemia compared with Gla-100 (nocturnal and at any time of day; Table 2). Nocturnal hypoglycemic event rates were consistently lower with Gla-300 than Gla-100. Severe hypoglycemia was rare in both treatment groups (2.3% with Gla-300 vs 2.6% with Gla-100). Weight gain with Gla-300 and
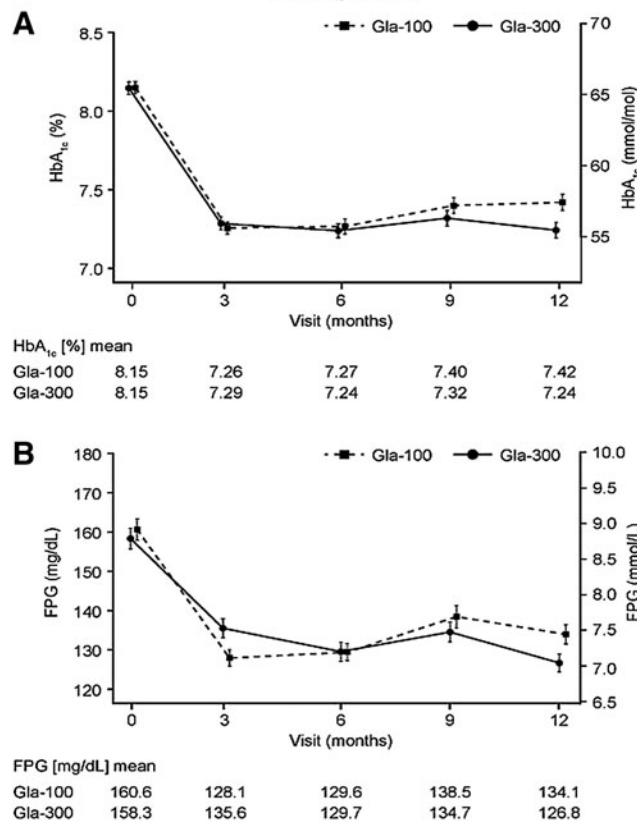
Table 1 – Glycemic control and weight change over 6 months in a meta-analysis of the EDITION 1, 2 and 3 studies

		HbA$_{1c}$ (%)*	
mITT population		Gla-300 (N=1239)	Gla-100 (N=1235)
Baseline	*Mean*	8.30	8.31
Change from baseline to month 6	*LS mean (SE)*	−1.02 (0.03)	−1.02 (0.03)
		Weight (kg)†	
Safety population		Gla-300 (N=1242)	Gla-100 (N=1246)
Baseline	*Mean*	99.89	99.94
Change from baseline to month 6	*LS mean (SE)*	0.51 (0.10)	0.79 (0.10)

*MMRM, mixed model for repeated measurements. †ANCOVA, analysis of covariance. mITT, modified intent-to-treat.

Table 2 – Hypoglycemic events over 6 months in a meta-analysis of the EDITION 1, 2 and 3 studies (safety population)

		Nocturnal hypoglycemia (00:00–05:59 h)			Hypoglycemia at any time of day (24 h)		
		Gla-300 (N=1242)	Gla-100 (N=1246)	RR* (95% CI)	Gla-300 (N=1242)	Gla-100 (N=1246)	RR* (95% CI)
Any hypoglycemia	*% people ≥1 event*	31.7	41.3	0.77 (0.69 to 0.85)	67.8	73.8	0.92 (0.87 to 0.96)
	Events/participant-year	2.25	3.30	0.68 (0.57 to 0.82)	15.87	18.62	0.85 (0.76 to 0.96)
Confirmed (<54 mg/dL [<3.0 mmol/L]) or severe hypoglycemia	*% people ≥1 event*	9.7	13.2	0.73 (0.59 to 0.91)	26.9	33.3	0.81 (0.72 to 0.90)
	Events/participant-year	0.37	0.56	0.67 (0.50 to 0.91)	1.93	2.08	0.93 (0.76 to 1.13)
Confirmed (≤70 mg/dL [≤3.9 mmol/L]) or severe hypoglycemia	*% people ≥1 event*	30.0	39.8	0.75 (0.68 to 0.83)	65.5	72.0	0.91 (0.87 to 0.96)
	Events/participant-year	2.10	3.06	0.69 (0.57 to 0.84)	15.22	17.73	0.86 (0.77 to 0.97)
Severe hypoglycemia	*% people ≥1 event*	0.6	1.0	0.71 (0.32 to 1.59)	2.3	2.6	0.85 (0.52 to 1.39)
	Events/participant-year	0.02	0.03	0.70 (0.35 to 1.42)	0.11	0.11	0.98 (0.51 to 1.86)

CI, confidence interval. *RR, relative risk for % people ≥1 event; RR, rate ratio for events/participant-year.

Gla-100 was slight (LS mean change [SE]: 0.51 [0.10] kg and 0.79 [0.10] kg, respectively), with a trend for less weight gain with Gla-300 (LS mean difference: −0.28 [95% CI: −0.55 to −0.01] kg, p=0.039).

Conclusion: Gla-300 provides comparable glycemic control to Gla-100 in type 2 diabetes mellitus, with consistently less hypoglycemia at any time of day and less nocturnal hypoglycemia.

Study sponsored by Sanofi (NCT01499082/NCT01499095/NCT01676220)

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INSULIN GLARGINE 300 U/ML VS 100 U/ML: GLUCOSE PROFILES OF MORNING VS EVENING INJECTIONS IN ADULTS WITH T1DM MEASURED WITH CONTINUOUS GLUCOSE MONITORING (CGM)

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Background and aims: Euglycemic clamp studies have shown that insulin glargine 300 U/mL (Gla-300) provides evenly distributed 24-hour insulin exposure and glucose utilization, with consistently low fluctuation.

Materials and methods: In this multicenter, 16-week, open-label, phase-2, parallel-group, two-period-crossover study, 59 adults with T1DM were randomized (1:1) to once-daily injections of Gla-300 or Gla-100. Injection time was randomized (1:1) during the first period to morning or evening and crossed-over in the second period. The primary efficacy endpoint, measured by CGM, was the mean percentage of time within a glucose range of 80–140 mg/dL (4.4–7.8 mmol/L) during the last 2 weeks of treatment in each period (weeks 7–8 and 15–16). Other glucose control endpoints, including variability metrics and safety, were assessed.

Results: Overall, the percentage of time within the 80–140 mg/dL glucose range was similar for participants receiving Gla-300 vs Gla-100 (LS mean difference [95% CI] 0.75% [−3.61 to 5.12], NS), but numerically greater during the last 4 hours prior to injection for Gla-300 vs Gla-100 (LS mean difference 3.73% [−1.97 to 9.42]). Pooled average glucose profiles showed more constant glucose levels with Gla-300 vs Gla-100 for both morning and evening injections (Figure). All measured intra-subject variability metrics were consistently lower with Gla-300 vs Gla-100. Hypoglycemic events were numerically lower or similar for Gla-300 vs Gla-100 (Table).

Conclusion: Gla-300 provided more stable 24-hour glucose levels irrespective of time of injection (morning or evening), and lower glucose variability compared with Gla-100.

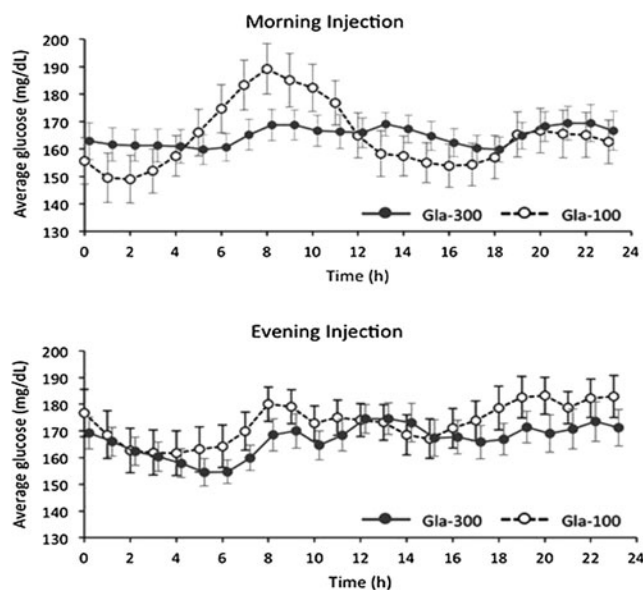Study sponsored by Sanofi (NCT01658579)

Table. Hypoglycemic events

	Gla-300 (N=30)	Gla-100 (N=29)
Hypoglycemia (safety population)*		
Any time (24 h):		
Confirmed (≤3.9 mmol/L) or severe hypoglycemia	1173 (126.5)	1181 (138.0)
Confirmed (<3.0 mmol/L) or severe hypoglycemia	282 (30.4)	395 (46.1)
Nocturnal (00:00–05:59 h):		
Confirmed (≤3.9 mmol/L) or severe hypoglycemia	111 (12.0)	165 (19.3)
Confirmed (<3.0 mmol/L) or severe hypoglycemia	37 (4.0)	77 (9.0)

*Based on case report form data; presented as total number of events (rate, calculated as events per participant-year)

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PHYSIOLOGICAL AND TECHNICAL STRESS TEST FOR MEDTRONIC'S ARTIFICIAL PANCREAS SYSTEM IN A SUPERVISED OUTPATIENT SETTING

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Background: A closed-loop system for maintaining sensor glucose (SG) at a pre-specified target was tested. The system's algorithm required users to deliver pre-meal boluses and adjusted the insulin infusion rate every 5-minutes. The safety and efficacy of the system and its safeguards were evaluated by introducing several challenges in a supervised outpatient setting.

Methods: Fourteen subjects with T1DM were recruited and stayed in a hotel for 3 days with no dietary or activity restrictions. The algorithm was initiated on day 1 before lunch and continued until ∼7:00 AM on day 3. To test the algorithm's performance and safety features, no pre-dinner bolus was given on day 1, sensor/pump communication was disrupted for 2 hours after breakfast on day 2, and subjects exercised for 1 hour after lunch on day 2.

Results: The average ± SD SG value including and excluding day 1 were 165 ± 22 and 147 ± 30 mg/dL, respectively. The average time spent with SG 70–180 mg/dL on days 1, 2, and 3 were 45%, 73%, and 78%, respectively. The average time spent with SG < 70 mg/dL for all 3 days was 1%. No adverse events were observed during the disrupted communication period, or during or after the exercise challenge.

Conclusion: The new closed-loop system provided good glycemic control in a supervised outpatient setting. The system performed well during periods of missed meal bolus, exercise, and disrupted sensor/pump communication. No DKA was observed during the missed pre-meal bolus challenge. These early findings support the progression to larger-scale testing over a longer period.

Morning Injection

Evening Injection

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OUTPATIENT DAY AND NIGHT GLUCOSE CONTROL USING A HYBRID CLOSED LOOP SYSTEM FOR THE MANAGEMENT OF TYPE 1 DIABETES

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Closed loop insulin delivery investigation has moved to the outpatient setting. In this randomized cross-over trial, we compared sensor augmented pump therapy with threshold suspend (SAPT + LGS) to a closed loop system with meal announcement in a free living ambulatory setting in patients with type 1 diabetes. We used the Medtronic Hybrid Closed Loop (HCL) system consisting of a Medtronic MiniMed insulin pump, Medtronic MiniMed Enlite II glucose sensor, Medtronic MiniMed Minilink REAL time sensor, Medtronic MiniMed Translator, and an Android mobile device with the HCL algorithm (proportional integrative derivate minus insulin feedback and additional safety parameters). All participants were optimized prior to an initial 48 hr in-clinic training period, followed by 5 days as an outpatient with remote monitoring.

8 patients (all female, mean age 25 ys (13–40), length of diagnosis 14 ys (4.2–25.6), mean HbA1c 7.5% (6.70–8.2) were studied. To date we have completed 840 hours of HCL and 840 hours of SAPT + LGS in the ambulatory setting.

The mean sensor glucose value during HCL over the 5 day period was 8.8 ± 3.1 mmol/L compared to 9.1 ± 3.3 mmol/L (p < 0.001) during SAPT + LGS. The percentage of time with a low glucose value (< 3.9 mmol/L) was reduced to 1.55% using HCL from 3.51% during SAPT + LGS (p < 0.001). Percentage time spent in target range (4.0–10 mmol/L) was 67.9% for HCL vs 62.2% for SAPT + LGS (p < 0.001). We conclude that the Medtronic Hybrid Closed Loop (HCL) system delivers improved mean sensor glucose values, and reduces hypoglycaemia in free living conditions.

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EFFICACY OF DUAL-HORMONE ARTIFICIAL PANCREAS TO ALLEVIATE THE CARBOHYDRATE COUNTING BURDEN IN TYPE 1 DIABETES: RANDOMIZED CROSSOVER TRIAL

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Objective: We examined if the artificial pancreas, delivering insulin and glucagon based on glucose sensor readings, could alleviate the burden of carbohydrate counting without degrading glucose control.

Research design and methods: Twelve adults were admitted three times from 7AM until 9PM and consumed low carbohydrate (breakfast; Women 30 g – Men 50 g), medium carbohydrate (dinner; Women 50 g – Men 70 g), and large carbohydrate (lunch; Women 90 g – Men 120 g) meals. For each visit, glucose levels were randomly regulated by 1) conventional pump therapy with patients informed of the meals carbohydrate content; 2) artificial pancreas accompanied with prandial boluses matching the carbohydrate of the meals based on individualized insulin-to-carbohydrate ratios (artificial pancreas with carbohydrate counting); or 3) artificial pancreas uninformed of the meals' carbohydrate content but accompanied with prandial boluses based on qualitative meal size assessment taking into account individualized insulin-to-carbohydrate ratios (artificial pancreas alleviating carbohydrate counting).

Results: The artificial pancreas without carbohydrate counting achieved similar control to when accompanied with carbohydrate counting after the small and medium meals (glucose incremental AUC 1.31 [0.20–3.32] vs 1.11 [0.33–2.29], p = 0.54; and AUC 0.44 [−1.21–1.73] vs 1.01 [0.45–1.76] mmol/L.h, p = 0.38) but yielded higher post-meal excursions after the large meal (glucose AUC 3.32 [0.88–4.46] vs 1.44 [−0.34–1.88] mmol/L.h, p = 0.004). The artificial pancreas alleviating carbohydrate counting yielded similar mean glucose compared to when accompanied with carbohydrate counting (8.4 ± 1.7 and 8.2 ± 2.1 mmol/L, p = 0.52).

Conclusions: The dual-hormone artificial pancreas is a promising therapy to alleviate the burden of carbohydrate counting without compromising glucose control.

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BIHORMONAL ARTIFICIAL PANCREAS WITH COORDINATED INSULIN-GLUCAGON ACTION: A MULTIVARIABLE APPROACH TO GLYCEMIC CONTROL

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An important challenge for artificial pancreas (AP) devices is tight glucose control without late hypoglycemia due to an excess of insulin delivery. Bihormonal devices with the concomitant administration of glucagon have been proposed. Clinical evaluation of bihormonal AP prototypes has demonstrated its feasibility. Recently, outpatient studies by Russell et al. also demonstrated its ability to reduce mean glucose and frequency of hypoglycemia, although glucagon was unable to completely eliminate hypoglycemic periods.

Current bihormonal controllers are based on uncoupled controllers for insulin and glucagon delivery, the latter being activated when glucose is below a given threshold. However, insulin and glucagon secretion by the pancreas is interrelated. Beta cells play a role in the signaling of glucagon secretion. Recently, a link between glucagon and insulin secretion in T2DM has also been reported. In this work, a multivariable approach incorporating insulin and glucagon coordination is proposed. A multiple-input-single-output controller is designed. It is composed of a central controller computing a virtual control action that represents the 'control effort' required for tight glucose control. This control effort is then distributed among insulin and glucagon signals following a given coordination law.

A proof-of-concept study has been conducted using the Imperial College London's bihormonal T1DM simulator. Compared to current bihormonal approaches, coordinated action

significantly improves postprandial control, with a reduction of time in hyperglycemia while avoiding hypoglycemia. These results justify the need for an increased understanding of the insulin and glucagon interplay that will translate to a more faithful bio-inspired approach for bihormonal control.

Funding: MINECO-DPI2010-20764-C02/DPI2013-46982-C2-1-R;EU-FEDER;WellcomeTrust

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HYBRID CLOSED-LOOP CONTROL USING THE MEDTRONIC 670G AND ENLITE3 SYSTEM IN TYPE 1 DIABETES AT DIABETES CAMP

T. Ly[1], A. Roy[2], B. Grosman[2], J. Shin[2], A. Campbell[2], S. Monirabbasi[2], B. Liang[2], S. Shanmugham[1], P. Clinton[1], B. Buckingham[1]

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The Medtronic 670G is the first fully integrated hybrid closed-loop system consisting of an Enlite3 glucose sensor and a proportional-integral-derivative algorithm incorporated into an insulin pump allowing for continuous closed-loop control.

The objective of this study was to test the safety and efficacy of a preliminary algorithm in subjects with type 1 diabetes. Twenty subjects were randomized to either hybrid closed-loop control with 670G (intervention) or 530G with threshold suspend at 60 mg/dL (control) over 6 days and nights in a diabetes camp setting. Both groups utilized premeal boluses.

The mean $\pm$ SD age was 18.6 ± 3.7 y, duration of diabetes was 9.1 ± 4.7 y, A1C was $8.6 \pm 1.5\%$ and insulin dose 0.8 ± 0.2 u/kg/day. Subjects in the 670G group remained in closed loop for $93 \pm 3\%$ of study time.

Glucose control for both groups are shown in the table. The percent time in range, 70–180 mg/dL, during the day was similar between the groups: 68.5% vs. 69.3%, control vs. 670G, respectively. During the overnight period, however, there was less nocturnal hypoglycemia < 70 mg/dL, in the 670G group, $p = 0.003$.

Hybrid closed-loop control with the fully integrated 670G system is safe and demonstrates less nocturnal hypoglycemia compared to threshold suspend technology alone.

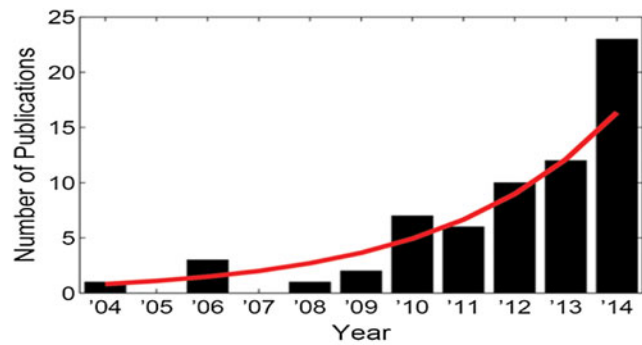| DAY 07:00 - 23:00	530G	670G	P-value
Mean glucose	153 ± 6	159 ± 8	0.530
% 70–180	68.5 ± 3.7	69.3 ± 4.4	0.891
% 70–150	54.0 ± 4.2	48.5 ± 5.0	0.385
% <70	3.4 ± 0.9	1.8 ± 1.1	0.253
NIGHT 23:00-07:00			
Mean glucose	146 ± 6	147 ± 7	0.919
% 70–180	66.0 ± 4.3	79.0 ± 5.0	0.053
% 70–150	54.0 ± 5.2	59.9 ± 6.1	0.454
% <70	5.2 ± 0.8	1.3 ± 0.9	0.003*

Glucose units - mg/dL

Figure 1: Number of published studies per year from 2004-2014 with fitted exponential curve.

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TRENDS IN THE CLINICAL DEVELOPMENT OF AN ARTIFICIAL PANCREAS: GUIDANCE FOR THE FUTURE

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The number of publications reporting clinical evaluation of closed-loop control in type 1 diabetes has increased exponentially over the past 10 years (Figure 1). We have assimilated details related to the publication, trial design, control algorithm, hardware, protocol, and results of 65 studies (to date) in an online database (www.thedoylegroup.org/apdatabase) to be used as a resource to improve artificial pancreas (AP) research. This tool can be used to analyze trends and locate relevant references for various choices of study parameters. The database has received 151 unique hits during the past month, after being available for public use for only 3 months. Using the database, we found that model predictive control was the most frequently used algorithm (32 studies), followed by PID (16) and fuzzy logic (9). Most systems used insulin-only control, but 17% added glucagon regulation. A total of 18 studies have included exercise during closed-loop control. Meal compensation strategies have become more diverse, with 8, 9, and 11 studies in 2014 including a meal with no, partial, or full bolus, respectively. The most striking development is the increased number of outpatient studies, with 13 out of 45 publications from 2012–2014 including outpatient results. Great strides have been made toward putting the AP in the hands of patients. Still, the disparities between protocols evident in the database make it difficult to judge overall progress, revealing the need for a benchmark test that will ensure the safety and efficacy of an AP system for meal, overnight, and exercise challenges.

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METABOLIC CONTROL WITH THE BIO-INSPIRED ARTIFICIAL PANCREAS (BIAP) IN ADULTS WITH TYPE 1 DIABETES: A 24-HOUR RANDOMISED CONTROLLED CROSSOVER STUDY

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Baseline demographics (n=12)	
Characteristic	**Results (mean (SD))**
Age (years)	45 (10)
Sex	Male 42% Female 58%
BMI (kg/m^2)	25 (4)
Duration of diabetes (years)	22 (12)
Duration of insulin pump therapy (years)	3.4 (4)
Insulin requirements (units/kg)	0.5 (0.1)
HbA1c (%) (mmol/mol)	7.4(0.7) 58 (8)

Objective: To evaluate the Bio-inspired Artificial Pancreas system (closed-loop) over 24 hours compared to standard pump therapy (open-loop). In addition to glucose outcomes we investigated concentrations of insulin and other metabolites including lactate, beta-hydroxybutyrate (BOHB), non-esterified fatty acids (NEFAs).

Method: Randomised controlled open-label crossover study. Informed written consent was obtained prior to screening. Participants were randomly assigned to attend either a 24-hour closed-loop or open-loop visit. Three standardised meals were provided at 19:00 h, 07:00 h and 12:00 h. A meal announcement strategy was employed. After completion of either visit participants crossed over following a minimum 1-week washout period. The primary outcome was percentage time spent in the target range (3.9–10 mmol/l). Secondary outcomes included % time in hypoglycaemia (<3.9 mmol/L) and hyperglycaemia (>10 mmol/L).

Results: Twelve adults participated. The baseline demographics are outlined in the table below. No significant difference in percentage time in target was observed between closed- and open-loop (71% (61.0–73.8) vs. 66.9% (55.4–82.5) respectively, p=0.94). The percentage time in hypoglycaemia was reduced with closed-loop (3.0% (0.0–7.0) vs. 17.9% (8.4–33.8), p < 0.01) whereas percentage time spent in hyperglycaemia was increased (28.9% (23.6 – 36.8) vs. 10.1% (7.7–15.1), p=0.01). The mean concentrations of lactate, BOHB and NEFAs did not differ significantly between closed- and open-loop.

Conclusion: The BiAP was safe and reduced hypoglycaemia compared to standard pump therapy, particularly overnight. This was at the expense of more time spent in hyperglycaemia during closed-loop, which could be counteracted by further algorithm tuning in future BiAP study phases.

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SIMULATED TRIAL OF AN ARTIFICIAL PANCREAS USING ACCELEROMETERS AGAINST LARGE UNANNOUNCED MEALS

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Closed-loop control of blood glucose (BG) levels in people with type 1 diabetes can reduce patient burden and lower the incidence of complications. Added accelerometers can detect exercise and sleep, improving performance. We tested a revised multiple model probabilistic predictive controller (MMPPC) in 100 simulated adult admissions lasting 32 hours each, with three large meals (1 g CHO/kg each), and unknown sleep times but with known accelerometer data.

The MMPPC algorithm explicitly estimates and predicts BG uncertainty based on past and potential future meals, endogenous glucose production, and insulin sensitivity. When the torso is vertical (during the day), insulin boluses are calculated to lower predicted BG levels until there is a roughly 3% risk of BG levels below 80 mg/dl. When sleep is anticipated, the bolus calculation fades into a less aggressive sleep mode. When the patient's torso is horizontal (presumed sleep), the MMPPC targets a BG of 100 mg/dl with basal like corrections providing smooth corrections, and mitigating the effect of pressure-induced sensor attenuations.

Using the UVa/Padova simulator this controller achieved a mean glucose of 147 mg/dl, 5 mg/dl lower than our previous controller. It also lowers the percentage time below 70 mg/dl by 50% to 0.19%. Missing dinner and their evening snack, totaling 44% of the total daily carbohydrate intake, the average time below 70 mg/dl increased by an average of 9 minutes to 0.8%. These results hold regardless of the patient's simulated sleep/wake schedule.

This promising control algorithm will undergo clinical testing in late 2014.

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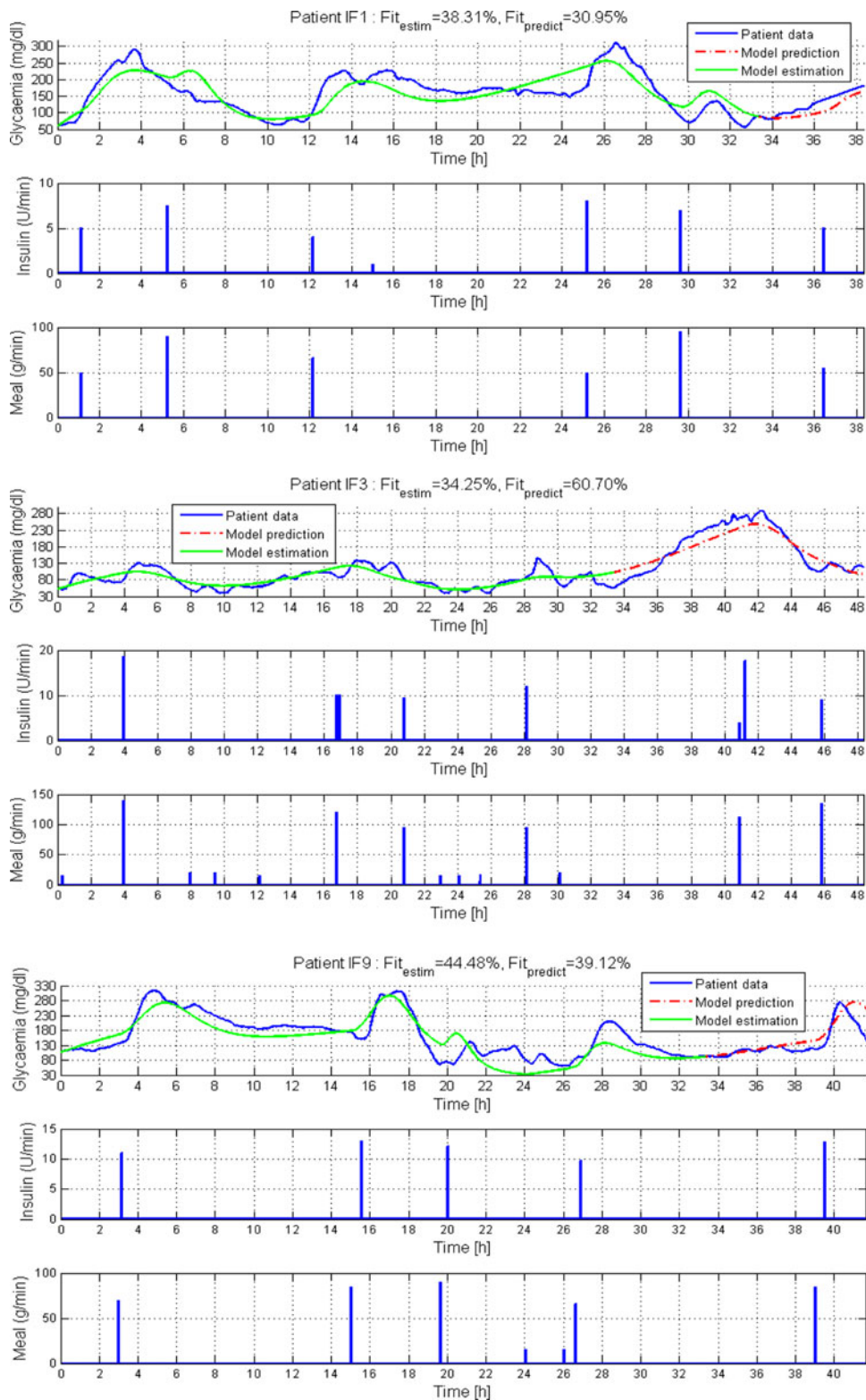### A NEW NONLINEAR CONTROL MODEL OF THE GLUCOSE METABOLISM FOR T1DM PATIENTS

I. Ben Abbes[1], J.Y. Poirier[1], I. Guilhem[1]

[1]Department of Endocrinology - Diabetes and Metabolism, University Hospital of Rennes, Rennes, France

Objective: In this contribution, we present a new nonlinear control model of the glucose metabolism for T1DM patients with parameters being identifiable from easily available patients' treatment data (i.e. data from the insulin pump, CHO of the meals and CGM).

Methods: The proposed nonlinear model is composed of five time continuous states equations and six parameters. Its design is determined in two steps. Firstly, two successive remote compartments are introduced to account for the insulin and glucose distribution in the organism. Secondly, the action of insulin and the meal on the glycaemia are modeled through original nonlinear forms validated by studies of the temporal dependence between variations of the glycaemia and insulin/meals.

Results: Data issued from the treatment of three real T1DM patients are used to estimate the parameters and validate the model. The time length is 2001 min (>33 h) with four meals (some extra-meals for hypo-correction) associated with bolus. The obtained mean estimation fit is 39% (values = 38%, 34, 44%)

Patient IF1 : Fit$_{estim}$=38.31%, Fit$_{predict}$=30.95%

Patient IF3 : Fit$_{estim}$=34.25%, Fit$_{predict}$=60.70%

Patient IF9 : Fit$_{estim}$=44.48%, Fit$_{predict}$=39.12%

which indicates a good approximation of the patients' glucose metabolism. Furthermore, the model forecasts accurately the glycaemia during at least five hours after the identification of its parameters. The mean prediction fit is 44% (values = 31%, 61%, 39%).

Conclusion: This novel T1DM control model represents accurately the glucose metabolism of real patients from their treatment data and can be used to predict accurately the upcoming values. This new model could then be used in a predictive controller.

Reference	n	Reduction in hypoglycemia	Reduction in hyperglycemia	Characteristics of 2-hour pump suspension events		
				Percentage of events lasting for 2 hours	SG after 2 hours (basal delivery resumed)	SG after 4 hours (2 hours after basal resumption)
[6]	21 LGS users vs 16 non-users	Fewer BG <70 mg/dL in LGS users (p<0.001)	Fewer BG >250 mg/dL in LGS users (p=0.03)	7%	110.7 ± 34.6 mg/dL (mean ± SD)	163.3 ± 42.1 mg/dL (mean ± SD)
[7]	121 TS users vs 126 non-users	53% reduction in SG ≤50 mg/dL in TS users (p<0.001)	No significant reduction in SG ≥250 mg/dL	9.4%	92.6±40.7 (mean ± SD)	168.8±64.6 (mean ± SD)
[8]	14,673 full-time TS users vs 2249 non-users	62% reduction in SG≤50 mg/dL in full-time TS users (p<0.001)	5.6% reduction in SG ≥300 mg/dL in full-time TS users (p<0.001)	10%	87 mg/dL (median)	median 164 mg/dL (median)

[1] Ly et al, Diabetes Care 35:1462, 2012; [2] Danne et al., Diabetes Technol Ther 13:1129, 2011; [3] Choudhary et al., Diabetes Care. 34:2023, 2011; [4] Garg et al., Diabetes Technol Ther 14:205, 2012; [5] Agrawal et al., J Diabetes Sci Technol. 5:1137, 2011 [6] Elbarbary, Pediatric Diabetes 15(S19):35, 2014; [7] Bergenstal et al., N Engl J Medicine 369:224, 2013; [8] Agrawal et al., Diabetes Technol Ther, in press, 2014

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Hypoglycemia Mitigation with Threshold Suspend: Clinical Trial and Real-World Outcomes

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[2]The Center for Endocrinology, Diabetes & Metabolism, Children's Hospital Los Angeles, USA

The Threshold Suspend feature automatically stops insulin delivery in the presence of sensor-detected glucose concentrations at or below a pre-specified threshold value. Usage and effectiveness of the feature with respect to hypoglycemia mitigation and prevention were studied in several earlier prospective [1–4] and retrospective [5] studies. Recent results from a prospective observational study of 37 adolescents with type 1 diabetes who fasted during Ramadan [6] were compared with results from the ASPIRE In-Home randomized controlled trial of 247 subjects [7] and with results from a retrospective observational study of CareLink uploads from 16,922 routine users of the MiniMed 530G/Enlite system [8]. The Table shows that consistent and statistically significant reductions in the percentage of sensor or blood glucose values are reflective of hypoglycemia.

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USE OF MODEL PREDICTED BOLUS ESTIMATION (MPB) TO OPTIMIZE INSULIN DOSING STRATEGIES COVERING HIGH FAT MEALS

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Background: Data exist showing High Fat (HF) meals require more insulin than Low Fat (LF) meals with identical carbohydrate (CHO) content. The objective of the present study was to optimally define how the DOSE (U) should be adjusted, what percentage of DOSE should be given immediately (SPLIT), and how long to extend the remaining portion (DURATION).

Methods: Adult subjects (N=3) with T1D on insulin pump therapy were admitted to the Joslin CRC on 2 to 7 occasions. On the first 2 occasions, subjects were given LF (50 g carbohydrate [CHO], 4 g protein [P], 9 g fat [F]) and HF (identical CHO, 44 g P, 36 g F) meals with DOSE calculated following usual-care (UC) settings. Subjects with 6 hr postprandial BG exceeding target underwent repeat assessments, with DOSE, SPLIT, and DURATION optimized by MPB. The MPB model was identified from the first meal and first-reassessment DOSE was constrained to be ≤175% UC.

Results: UC DOSE was insufficient to return BG to target in all HF meals, despite returning BG to target in all LF meals (p=0.1; chi2). HF meal DOSE was increased by 75% in each subject (maximum allowed on first repeat assessment); SPLIT and DURATION were variable. In 1 of the 2 subjects with repeat meal data available, the increase in DOSE was insufficient to return BG to target.

Conclusions: HF meals may require 75% or more insulin to achieve target compared with LF meals; MPB estimation provides a means to optimize SPLIT and DURATION.

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D-NAV : A REAL–WORLD EVALUATION OF A NOVEL ASSISTIVE TECHNOLOGY (D-NAV) TO OPTIMISE GLYCAEMIC CONTROL IN THOSE WITH TYPE 2 DIABETES REQUIRING INSULIN THERAPY

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Aims: Frequent dosage adjustment is essential for effective and safe insulin therapy and glycaemic control optimisation. We evaluated the effectiveness of d-Nav™ a handheld device that automates insulin dosage titration using Diabetes Insulin Guidance System [DIGS™] software and an on board glucose

monitor. DIGS^{TM} software identifies glucose patterns and recommends weekly insulin dosage updates, similar to clinician recommendations.

Methods: An exploratory single-centre pilot evaluation of the use of d-Nav in patients aged $\geq$ 21 years with an HbA1c level $\geq$ 53 mmol/mol ($\geq$ 7.0%) who were receiving insulin therapy for at least 1 year. Patients were asked to use d-Nav to monitor their blood glucose before each insulin injection and when they suspected hypoglycaemia to allow d-Nav to adjust insulin dosage. HbA1c and information on hypoglycaemia was collected during scheduled 3-monthly clinic visits. Patients were followed for a minimum of 6 months. Institutional Review Board waived the need for informed consent.

Results: A total of 96 patients (n = 94 type 2, n = 2 type 3 diabetes) completed the evaluation. The mean ($\pm$ sd) HbA1c for active users decreased from 77 $\pm$ 15 mmol/mol (9.2 $\pm$ 1.4%) at baseline to 62 $\pm$ 13 mmol/mol (7.8 $\pm$ 1.2%) at the 3–5 month clinic visit and to 58 $\pm$ 13 mmol/mol (7.5 $\pm$ 1.2%) at the 6–12 month clinic visit. The decreases were statistically significant at both post-baseline visits (both P < 0.001). The frequency of minor hypoglycaemia (blood glucose $\leq$ 3.6 mmol/l) was low and well within the tolerated range.

Conclusions: d-Nav was shown to be a highly effective solution for blood glucose management in insulin users and warrants further investigation.

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DEVELOPMENT OF A MOBILE APPLICATION TO COMPUTE FOOD CARBOHYDRATES AND FIRST EVALUATION IN PATIENTS WITH INSULIN-TREATED DIABETES

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Background: To estimate meal carbohydrates (CHO) is needed to adjust insulin doses by patients with type 1 diabetes (T1D). We developed an Android application (APP) to help them in this task.

Methods: Ten T1D patients (4 males/6 females), aged 21–61 (range), with HbA1c of 6.5–8.5%, volunteered to use the APP uploaded on a cellphone for one week. Each meal composition was entered in APP on blind mode, i.e. with no sent back information, while patient CHO self-computing was written in a logbook. Data collected included, beside meal contents and CHO computed both by APP and patient, the time needed for entering meals in APP and postprandial blood glucose levels.

Results: The number of analyzed meals was 168. Average APP-computed CHO were 74.1 $\pm$ 32.5 g per meal. Patients underestimated CHO in 61% meals, with a mean difference (delta CHO) of 2.8 $\pm$ 8.9 g per meal (9.6 $\pm$ 7.9% of total CHO). Food with high CHO content were always underestimated by patients. When delta CHO was < $-$15 or $-$10 g (overestimation), postmeal hypoglycaemia occurred in 100 or 80% meals, respectively. When delta CHO was >15 or 10 (underestimation), 61 or 32% meals were followed by hyperglycaemia, respectively. Mean time to enter a meal diminished by 21% over the study week.

Conclusion: Beside confirmed underestimation of meal CHO by T1D patients, our study suggests an APP computing meal CHO could be helpful to reduce it. Further evaluation of this APP about its outcomes on glucose control on longer term is scheduled.

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FACEBOOK AS A USEFUL TOOL TO IMPROVE GLUCOSE CONTROL IN PATIENTS WITH TYPE 1 DIABETES: ONE YEAR FOLLOW-UP STUDY

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Aims: To evaluate the impact of Social Media (Facebook) as a tool to improve control in patients with type 1 diabetes.

Materials and methods: A total number of 441 patients (14.2 $\pm$ 2.7 years old), with type 1 diabetes (4.4 $\pm$ 2.9 years), 42% on insulin pump and 58% on MDI and HbA1c of 7.9 $\pm$ 1.2%, were analyzed in two groups:

Internet group: 228 patients, who participated in a Facebook group where support for education (insulin change, carb intake, exercise, hypoglycemic and hyperglycemic events). Patients should have at least one advice per 3 months during the study.

Regular group: as controls, 213 patients with type 1 diabetes, age- and sex-matched, with similar HbA1c at baseline, were randomly selected who did not have Facebook profile. Patients should have at least one visit per 3 months during the study.

Diabetes Quality of Life for Youth Inventory (DQOLY) and Hba1C at baseline and after one year was performed.

Results: Significant decrease of 0.7% in HbA1c was found in internet group (7.9 $\pm$ 1.2% vs. 7.2 $\pm$ 0.8%, P < 0.05), compared with 0.2% in the regular group (7.9 $\pm$ 1.4% vs. 7.6 $\pm$ 1.8%, P = 0.72). DQOLY questionnaires showed a significant improvement (P < 0.05) only in patients from internet group.

Conclusion: Social media like Facebook is cheap and effective tool to improve diabetes control in type 1 diabetes patients. Facebook can help the diabetes team how to understand and treat patients more systematically.

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CONTINUOUS GLUCOSE MONITORING ASSESSING THE CLINICAL IMPACT OF AN ALGORITHM DRIVEN BASAL-BOLUS INSULIN REGIMEN IN NON-CRITICALLY ILL INPATIENTS WITH T2DM

K. Donsa[1], K.M. Neubauer[2], J.K. Mader[2], B. Höll[1], S. Spat[1], P. Beck[1], F. Aberer[2], J. Plank[2], T.R. Pieber[2], L. Schaupp[2]

[1]*HEALTH - Institute for Biomedicine and Health Sciences, JOANNEUM RESEARCH, Graz, Austria*
[2]*Department of Internal Medicine Division of Endocrinology and Metabolism, Medical University of Graz, Graz, Austria*

Background: Continuous glucose monitoring (CGM) displays diurnal glycaemic profiles and detects responsiveness patterns to therapeutic efforts. This study aimed to test the capability of CGM for assessing the clinical impact of an algorithm driven basal-bolus-insulin regimen and to compare CGM to standard blood glucose (BG) measurements in non-critically ill T2DM inpatients.

First day with CGM

Last day with CGM
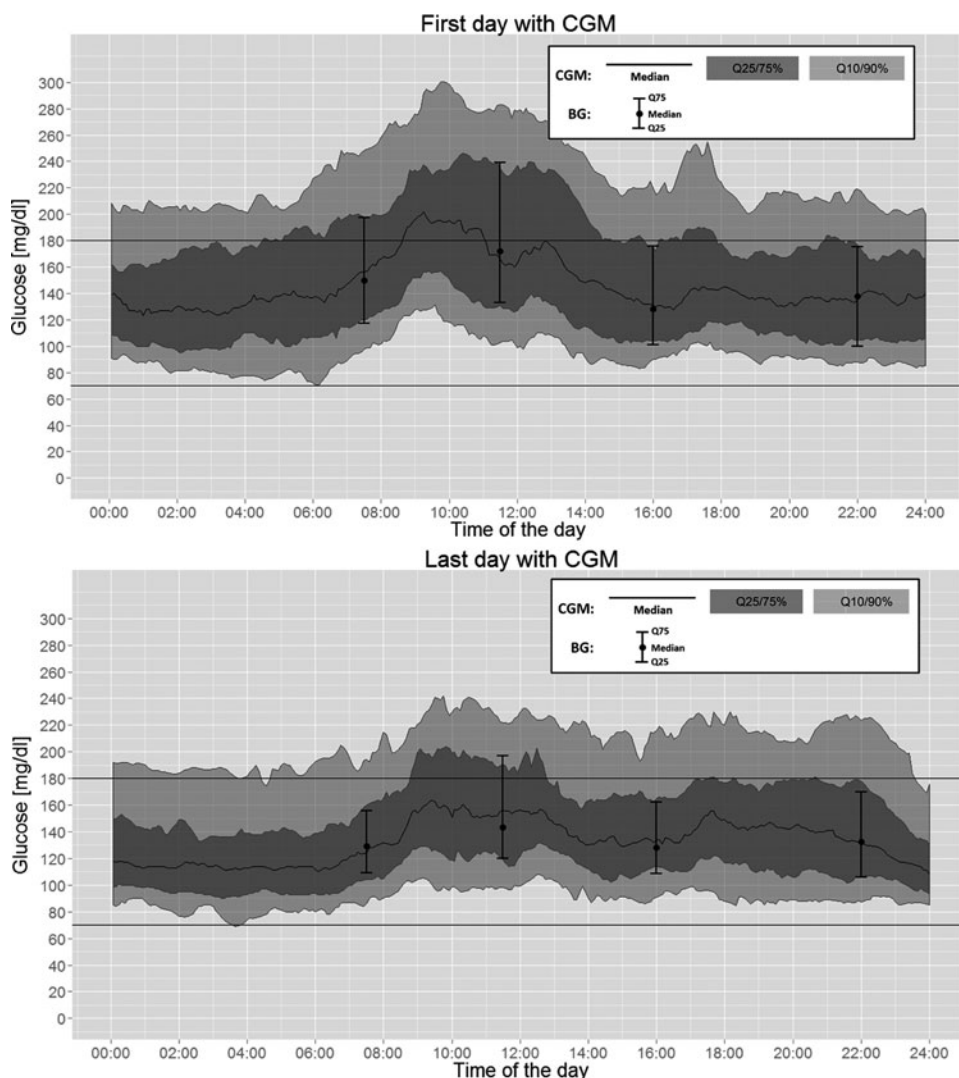
Methods: 84 patients (age 68 ± 10 years, HbA1c 72 ± 28 mmol/mol and BMI 31 ± 7 kg/m^2) were treated with an algorithm driven basal-bolus-insulin therapy based on four daily BG measurements. CGM was performed with the iPro2 system (MiniMed Medtronic) and calibrated retrospectively. Percentages of glucose readings in the range 70–180 mg/dl and the coefficient of variation (CV) were calculated for the first and the last treatment day.

Results: 140,424 CGM and 2,066 BG measurement values were analysed. The number of values (CGM/BG) in the range 70–180 mg/dl significantly increased over time from 67.7/67.2% (day one) to 77.5/78.6% (last day), $p < 0.04$. Also the glucose variability (CGM/BG), expressed by the CV, significantly improved over time from 39.6/40.6% (day one) to 36.9/36.8% (last day), $p < 0.03/p = 0.05$.

Conclusion: The therapy yielded a high number of readings (CGM&BG) in the range 70–180 mg/dl and lower glucose variations at the end of the hospital stay. A notable consistency between the parameters describing the therapy performance obtained by CGM and BG measurements was found, even though the number of CGM values was 70-fold higher than the number of BG measurements.

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ROLE OF MOBILE TECHNOLOGY TO IMPROVE DIABETES CARE IN ADULTS WITH TYPE 1 DIABETES: THE REMOTE-T1D STUDY

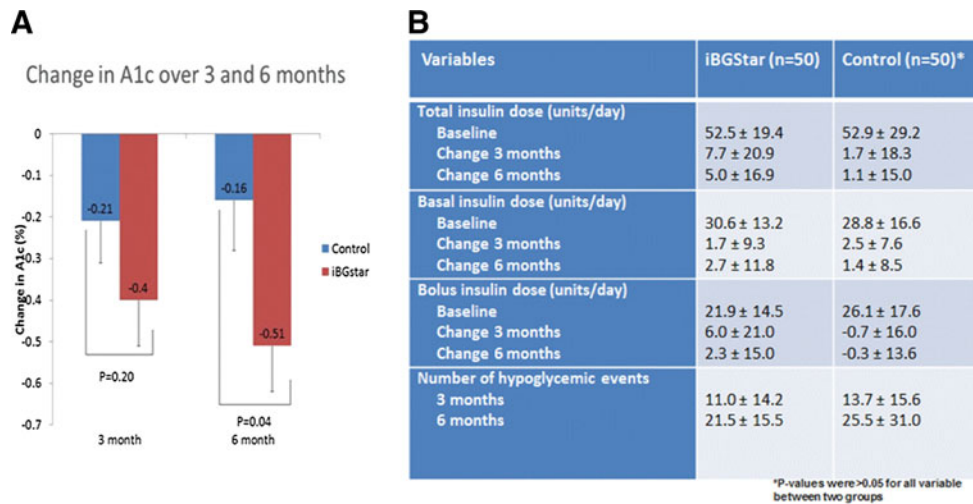*V. Shah[1], W. Hiatt[2], P. Gottlieb[1], C. Beatson[1], J. Snell-Bergeon[1], S. Garg[1]*

[1]*Barbara Davis Center for Diabetes, University of Colorado School of Medicine, Aurora, USA*
[2]*Colorado Prevention Center, University of Colorado School of Medicine, Aurora, USA*

Background: Role of mobile technology on patient reported outcomes (PRO) and glycemic control in adults with type 1 diabetes (T1D) needs further evaluation.

Methods: This single-center, prospective, 6-month, open-label, investigator-initiated study randomized 100 subjects with T1D in a 1:1 fashion to a control group; Self-Monitoring of Blood Glucose (SMBG) with Accu-Chek Nano® and an intervention group using SMBG with iPhone plus glucose meter (iBGStar®). Primary end points was change in PRO.

Results: Baseline demographics and A1c values were similar in the two groups. There was a significant reduction in

Change in A1c over 3 and 6 months

Variables	iBGStar (n=50)	Control (n=50)*
Total insulin dose (units/day)		
Baseline	52.5 ± 19.4	52.9 ± 29.2
Change 3 months	7.7 ± 20.9	1.7 ± 18.3
Change 6 months	5.0 ± 16.9	1.1 ± 15.0
Basal insulin dose (units/day)		
Baseline	30.6 ± 13.2	28.8 ± 16.6
Change 3 months	1.7 ± 9.3	2.5 ± 7.6
Change 6 months	2.7 ± 11.8	1.4 ± 8.5
Bolus insulin dose (units/day)		
Baseline	21.9 ± 14.5	26.1 ± 17.6
Change 3 months	6.0 ± 21.0	-0.7 ± 16.0
Change 6 months	2.3 ± 15.0	-0.3 ± 13.6
Number of hypoglycemic events		
3 months	11.0 ± 14.2	13.7 ± 15.6
6 months	21.5 ± 15.5	25.5 ± 31.0

*P-values were >0.05 for all variable between two groups

glycosylated hemoglobin (A1c) value at 6 months in iBGStar® group compared to control group (Figure A). There was tendency towards a non-significant increase in total insulin dose in iBG-Star® group with no difference in hypoglycemic events at 6 months in the iBGStar group compared to controls (Figure B). The Hypoglycemia Fear Scale (PRO) improved compared to baseline in both groups at 6 months (-1.4 ± 10.0 vs -3.9 ± 12.5, p = 0.31).

Conclusions: The use of iBGStar versus control resulted in better glycemic control at 6 months with no increased risk of hypoglycemia and improvement in PRO in both groups.

Investigator Initiated Study sponsored by Sanofi; NCT 1825382

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SAFETY AND EFFICACY OF STANDARDISED GLYCAEMIC MANAGEMENT BY USING THE GLUCOTAB SYSTEM FOR PATIENTS WITH DIABETES MELLITUS TYPE 2 AT DIFFERENT HOSPITAL WARDS

K.M. Neubauer[1], F. Aberer[1], J.M. Mader[1], B. Höll[2], L. Schaupp[1], S. Spat[2], P. Beck[2], K. Donsa[2], J. Plank[1], T.R. Pieber[1]

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[2]HEALTH, Joanneum Research GmbH, Graz, Austria

Background: Evidence based electronic decision support systems are recommended to improve glycaemic management in hospitalised patients with diabetes mellitus type 2 (T2DM). The aim of the intervention study was to investigate the safety and efficacy of the electronic workflow and decision support system GlucoTab at four different hospital wards.

Methods: 99 hospitalised patients with T2DM at four different wards (Endocrinology (n = 42), Cardiology (n = 30), Nephrology (n = 15), Plastic Surgery (n = 12)) received standardised glycaemic management according to the GlucoTab system. The system assists health care professionals in organizing the treatment workflow and provides insulin dosage suggestions based on

a basal bolus dosing algorithm for achieving blood glucose values between 70- < 180 mg/dl.

Results: No severe hypoglycaemic event (< 40 mg/dl) occurred at any ward. In total 1.9% of blood glucose measurements (BG) were between 40- < 70 mg/dl (range 0.3% (Cardiology) to 3.0% (Endocrinology)). 25.7% of BG were > 180 mg/dl (Endocrinology: 22.6%, Cardiology: 29.1%, Nephrology: 34.4%, Plastic Surgery: 14.6%). 72.4% of BG were in target 70- < 180 mg/dl (range 64.6% (Nephrology) to 83.6% (Plastic Surgery)). The mean daily BG was 154 ± 35 mg/dl (Endocrinology: 150 ± 35 mg/dl, Cardiology: 163 ± 33 mg/dl, Plastic Surgery: 134 ± 31 mg/dl, Nephrology: 162 ± 34 mg/dl).

Conclusion: The GlucoTab system safely supported standardised glycaemic management at all different wards. However, differences in the efficacy of glycaemic control were observed. Future algorithm modification will focus on specific patient groups.

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HI-TOUCH/HI-TECH: DIABETES MANAGEMENT MANUAL, A TYPE 1 DIABETES GUIDE TO THE UNIVERSE, WITH EMBEDDED VIDEOS, INTERACTIVE ELEMENTS & UNLIMITED UPDATES

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The first of its kind eBook patient self-management manual for type 1 diabetes, *A Type 1 Diabetes Guide to the Universe*. The book uses the cutting edge technology of iBooks Author and the iBooks publishing platform to create a truly unique and novel learning and psychologically supportive, healing experience for patients and their families, achieving an optimal balance of hi-tech and hi-touch. It has 5 ½ hours of embedded videos of interviews of children with diabetes, siblings, parents and adults with type 1 from the US, Canada, the UK, Australia and New Zealand talking about their experiences, conveying a sense of hope to the reader. In addition there are iBook Author interactive elements throughout the book - quizzes, photo galleries &
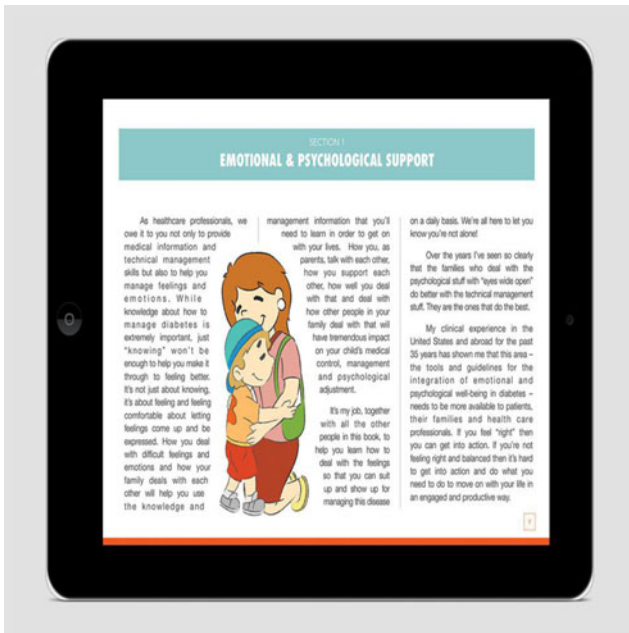
educational pop-up call-outs. The book integrates the author's unique Family Approach to Diabetes Management. Comprehensive in scope covering all aspects of diabetes self-management while integrating the psychological, emotional and family dynamic aspects that are so critical in helping patients and their families cope effectively. Videos of Joe throughout the book give the reader the feel that they are ''in Joe's office'' having a consultation. In both mg/dl & mmol, updates are unlimited and free after purchasing, allowing the book to be organic and up to date over time. This book is the first of its kind and is an invaluable resource for patients, their families and healthcare professionals.

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PERFORMANCE EVALUATION OF THE CONTOUR BLOOD GLUCOSE MONITORING SYSTEM, WITH AN UPDATED METER ALGORITHM, IN THE HANDS OF USERS

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Background: The accuracy and ease of use of an updated CONTOUR blood glucose monitoring system (BGMS) containing an updated meter algorithm and using currently available CONTOUR test strips were assessed.

Methods: Untrained subjects (N = 372) with or without diabetes were enrolled at 2 clinical sites and performed fingertip self-tests. Study staff tested fingertip blood from all subjects and venous blood from subjects with diabetes. Meter and YSI reference results were compared. The primary objective was per ISO 15197:2013 Section 8 accuracy criteria ($\geq$95% of fingertip self-test results within $\pm$ 15 mg/dL [0.8 mmol/L] and $\pm$ 15% of reference at YSI glucose concentrations < 100 mg/dL [5.6 mmol/L] and $\geq$ 100 mg/dL [5.6 mmol/L], respectively) for persons with diabetes (N = 329). Subjects completed a questionnaire about

Table 1. Summary of Evaluable* BGMS Accuracy Results For Subjects With Diabetes

Test	N	$\pm$5 mg/dL (0.3 mmol/L)[†] or $\pm$5%[‡]	$\pm$10 mg/dL (0.6 mmol/L)[†] or $\pm$10%[‡]	$\pm$15 mg/dL (0.8 mmol/L)[†, §] or $\pm$15%[‡,§]	$\pm$20 mg/dL (1.1 mmol/L)[†] or $\pm$20%[‡]
		Percent of meter results within specified error limits			
Fingertip subject self-test	324	61.7%	90.7%	97.8%	98.8%
Fingertip staff test	326	64.7%	96.0%	99.7%	99.7%
Venous test	318	77.7%	98.1%	100.0%	100.0%

BGMS, blood glucose monitoring system.
*Of 329 subjects, 324 results for fingertip self-testing, 326 results for study staff fingertip testing, and 318 results for venous testing from persons with diabetes were evaluable per protocol.
[†]For glucose values <100 mg/dL (5.6 mmol/L).
[‡]For glucose values ≥100 mg/dL (5.6 mmol/L).
[§]ISO 15197:2013 Section 8 accuracy criteria.

ease of use of the BGMS and the user instructions, per ISO 15197:2013 Section 8 (acceptance criterion was ≥90% of subjects responding 'strongly agree,' 'agree,' or 'neutral' to each of 6 statements).

Results: BGMS accuracy results are shown in Table 1. For subjects with diabetes, 97.8% of subject fingertip, 99.7% of study staff fingertip, and 100% of venous results met ISO15197:2013 accuracy criteria. Furthermore, ≥99.1% responded 'strongly agree,' 'agree,' or 'neutral' to all ease of use questionnaire statements.

Conclusion: The CONTOUR BGMS exceeded ISO 15197:2013 Section 8 accuracy criteria for capillary self-testing and demonstrated ease of use in the hands of users.

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A FEASIBILITY STUDY OF A NOVEL REDUNDANT ELECTROCHEMICAL SENSOR FOR CONTINUOUS GLUCOSE MONITORING IN PATIENTS WITH TYPE 1 DIABETES (TID)

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Background: A glucose-sensor incorporating multiple sensing elements may improve accuracy and reliability. Harmony (Medtronic, Northridge CA) is a redundant electrochemical sensor with sensing elements on both planar surfaces. A diagnostic algorithm combines the output from the two sensing elements with the aim of producing one robust accurate glucose-sensor value.

Aim: To evaluate the Harmony sensor performance in adults with T1D.

Method: Fifteen adults with T1D wore two identical Harmony sensors continuously for 168 hours. On Day 4 and Day 8 post sensor insertion venous samples were collected every 15 minutes for YSI plasma glucose measurements for half-an-hour before and 3-hours post a standardised meal. Between study visits, participants wore sensors at home and performed capillary glucose testing 6–8 times daily. Sensor glucose values were processed prospectively and displayed only when trace characterisation algorithms deemed values to be sufficiently robust. Sensor glucose readings were compared to plasma and capillary glucose levels.

Results: The overall Mean absolute relative difference (MARD) was 10% during entire wear and 8% during the meal test period. All (100%) sensor glucose values fell within zone A and B of the consensus error grid. Average sensor display time was higher in the combined-redundant sensor than each of the two sensing electrodes alone (97% versus 95%; p < 0.001). Average sensor survival was 6.8 days.

Conclusion: Redundant electrochemical sensing technology is feasible. Harmony sensor performance compares favourably with available data for current generation glucose-sensors. Improved sensor accuracy, reliability and lifespan may facilitate artificial pancreas development.

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HEALTH ECONOMIC EVALUATION OF SENSOR-AUGMENTED PUMP WITH LOW GLUCOSE SUSPEND FUNCTION VERSUS PUMP THERAPY ALONE IN A RISK OF HYPOGLYCEMIA T1DM IN FRANCE

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Aims: Main objective of this study was to estimate health-economic impact of Sensor-Augmented Pump with Low Glucose Suspend function (SAP + LGS) compared to pump therapy alone (CSII) in a risk of hypoglycemia Type 1 Diabetes population (T1DM) in France.

Methods: Core Diabetes Model was used to project incidence of diabetes-related complications and Severe Hypoglycemic Events (SHE) over a lifetime horizon, based on a recently published Australian trial by Ly TT et al. comparing SAP + LGS versus CSII. This RCT demonstrated that after 6-month treatment the rate per 100 patient-months was 2.2 in CSII arm versus zero in SAP + LGS arm. The cohort characteristics used are presented in table 1. The quality of life was adjusted using a utility combining both the reduction of SHE and the reduced fear of hypoglycaemic event in SAP + LGS arm (0.038) versus CSII (−0.036).

Results: Improvement in Quality Adjusted Life Year (QALY) gained was 1.45 year in favour of SAP + LGS. Incremental Cost-Effectiveness Ratio (ICER) was 21,727€ per QALY. Additional SAP + LGS related costs were partially offset by the savings due to the reduction in SHE compared to the CSII arm. SHE related discounted costs in CSII arm were on average per patient 12,192€ over the remaining life-expectancy.

Table 1: Cohort Characteristics Used*	
Total randomized patients	n=95
SAP-LGS patients	n=46
CSII patients	n=49
Mean baseline age	18.6 years
Proportion of male	49.5%
Proportion of children	68.4%
Diabetes duration	11 years
Mean baseline HbA1c	7.5%
Hypo-unawareness	100.0%

*From Ly TT et al. JAMA. (2013)

Conclusion: Using a well-accepted simulation model in a risk of hypoglycemia T1DM, projection of the reduction of SHE for SAP + LGS versus CSII translated into cost-effective ratio, generally considered as very good value for money in France. Extensive sensitivity analysis on key drivers confirmed the robustness of results under a wide range of assumptions.

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HYPOGLYCAEMIA INDUCED BRAIN CONNECTIVITY CHANGES IN TYPE 1 DIABETES ASSESSED BY PARTIAL DIRECTED COHERENCE ANALYSIS OF EEG RECORDINGS

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Background: Several works have investigated hypoglycaemia-induced EEG changes, showing a power increase in the low frequency bands. A limited knowledge is available on how hypoglycaemia influences the connectivity between different brain areas. In this study, we use Partial Directed Coherence (PDC) to quantify the synchronization, i.e., functional interaction, between EEG channel-pairs during eu- and hypo-glycaemic conditions in type 1 diabetes (T1D).

Methods: Nineteen T1D patients undergoing a hyper-insulinaemic glucose clamp were studied during 1-hour intervals of euglycaemia and hypoglycaemia. EEG, according to the 10–20 system, and plasma glucose concentrations measured by YSI were observed in parallel. PDC was estimated, exploiting multivariate autoregressive models, from P3, P4 (parietal), C3, C4 (central) channels. PDC average values during the transition from eu- to hypo-glycaemia were evaluated in theta ([4–8] Hz) and alpha ([8–13] Hz) bands.

Results: The absolute values of PDC are low, while a significant change passing from eu- to hypo-glycaemia is observed in theta and alpha bands. In particular, both intra-hemispheric, i.e., P3-P4 (P4-P3) and C3-C4 (C4-C3), and inter-hemispheric, i.e., P3-C3 (C3-P3) and P4-C4 (C4-P4), PDC mean values decrease significantly (p < 0.05).

Conclusion: PDC mean values between parietal and central derivations tend to decrease passing from eu- to hypoglycaemia, suggesting that hypoglycaemia not only results in an increase of EEG power in low frequency bands, but also in a decrease of intra-hemispheric and inter-hemispheric coherence, related to progressive loss of cognitive function and altered cerebral activity. Future developments will include the extension of the database and of the considered EEG channels.

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LONG TERM RESULTS OF A FLUORESCENCE-BASED IMPLANTABLE GLUCOSE SENSOR

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Aim: To investigate the 90 day performance of a fluorescence-based implantable glucose sensor.

Methods: A small cylindrical sensor (3 × 14 mm) was implanted in the upper arm of type 1 diabetes patients. The sensor includes a temperature compensated fluorometer. Glucose values can be wirelessly transmitted and displayed on a smartphone. There were 41 implanted sensors, divided into 3 groups based on hardware differences. Mean absolute relative difference (MARD) for glucose values above 75 mg/dl was calculated. Venous samples collected every two weeks during 8 hours hospital stays, at 15 minutes intervals were used as reference for MARD calculation. Clarke Error Grid analysis completed the accuracy evaluation.

Results: Compared with group A (n = 6), Group B (n = 17) had a significantly higher longevity (64 ± 31 days group B vs. 28 ± 10 days group A, p < 0.01) and better MARD (11.8 ± 0.8% group B vs. 23.0 ± 1.5% group A, p < 0.01). There was a further improvement in group C (n = 18) for both longevity (64 ± 31 days group B vs. 87 ± 10 days group C, p < 0.01) and MARD (11.8 ± 0.8% group B vs. 10.9 ± 0.7% group C, p < 0.01). Similar improvements in sensor accuracy were shown by the Clarke Error Grid analysis showing a cumulative percentage for zone A + B of 85.5%, 98.5%, and 98.8% for group A, B, and C respectively.

Conclusion: Clinical data for a fluorescence-based implantable glucose sensor in type 1 diabetes patients showed 90 days very good results in terms of longevity and accuracy, particularly in sensor configuration available in group C. This particular sensor configuration looks ready for further 180 day testing.

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TIME LAG OF THE NEW DEXCOM G4 PLATINUM WITH MODIFIED SOFTWARE SYSTEM

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Background: Continuous glucose monitoring (CGM) systems estimate blood glucose levels using interstitial fluid. The physiology of glucose moving from blood to interstitial fluid has been estimated to happen in 5–6 minutes; CGM has reported time lags ranging from 5 to 20 minutes. The time it takes to display blood glucose estimates impacts the helpfulness of CGM.

Methods: The G4 PLATINUM with modified software system was evaluated in 51 diabetic subjects. Subjects participated in a 12 hr clinic session with the system and Yellow Springs Instrument (YSI) blood glucose measurements recorded every 5 and 15 minutes, respectively. Subject glucose levels were manipulated during their clinic stay allowing time lag estimation during recovery from hypoglycemia (YSI glucose ≤ 70 mg/dL). Time lag within 30 minutes was estimated for each system using the optimum of different statistics.

Results: There were a total of 2,378 YSI values collected from 50 subjects. The median time lag of the system was 6 minutes for each statistic (Figure 1) with averages ranging from 5 to 7 minutes. The majority (88%, 44 out of 50) of systems had a time lag within 10 minutes. Time lag during recovery from hypoglycemia was 4–6 minutes (Figure 2).

Conclusion: The time lag of this CGM is short and similar to physiological time lag. The system experienced similar time lag overall as while recovering from hypoglycemia, which may allow CGM users to utilize CGM trends for hypoglycemia management. The apparent time lag of glucose between venous blood and interstitial fluid can be minimized.
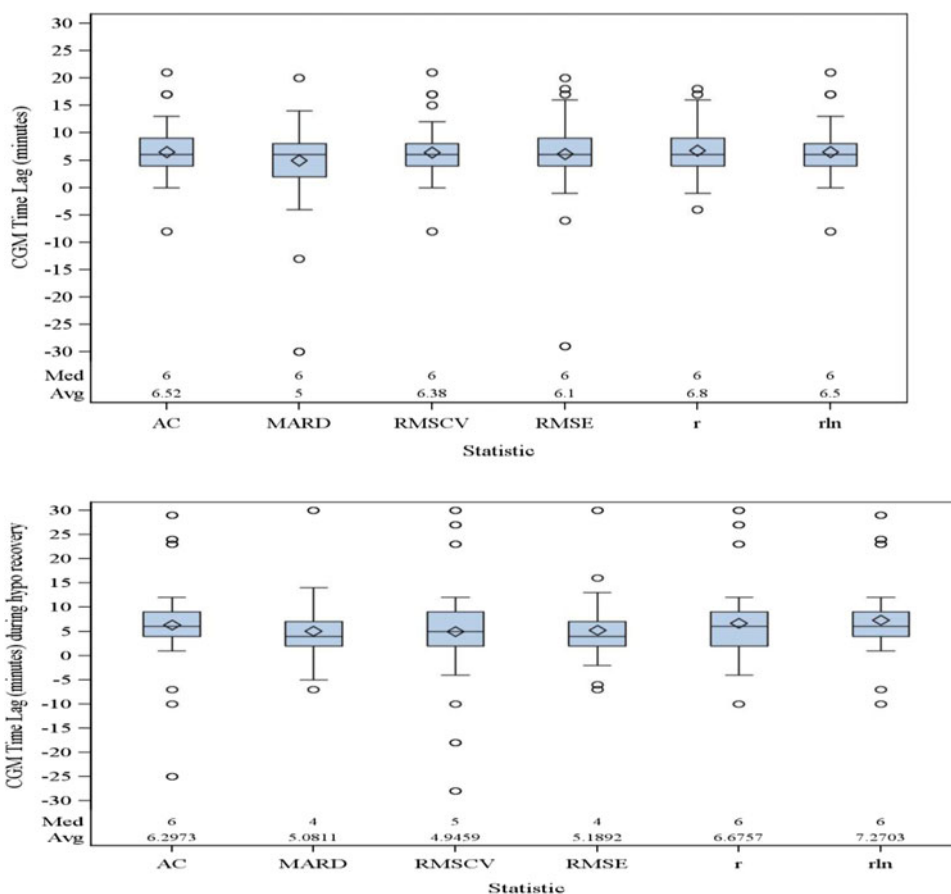
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EXPLOITING METER TECHNOLOGY TO IMPROVE SMBG AND GLYCAEMIC CONTROL IN SUBOPTIMALLY ADHERENT AND POORLY CONTROLLED INSULIN-USING INDIVIDUALS WITH DIABETES

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Background: Research has established that information, motivation, and skill demands of SMBG constitute significant challenges to patient adherence and achievement of glycaemic control. Improved meter technology may address these challenges by reducing information, motivation, and skill demands of SMBG. The current research examined the impact of innovative, integrated and simplified meter technology designed to substantially reduce demands of SMBG and improve adherence and glycaemic control.

Methods: 311 individuals with type 1 or insulin-treated type 2 diabetes performing SMBG at suboptimal frequencies and HbA1c $\geq 7.0\%$ were cluster-randomized to an integrated strip-free self-monitoring system (EXP; Accu-Chek® Mobile system, Roche Diagnostics) or single-strip meters (CNL). Patient-reported challenges of SMBG were assessed at baseline and diabetes regimen distress, SMBG frequency, HbA1c were measured at baseline, 12, and 24 weeks.
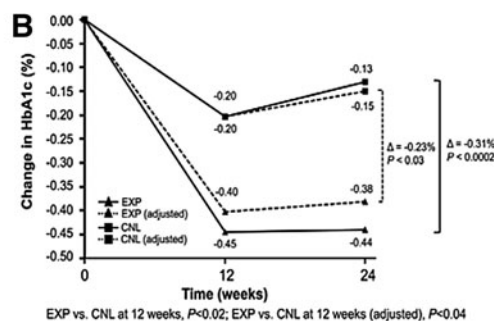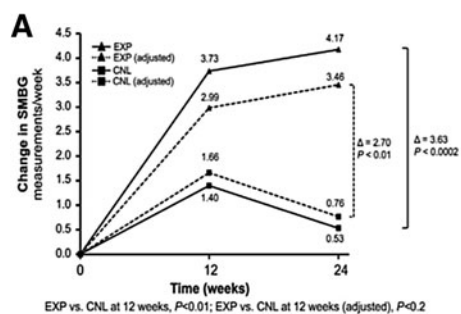
Results: At study baseline participants reported significant challenges to SMBG including feeling discouraged (32.5%), helpless (31.9%), and depressed (29.7%) in relation to self-monitoring and a substantial proportion (23.7%) reported that they were not motivated to maintain self-management. Moreover, 39.8% of participants reported one or more element of serious regimen-related distress at study baseline and 29.3% continued to report serious regimen-related distress at 24 weeks. Despite experiencing these motivational challenges to self-management, participants randomized to the integrated strip-free system showed significantly increased SMBG frequency and significantly improved glycaemic control across the study interval.

Conclusion: Integrated, simplified strip-free meter technology may result in meaningful increases in SMBG frequency and glycaemic control among individuals with suboptimal self-monitoring and glycaemic control who experience substantial motivational barriers to adherence.

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FEASIBILITY STUDY USE CASE AND PERFORMANCE OF A 90-DAY IMPLANTABLE CGM SYSTEM

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As CGM systems begin to consolidate more functionality into the wearable device as well as incorporate seamless connectivity to smartphones, the form factors and disposable components also become part of the scaling process. All of these system design features become a part of the user experience and play a role in compliance and overall use of the system's features and functionalities. A new implantable CGM system consisting of a fluorescence-based glucose Sensor, body-worn Transmitter and smartphone App has been developed. The small cylindrical Sensor has been designed to be inserted subcutaneously and provides 90 days of continuous measurements. The wearable Transmitter communicates with the passive Sensor via a near field communication (NFC) link as well as smartphone App via Bluetooth LE to display real time results. The Transmitter is powered with a rechargeable battery that can go from completely empty to fully charged in approximately 15 minutes and is attached via an adhesive patch or armband strap. This use case enables continuous usage throughout the day and night and can be taken off for a brief interval for recharging. This CGM system was used in a 14-subject, 90-day feasibility study where system performance and patient compliance were then analyzed. The sensor system achieved a full range MARD of 11.1%. Compliance metrics and subject use case benefits in HbA1c were assessed. Further detailed in Table 1, this study found an average median use time > 22 hrs/day over the full 90-day study duration.

Table 1: System Use Case Statistics for the 90 day study and Pre- and Post- Study HbA1c Measurements				
Subject ID	Median Wear Per Day (hrs)	MARD (%) (Full Range)	Pre-study HbA1c	Post-study HbA1c	HbA1c Difference
1	23.1	8.4	7.01	6.8	-0.21
2	23.1	11.9	n/a	6.78	n/a
3	23.1	9.8	n/a	7.1	n/a
4	23.6	9.7	n/a	8.17	n/a
5	23.4	9.9	n/a	n/a	n/a
6	23.3	7.9	7.9	6.66	-1.24
7	18.1	13.6	8.2	7.79	-0.41
8	22.5	13.4	9.6	8	-1.6
9	24	16.9	7.5	6.84	-0.66
10	23.1	10.7	7.13	7.32	0.19
11	22.8	18.2	8.77	7.49	-1.28
12	22.7	6.3	9.8	8.81	-0.99
13	13.5	10.6	13.7	9.35	-4.35
14	23.4	5.6	9.76	8.82	-0.94

This case report has been published in BMJ case report.

Lee SI, Narendran P. Intraperitoneal insulin therapy for a patient with type 1 diabetes with insulin injection site inflammation. BMJ Case Rep. 2014 Aug 21;2014. pii: bcr2014205278. doi: 10.1136/bcr-2014-205278.

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INTRAPERITONEAL INSULIN THERAPY FOR A PATIENT WITH TYPE 1 DIABETES WITH INSULIN INJECTION SITE INFLAMMATION

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Background: A 36-year-old Caucasian man with a 14-year history of type 1 diabetes (T1D) developed skin inflammation at the site of subcutaneous insulin injection after 10 years of basal bolus subcutaneous insulin therapy. This inflammation led to poor insulin absorption, poorly controlled blood glucose (glycated haemoglobin (HbA1c) 94 mmol/mol) and subsequently to ketoacidosis. The problem persisted despite a trial of continuous subcutaneous insulin infusion (CSII). Insulin autoantibody and skin prick test against common insulins were all negative.

Method: The patient was switched to treatment with continuous intraperitoneal insulin infusion (CIPII). The percutaneous port system consists of a metal body with a catheter placed intraperitoneally. We used the Accu-Check Diaport (Roche) CIPII device and Insuman Infusat (soluble insulin, 1.100 strength, Sanofi INS 1450).

Results: Two months post insertion, he developed cellulitis surrounding the port, this settled with intravenous antibiotics. At 3 months' follow-up, his HbA1c was 63 mmol/mol compared with 73 mmol/mol pre-CIPII. His Problem Areas in Diabetes (PAID) score improved from 67/80 pre-CIPII to 33/80 post-CIPII.

Discussion: CIPII closely approximates the physiological secretion of insulin because insulin is absorbed from the peritoneal space into the portal circulation. It has been shown to give good HbA1c control with acceptable morbidities and improves quality of life.

We present the use of CIPII as an alternative route of insulin delivery in a young adult with T1D. The only alternative approach would have been a pancreas transplant. CIPII is a better alternative because it is simpler, less invasive, and does not require lifelong immunosuppression.

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FACTORS ASSOCIATED WITH SUCCESSFUL CONTINUOUS SUBCUTANEOUS INSULIN INFUSION THERAPY IN TYPE 2 DIABETES PATIENTS— THE OPT2MISE TRIAL

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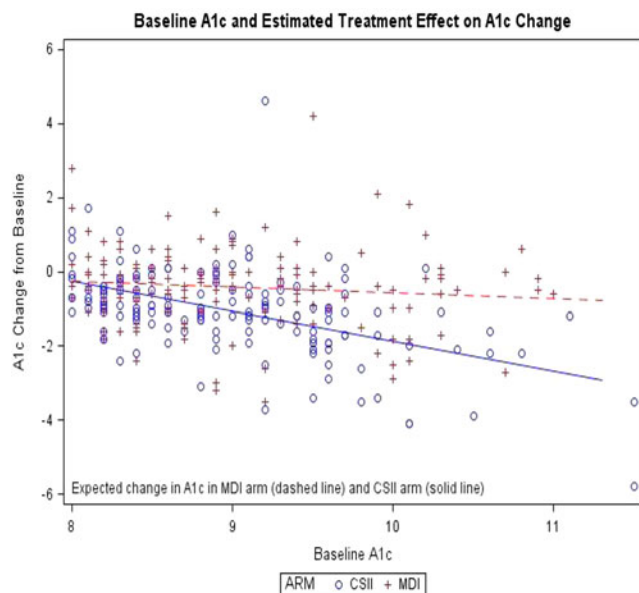[1]*Institute of Endocrinology, Sheba Medical center, Ramat gan, Israel*

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The OpT2mise study, demonstrated CSII provided significant improvement in glycemic control, as compared with injection therapy (MDI) in type 2 diabetes (T2D). We aimed to assess the association between baseline or treatment related factors with glycemic improvements seen in the CSII arm of the study.

331 uncontrolled T2D subjects subjects (45.6% women, 56.0 ± 9.6 yr, BMI 33.4 ± 7.3 kg/m^2, diabetes duration 15.1 ± 8.0 yr, HbA1c 9.0 ± 0.8%), were randomized to CSII or MDI regimen. Analysis was performed to assess the association of A1c change at 6 months with base line and study related factors.

CSII therapy achieved significantly greater A1c (-1.1%) reduction and more treatment satisfaction than MDI arm (-0.4%). The effect of in A1c change was dependent on baseline A1c ($p < 0.001$). CSII was superior to MDI in the observed range of baseline A1c values and the advantage of CSII over MDI increased with higher baseline A1c. Older age, longer duration of diabetes, low cognitive score and low SMBG use did not diminish the effect. In the CSII arm only 6-month satisfaction and number of boluses were associated with A1c reduction.

Conclusion: CSII in T2D patients was associated with greater improvement in A1c compared to MDI. Baseline A1c was a major predictor of glycemic response. A1c improvement in CSII arm was associated with treatment satisfaction and number of boluses without increase in total daily dose. Although CSII treatment involves the use of advanced technology, patients using less SMBG, had lower cognitive state or older achieved comparable improvement in glycemic control.

Baseline A1c and Estimated Treatment Effect on A1c Change

Expected change in A1c in MDI arm (dashed line) and CSII arm (solid line)

ARM o CSII + MDI

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FACTORS ASSOCIATED WITH SEVERE HYPOGLYCEMIA IN OLDER ADULTS WITH TYPE 1 DIABETES

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Background and Aims: In the T1D Exchange clinic registry, hypoglycemia-induced seizure or loss of consciousness within the prior year was reported by 21% of participants aged ≥ 65 years with ≥ 40 years T1D duration. We designed a case-control study to identify factors associated with severe hypoglycemia (SH) in older adults with T1D.

Methods: Cases ($n = 101$) aged ≥ 60 years with ≥ 20 years T1D duration and a SH event in the past year were age-matched to 100 controls without SH in the past 3 years. Data collection included 14 days of blinded CGM, various aspects of diabetes management, and cognitive, psychosocial, and functional measures.

Results: Cases and controls were nearly identical for age (mean 68 years), TID duration (mean 40 years), pump use (59%), HbA1c (mean 7.8%), and mean CGM glucose (175 mg/dL), but cases had more CGM glucose variability (CV, $p = 0.009$). Cases spent 65 minutes/day < 60 mg/dL, compared with 43 minutes/day in controls ($p = 0.12$). Hypoglycemia unawareness was strikingly more common in cases, with 45% reporting not feeling symptoms until glucose < 50 mg/dL versus 18% of controls ($p = 0.001$). Cases had slightly lower cognitive test scores than controls ($p = 0.04$) and higher Hypoglycemia Fear Survey scores ($p < 0.001$).

Conclusions: Tight glycemic control is not a key explanatory factor for the high rate of SH in older adults with longstanding T1D. Rather, an ominous combination of increased glycemic variability and hypoglycemia unawareness increases the SH risk. While CGM may effectively address the risk of SH in this population, U.S. Medicare does not currently cover CGM.

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DURABILITY OF INSULIN PUMP THERAPY EFFICACY IN A COHORT OF 161 PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Insulin pump therapy is effective in type 2 diabetes patients (T2D) uncontrolled by multiple daily insulin injections (MDI). We retrospectively analyzed on the long term efficacy of pump in a cohort T2D patients followed in one french center.

All 161 T2D patients who began insulin pump therapy between 1998 and 2012 were included in the survey. Patients characteristics included age 58.3 ± 9.8 yrs, BMI 33.2 ± 6.6 kg/m^2, A1c $8.95 \pm 1.68\%$. Insulin was used in 96% patients (MDI in 85%) for a mean of 6.75 ± 4.6 yr at a total daily dose (TDD) of 1.23 ± 0.88 U/kg/d. Metformine was used in 41% patients. Medical data were collected at pump initiation and thereafter yearly. At 1 year, HbA1c dropped by -1.29% ($p < 0.001$), 56.2% patients achieving an HbA1c $< 8\%$. HbA1c dropped by $-0.83 \pm 1.28\%$ in patients on a basal/bolus regimen. No change in A1c occurred when baseline HbA1c was $\leq 8\%$. Insulin TDD dropped by 13% ($p < 0.05$), body weight (BW) increased by 2.9 ± 7.6 kg ($p < 0.001$). Metformin intake had no influence on A1c or body weight changes. Mean duration of pump therapy was 5.13 ± 3.22 yrs. A1c and TDD remaining stable during 7 yrs follow-up ($p < 0.01$). Mean BW gain was 4 ± 11 kg at 5 yrs ($p < 0.05$).

In conclusion, pump therapy improves glycemic control with durability of such effect maintained several years after pump initiation.

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OPT2MISE: A RANDOMISED CONTROLLED TRIAL TO COMPARE INSULIN PUMP THERAPY WITH MULTIPLE DAILY INJECTIONS IN THE TREATMENT OF TYPE 2 DIABETES

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Background: Previous randomised controlled studies comparing the glucose-lowering efficacy of pump therapy and multiple injections in insulin-treated patients with type 2 diabetes have yielded unconclusive results.

Methods: OpT2mise was a large, multicenter, controlled trial that compared pump therapy with multiple injections in insulin-treated patients with type 2 diabetes. Patients (n = 495) with poor glycaemic control despite multiple injections with insulin analogues were enrolled into a 2-month dose-optimisation run-in period, after which patients with glycated haemoglobin A1c (HbA1c) $\geq 8.0\%$ and $\leq 12\%$ (n = 331) were randomised to pump therapy or to continue with multiple injections. The primary endpoint was the change in mean HbA1c from baseline to the end of the randomised phase.

Findings: At baseline, the mean HbA1c level was 9% in both groups. At 6 months, HbA1c had decreased by $1.1 \pm 1.2\%$ in the

pump therapy group, and $0.4 \pm 1.1\%$ in the multiple injections group, resulting in a between-group treatment difference of -0.7% (95% confidence interval [CI] -0.9 to -0.4, $P < 0.001$). The percentage of subjects achieving an HbA1c level $< 8\%$ in the pump therapy group was twice that in the multiple injections group. At the end of the study, the total daily insulin dose was 20.4% lower with pump therapy than with multiple injections, with no significant difference in body weight change between the two groups. No severe hypoglycaemia or ketoacidosis occurred in the pump therapy group.

Interpretation: In patients with sub-optimally-controlled type 2 diabetes, pump therapy significantly improved glycaemic control, compared with injection therapy, with lower insulin doses and maintained safety.

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THE IMPACT OF INSULIN PUMP THERAPY ON GLYCEMIC PROFILE OF PATIENTS WITH TYPE 2 DIABETES. DATA FROM THE OPT2MISE STUDY

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Aim: To further understand the mechanism underlying the differences between both types of therapies, a study on the glucose metrics, as a secondary endpoint, was performed.

Subjects and Methods: Subjects with poor glycemic control (n = 495) on MDI were enrolled into a run-in period for insulin dose optimization. Those showing an HbA1c $\geq 8\%$ and $\leq 12\%$ were then randomly assigned to CSII or continuing on MDI for 6 months. Blinded Continuous Glucose Monitoring (CGM, iPro2, Medtronic) data was collected for a 6 day period before and 6 months after randomization and changes in glucose metrics were evaluated (Glucose exposure, Glucose Variability and Glucose Ranges).

Results: Data on CGM were available for 290 patients (143 and 147; 123 and 112 in the CSII and MDI arms at baseline and 6 month). After 6 months, 24 h sensor glucose (SG) was reduced significantly more in CSII group (-17.1 mg/dl, $p < 0.05$), with less exposure to SG > 180 and SG > 250 mg/dl (-12.2%, $p < 0.001\%$, and -6.4%, $p < 0.05$), more time in target (70–180 mg/dl; 11.8%, $p < 0.001$) and no difference in time exposure to SG < 70 mg/dl. Concerning glucose variability, there were no difference in 24 h Standard Deviation (SD) SG, coefficient of variation (CV) or in mean amplitude of glucose excursions (MAGE).

Conclusions: CSII treatment in suboptimally controlled patients with T2D provides a significant improvement in glucose profile with increased time spent in target, less exposure to hyperglycemia and without an increase in the risk of hypoglycemia

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COMPOSITE ADIPONECTIN-RESISTIN AND INSULIN RESISTANCE INDEXES ARE CORRELATED WITH ADIPOSITY GLUCOMETABOLIC CONTROL AND CARDIOVASCULAR RISK IN TYPE 2 DIABETIC PATIENTS AND NON–DIABETIC INDIVIDUALS

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Objectives: Adiponectin and resistin are adipokines involved in insulin resistance, glucometabolic control and adiposity. There are evidences that hypoadiponectinemia and hyperresistinemia are associated with cardiovascular disease. The aim of this study was to assess the relationships of Adiponectin-resistin (AR) and insulin resistance (IR_{AR}) indexes with adiposity, glucometabolic control and cardiovascular risk in healthy subjects and patients with type 2 DM.

Methods: This observational case control study was conducted in the Departments of Physiology and Medicine, King Saud University, Riyadh. A total of 229 subjects with age range 24–65 years were studied. Body composition was assessed by bioelectrical impendence analyzer. Fasting blood samples were analyzed for glucose, glycosylated hemoglobin (HbA1c), high sensitivity C reactive protein (hsCRP), lipids, Lipoprotein(a), adiponectin and resistin levels. The AR and IRAR indexes were determined by the formulas; $1 + [\log_{10}(R_0)\text{-}\log_{10}(A_0)]$ and $\log_{10}(I_0 G_0) + \log_{10}(I_0 G_0)\log_{10}(R_0/A_0)$ respectively as previously described. [R_0 = fasting resistin, A_0 = fasting adiponectin, I_0 = fasting insulin and G_0 = fasting glucose]

Results: Serum adiponectin and resistin levels correlated inversely ($r = 0.158$, $P < 0.05$). AR and IRAR indexes were more strongly associated with adiposity, dyslipidemia and cardiovascular risk markers. AR index correlated positively with Triglycerides ($r = 0.354$, $P < 0.001$), hsCRP ($r = 0.264$, $P < 0.001$), HbA1c ($r = 0.425$, $P < 0.001$), fat mass ($r = 0.157$, $P < 0.05$), Waist hip ratio ($r = 0.212$, $P < 0.01$) and negatively with high density lipoprotein ($r = -0.327$, $P < 0.05$). IRAR relationships were even more strongly correlated with the above mentioned markers.

Conclusions: Adiponectin-resistin and insulin resistance indexes correlate significantly with adiposity, glucometabolic control and cardiovascular risk in type 2 diabetic patients and non diabetic individuals. They may prove to be useful integrated biomarkers to predict metabolic dysregulation and cardiovascular risk.

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DIABETES MANAGEMENT IN ITALIAN CHILDREN, ADOLESCENTS AND YOUNG ADULTS WITH TYPE 1 DIABETES (T1D) IN TEENS: ADVANCED VS CONVENTIONAL THERAPIES

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Table: Glycaemic control, diabetes management and acute complications in patients using advanced or conventional therapies

	8-12 years old (n=330)		13-18 years old (n=490)		19-25 years old (n=189)	
	AT (n=185)	CT (n=145)	AT (n=292)	CT (n=198)	AT (n=146)	CT (n=43)
Glycaemic control						
HbA1c [%], mean (SD)	7.7 (1.0)	7.9 (1.0)	7.8 (1.4)	7.9 (1.2)	7.7 (1.3)	7.5 (1.1)
HbA1c at target*, % of participants	46	37	44	38	33	26
Diabetes management						
SMBG [times per day] mean (SD)	5.4 (1.5)	5.2 (1.6)	4.5 (1.6)	4.6 (1.9)	3.9 (1.4)	3.6 (1.2)
CGM, % of participants	8.6	0.7	4.5	1.0	2.7	2.3
Acute complications in the past 3 months (% of participants)						
Severe hypoglycaemia†	2.2	2.1	1.0	0	2.7	0
DKA	3.8	0.7	2.1	1.0	3.4	2.3

AT, advanced therapy; CGM, continuous glucose monitoring; CT, conventional therapy; DKA, diabetic ketoacidosis; SD, standard deviation; SMBG, self-monitoring of blood glucose

*HbA1c targets were defined as <7.5% (ISPAD) for participants aged ≤18 years and <7% (ADA) for participants aged >18 years; †Resulting in seizure or loss of consciousness

Objectives: TEENs is the largest worldwide, contemporary, observational study of T1D in 8-25-year-old (y/o) patients, aiming to assess disease management and psychosocial parameters to identify approaches to optimise diabetes outcomes. This report describes outcomes in Italian patients using advanced therapies (AT; insulin pump using analog insulin, basal-bolus with analog insulin) *vs* conventional therapies (CT; human insulin, non-analog insulin).

Methods: 23 centres collected data by interview, medical record review and participant/parent survey from 1009 Italian youths (mean[SD] diabetes duration: 7.52[4.64] years). HbA1c was measured uniformly using A1cNow™ (Bayer, reference range 4–6%). Diabetes-specific emotional burden was assessed using the Problem Areas In Diabetes (PAID; ages 13–25 y/o) survey.

Results: Overall, 40% of participants attained HbA1c targets and 62% used AT. Across age groups, numerically more AT users achieved HbA1c targets compared with CT users (**Table**). While SMBG frequency was similar across groups, a higher proportion of AT users used CGM compared with the CT group. A higher rate of DKA (all age groups) and severe hypoglycaemia (13–25 y/o) was reported for the AT group. Overall diabetes-related emotional burden was similar between treatment groups (AT *vs* CT, mean[SD]; PAID 13–18 y/o 24[18] *vs* 25[18]; 19–25 y/o 22[17] *vs* 22[21]).

Conclusions: In Italy, 40% of patients attained HbA1c targets with a mean(SD) HbA1c of 7.8(1.2). A higher proportion of patients at target were using AT compared with CT. Opportunities exist to further improve HbA1c target attainment, and reduce acute complications and disease burden for youth with T1D.

Study funded by Sanofi

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INCREASED ARTERIAL WALL STIFFNESS IN CHILDREN WITH TYPE 1 DIABETES AND BAD METABOLIC CONTROL: EARLY MARKER OF VASCULAR COMPLICATIONS?

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Background: The prevalence of cardiovascular risk factors is underestimated in children with type 1 diabetes (T1D).

Aim: To investigate the relationship among the arterial stiffness and factors associated with metabolic control of diabetes such as HbA1c levels, duration of diabetes and mode of insulin treatment.

Patients and Methods: We have examined 39 children with type 1 diabetes (25 males), aged 11–18 years (median 16), diabetes duration 3–16 years (median 9), 20 and 19 treated with CSII and MDI, respectively. All subjects have measured HbA1c (44–122, median 78 mmol/mol; IFCC). Arterial stiffness was measured as carotid-femoral pulse wave velocity (PWV) (PulsePen, DiaTecne). Adjustment included gender, age, heart rate and mean arterial pressure.

Results: Increased arterial stiffness was found in 8 (21%) patients. We found significant association between increased PWV and higher HbA1c level ($p < 0.001$) whereas duration of T1D and insulin treatment mode were not associated.

Conclusions: Higher HbA1c levels were associated with significant increase of arterial stiffness in young patients with type 1 diabetes. Identifying early vascular abnormalities in youth with T1D will allow implementation of more aggressive risk factor management.

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REDUCTION OF SILENT OCCLUSION OCCURRENCE
DURING CONTINUOUS SUBCUTANEOUS INSULIN
INFUSION

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Background: Continuous subcutaneous insulin infusion
(CSII) sets' failure modes include leakage, pump occlusion
alarms, and sub-alarm "silent" occlusions; these can impede in-
sulin delivery and contribute to lack of glycemic control. A novel
CSII polymer catheter set was evaluated against commercial sets
for delivery reliability using multiple insulin pump types.

Method: CSII flow performance was examined during 4.5 hr
placebo delivery at clinically relevant rates (1 U/hr basal, 10 U/
bolus) in 12 nondiabetic Yorkshire swine using BD's investiga-
tional 6 mm polymer set and 3 commercial sets (Animas Inset®,
Medtronic Quick-set®, Accu-chek® Ultraflex; all 6 mm length)
with their recommended pump (Animas OneTouch® Ping®, Med-
tronic MiniMed Paradigm® Revel™, & Roche Accu-Chek® Spirit,
respectively). Flow performance was monitored using in-line in-
fusion pressure and analyzed with a proprietary pressure/flow al-
gorithm that identified periods of sub-alarm flow interruptions
("silent" occlusions) with 30 minute minimum threshold. Animal
studies were IACUC approved and NIH/AAALAC compliant.

Results: When BD's investigational set was used, reductions in
mean percent time of silent occlusion were observed compared to
Animas/Inset®, Medtronic/Quick-set®, and Roche/Ultraflex by 79%,
77%, and 74%, respectively. Reductions at p-values of 0.0066, 0.0159
and 0.0535, respectively, were shown per non-parametric testing as
data was non-Gaussian. There were no statistically significant dif-
ferences in leakage or occlusion alarm occurrences amongst devices.

Conclusions: The investigational set showed improved in-
sulin flow reliability relative to comparators based on detectable
silent occlusions. More reliable insulin flow may provide benefit
in reducing complications due to undetected insulin set failure.
Ongoing efforts include examining pressure/flow algorithm op-
timization and clinical detection of silent occlusions.

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HEALTHCARE PROVIDERS AND THEIR PATIENTS
WITH TYPE 1 DIABETES HAVE DIFFERING
PERCEPTIONS OF THE IMPORTANCE
OF VARIOUS INSULIN PUMP FEATURES

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Aims: Latest generation insulin pumps (LGIP) offer advanced
features that are designed to assist individuals with diabetes
better manage their disease. However, are healthcare profes-
sionals (HCPs) and their patients aligned in their perceptions
regarding the importance of these features? We conducted a
survey of HCPs and their patients with type 1 diabetes to address
this question.

Methods: HCPs and their patients from 82 centers in five
countries responded to the survey. All patients had recently
transitioned to an LGIP (Animas® Vibe™), enabled with con-
tinuous glucose monitoring (CGM), following previous treat-
ment with an earlier generation insulin pump, multiple daily
injections (MDI) or no previous insulin treatment. Patients were
surveyed via a 50-item online questionnaire, which included
questions to assess their perceptions of the value and importance
of the LGIP features. HCPs completed a shorter version of the
questionnaire. Respondents rated specified features of the LGIP
'important' or 'less important'.

Results: A total of 356 patients, age 12–79 years, and 121
HCPs, responded to the survey. Alignment of perceptions be-
tween groups was mostly strong; however, notable differ-
ences were seen in perceived importance of certain convenience/
utility features (high-contrast screen, waterproofness) and clin-
ically relevant features (ezBG, downloading capability).
(Table 1)

Table 1. Percentage of patients and HCPs who considered the LGIP advanced features "important"

Feature	Rated "Important"	
	Patient n=356	HCP n=121
Ease of use (e.g. menu, navigation, instructions, etc.)	96.6%	100.0%
Giving a bolus at meal or snack time	95.3%	96.6%
Warnings and alarm safety system	93.5%	86.8%
Size	90.6%	85.8%
Ease of customizing profiles (e.g. basal rates, exercises, etc.)	88.3%	87.5%
Weight	83.9%	80.7%
Continuous Glucose Monitoring (CGM) option	80.9%	81.8%
Waterproofness	**73.9%**	**61.1%**
ezBG feature (automatic calculation of correction bolus doses)	**71.3%**	**90.2%**
Low bolus increment of 0.05 U	67.9%	61.2%
Low basal increment of 0.025 U	66.6%	71.6%
High-contrast color screen	**63.7%**	**84.5%**
Downloading capability	**62.4%**	**87.5%**
Customizable in-pump food database option	36.2%	34.8%

Conclusions: Because improving glycemic control is a shared goal, it is important that HCPs and patients discuss the importance of pump features. HCPs should explain and encourage use of clinically relevant features with their patients but also discuss the convenience/utility features that will reduce the burden of diabetes and enhance optimal diabetes self-management.

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SIMPLE CSII PROVIDES ACCURATE BASAL INSULIN DELIVERY

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Objective: A unique advantage of continuous subcutaneous insulin infusion (CSII) over insulin injections is the ability to deliver basal insulin that mimics physiologic interprandial insulin secretion, which can reduce glycemic variability and minimize hypoglycemia risk. New insulin delivery devices, developed to deliver simple insulin infusion (SII), provide ''flat basal'' infusion similar to durable insulin pumps but without the complexity and extensive training requirements. We assessed the accuracy of basal insulin infusion in the PaQ insulin delivery device (CeQur, Horw, Switzerland), which provides three days of continuous insulin infusion for individuals with type 2 diabetes.

Methods: In accordance with recommended test methodology (International Electrotechnical Commission [IEC] 60601-2-24 standard for infusion pump performance), we assessed the accuracy of the PaQ device at 10.0 μl/h) over two time periods: first 24 hours (T1); and the subsequent 25 hours (T2). The flow was calculated for every two successive 15 minutes intervals. Percent of variation [E_p(max.) and E_p(min.)] and overall mean percent error were plotted on a trumpet curve. E_p(max.) and E_p(min.) were calculated for the 15, 60, 150, 330, 570 and 930 minute observation windows.

Results: Overall flow rate was 9.908 μl/h (average 9.860 μl/h) during T1 and 9.934 μl/h (average 9.930 μl/h) during T2, resulting in an Overall Error, A (%) of -0.66%. **(Figure 1A)** Average flow rate over the 49 hours was 9.96 μl/h.

Conclusions: Basal insulin infusion of the PaQ device is accurate, consistent over time and appears to be comparable with durable insulin pump devices. **(Figure 1B)**

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INSULIN PUMP THERAPY REDUCES POSTPRANDIAL GLUCOSE VARIABILITY IN PATIENTS WITH TYPE 1 DIABETES

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Background: Postprandial glycaemia is associated with increased coronary heart disease and cardiovascular events. Total glucose exposure, including postprandial hyperglycaemia and glucose variability, should be considered when evaluating the patient's risk for complications. Our aim was to assess the impact of insulin pump therapy on postprandial glucose variability.

Research Design and Methods: We retrospectively analysed continuous glucose monitoring data from 22 type 1 diabetic patients under insulin pump (IP) therapy and 39 patients under multiple daily injection (MDI) regimen. iPro[TM]2 CGM device (Medtronic, Northridge, CA) was used in all patients.

Results: Duration of disease and HbA1C was similar in both groups (19.4 and 16.4 years, p=0.212; 7.98% and 7.89%, p=0.787 for IP and MDI groups, respectively). Patients under IP were less time in hypoglycaemia than patients treated with MDI (5.9% versus 10% of the total continuous glucose monitoring time). Patients under IP therapy had mean postprandial glucose higher than those treated with MDI at breakfast and lunch (162.1 versus 150.9 mg/dL, p<0.001; 157.9 versus 154.2 mg/dL, p<0.001, respectively), but not at dinner (155.4 versus 159.2 mg/dL, p=0.002). Though, percentage coefficient of variation was lower in the patients treated with IP than MDI in all meals (breakfast 42.7% versus 50.3%, p<0.001; lunch 43.4% versus 45.9%, p<0.001; dinner 44.4% versus 45.5, p=0.001, respectively).

Conclusions: Insulin pump therapy effectively reduces hypoglycaemia and postprandial glucose variability in patients with type 1 diabetes. Intervening in all components of glucose exposure is required for optimal diabetes control.

Figure 1. Flow rate accuracies for PaQ simple infusion device (A) and ACCU-CHEK® Spirit insulin pump (B)
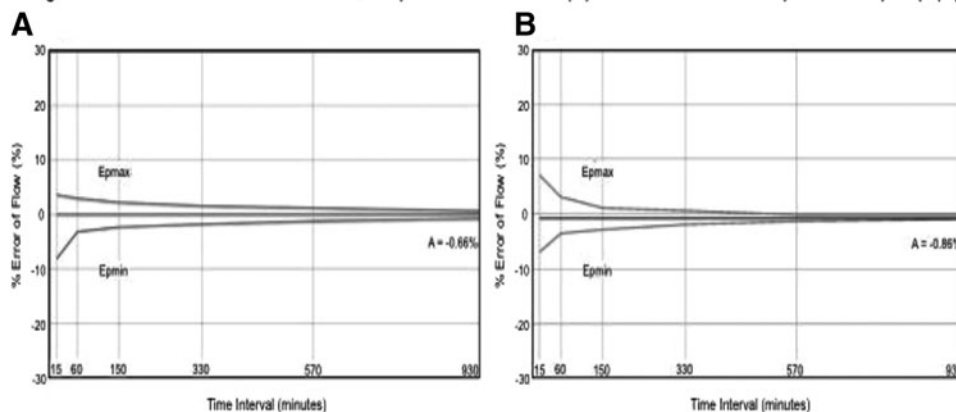
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INTRAPERITONEAL GLUCOSE SENSING – RAPID AND ACCURATE

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A rapid, accurate and robust glucose measurement is needed for making a safe artificial pancreas for treatment of diabetes mellitus type 1 and 2. Non-invasive or minimally invasive approaches such as subcutaneous (SC) glucose sensors are known to have slow response and poor robustness towards local tissue effects such as mechanical pressure, temperature, etc.

The present pilot study demonstrates that an intraperitoneal (IP) glucose sensor can have substantially faster and distinctive response than SC sensors. Intra-arterial (IA), IP and SC glucose sensors have been tested on two anaesthetized non-diabetic pigs during experiments with intravenous infusion of glucose boluses, enforcing glucose level excursions within the range 5–22 mmol/L.
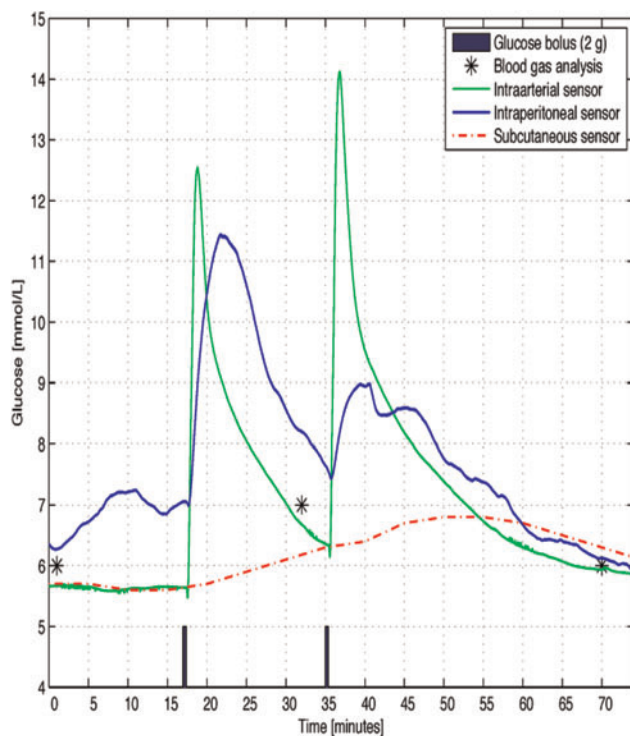

Figure 1: Segment of recorded data from animal trial with IA, IP and SC sensors. Includes three analysed samples from an artery [in black]. Two glucose boluses (2 grams each) were infused intravenously [in dark blue].

Off-the-shelf amperometric enzyme-based (glucose oxidase) sensors were used for the SC case. Optical interferometric phenylboronic acid based sensors were used for IA and IP measurements. Results shown in Fig. 1 indicate that IP measurements can reflect change in plasma blood glucose already within 1–2 minutes.

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EFFECT OF ACETAMINOPHEN ON CGM GLUCOSE IN AN OUT-PATIENT SETTING

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Acetaminophen is known to interfere with continuous glucose monitoring (CGM) by falsely elevating CGM glucose values. However, limited published data exist documenting the magnitude of this relationship. We hypothesized that oral acetaminophen would cause elevation of CGM glucose values in relationship to glucose meter values.

Participants (n=15, 60% male, age=31.2 ± 8.5 years, HbA1c=$7.5 \pm 0.8\%$) were enrolled in an out-patient study using the DexCom G4® system. Participants consumed breakfast with a standardized 1000 mg dose of acetaminophen. Glucose meter (Bayer Next®) values were taken at baseline, 0.5, 1, 2, 4, 6 and 8 hours, and differences between CGM and meter glucose values were calculated for each time point.

Least squares means and 95% CIs from a mixed model of the difference at each time point are displayed (Figure). Statistically significant differences existed at 1, 2, and 6 hours after acetaminophen ingestion (p=0.001, 0.0004, and 0.036 respectively). The greatest mean difference was 59 mg/dl with an upper 95% CI limit of 90 mg/dl. Individual variation requires further investigation.

Acetaminophen falsely elevates CGM glucose values compared to home glucose meter values. Implications of these data include use of CGM glucose as a replacement for meter glucose for insulin dosing decisions and applications for closed-loop systems.


Least squares means and 95% CIs for CGM glucose-meter glucose by time point.
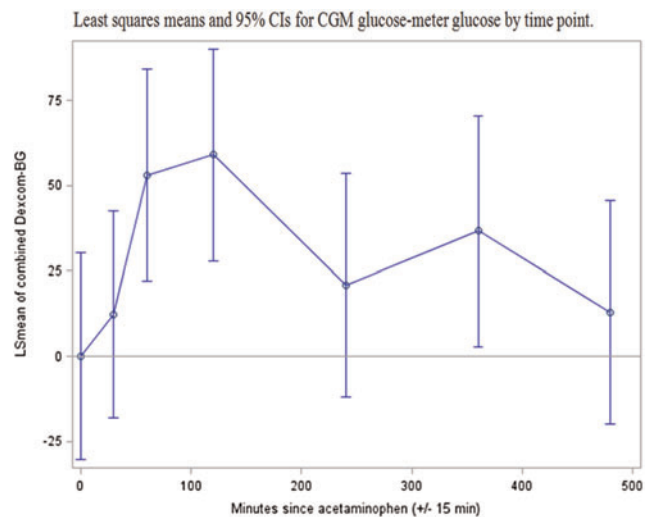
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EFFECT OF GLUCOSE REFERENCE MEASUREMENT DISTRIBUTION ON MARD PERFORMANCE MEASURE FOR CGM

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The mean absolute relative difference (MARD) is commonly used toquantify the performance of CGM sensors. It is well
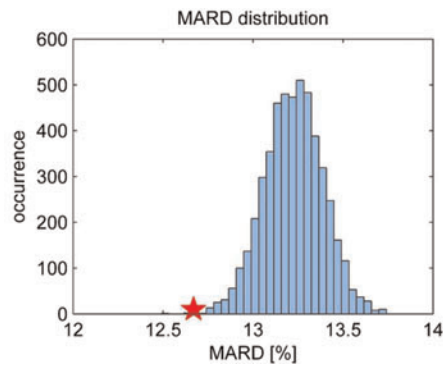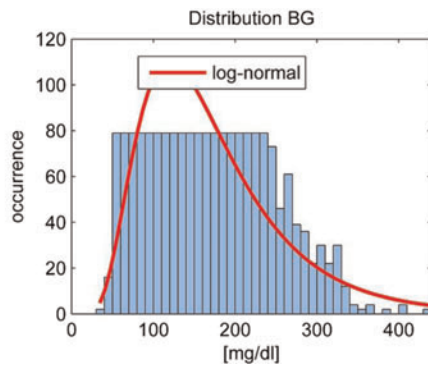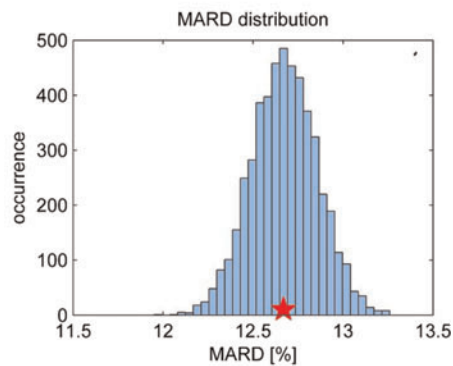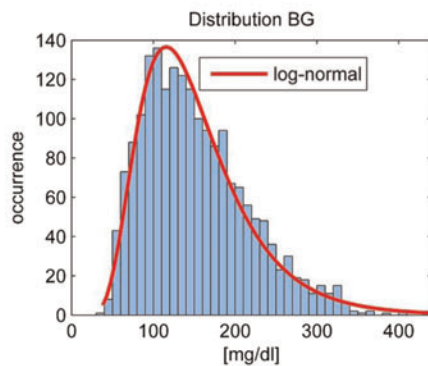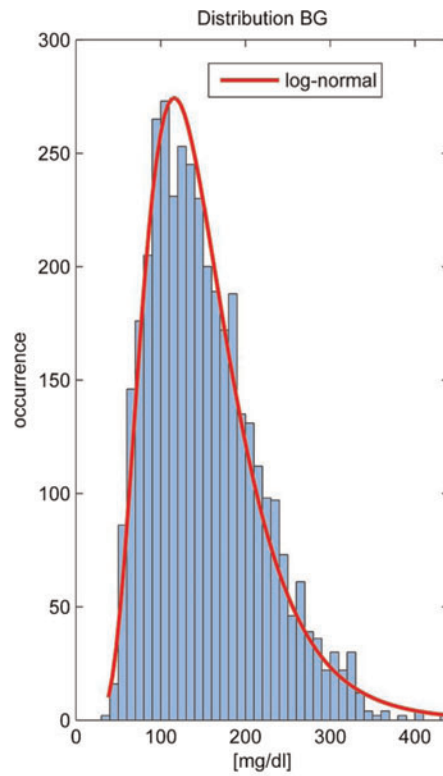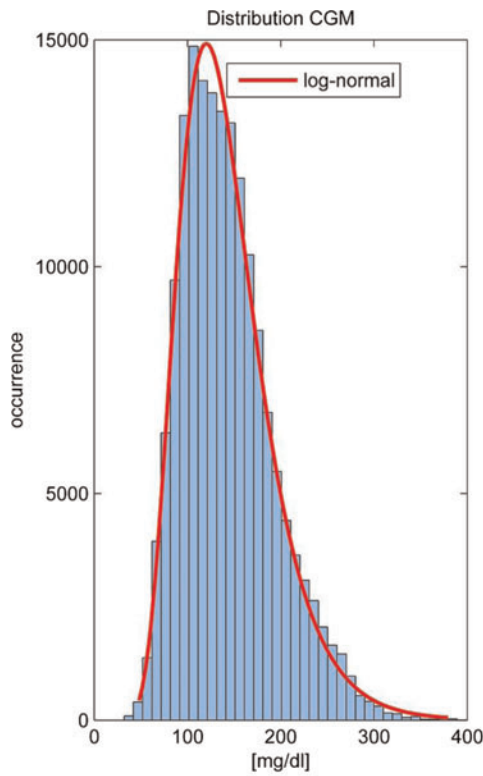
known that there are significant differences in the MARD if different glucose ranges are considered (e.g. in hypo-, normo- or hyperglycemia). Here, we analyzed the effect of the distribution of glucose reference measurements on MARD.

Methods: Data from 12 patients wearing several sensors in parallel (Freckman et al., J. of Diabetes Science and Technology 7(4), pp. 842–853) were analyzed. The original distribution of CGM values and paired reference measurements was close to a log-normal distribution (Fig. 1). Retrospectively, reference measurements were removed for MARD calculation in two ways: a) by maintaining a log-normal distribution, b) by changing to a uniform distribution. Points to remove were selected randomly; computation was repeated many times (Monte Carlo simulation) to obtain a statistically significant result.

Results: Initially available paired reference measurements (N = 4757, 3839, 4259 for sensors A/B/C respectively) were reduced to N* = 2371, 1913, 2124. Initial MARD values (16.52%, 12.67%, 17.06%) changed to $16.52 \pm 0.24\%$, $12.67 \pm 0.19\%$ $17.07 \pm 0.27\%$ when maintaining the log-normal distribution and to $16.51 \pm 0.21\%$, $13.22 \pm 0.16\%$, $18.25 \pm 0.24\%$ when changing to a uniform distribution (mean $\pm$ std). See Fig. 2 for results on sensor B.

Conclusions: The distribution of the paired reference measurements greatly affects the MARD. In case the distribution keeps log-normal (which is the standard case) a reduced amount of paired measurements still enables bias-free estimation of the MARD. In case the distribution changes, different glucose regions get more pronounced, thus significantly affecting the resulting MARD.

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ENDURANCE EXERCISE AND CONTINUOUS GLUCOSE MONITORING—EFFECTS ON TISSUE GLUCOSE LEVELS: TEAM BLOOD GLUCOSE CYCLING RESEARCH

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Introduction: Maintaining stable glycaemia during physical activity can be challenging for people with type 1 diabetes. Glucose excursions during and after exercise remain a barrier.
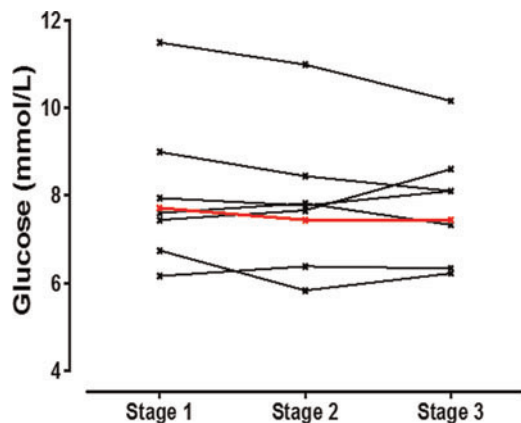
FIG. 1. Median glucose level for individual riders with diabetes during each stage of the Grand Tour (and overall median, red line)

We used CGM in a multi-day cycling event to study the impact of endurance exercise on glucose homeostasis.

Methods: Team Blood Glucose cycled from Barcelona to Vienna in 2014. The event comprised three five-day stages (mean distance 159 km/day) with a rest day between each stage. Volunteers wore Dexcom G4 continuous glucose monitoring devices, calibrated with capillary blood glucose at least twice daily. Those with diabetes self-adjusted their insulin dosage, with peer-support.

Results: We recruited 11 volunteers (n = 7 with diabetes, n = 4 without diabetes, age 26–49 years) who cycled all stages. Of those with diabetes, continuous subcutaneous insulin infusion (n = 5) and multi-dose injections (n = 2) were used. Median glucose for those with diabetes was significantly (p < 0.001) reduced between Stage 1 and Stage 2 but there was no difference between Stage 2 and Stage 3 (Fig. 1). There was no difference in glycaemic variability between Stages in the riders with diabetes.

Median glucose ($\pm$ IQR) of participants without diabetes was significantly (p < 0.001) reduced between Stage 1 (5.72 $\pm$ 4.88-6.66 mmol/l), Stage 2 (5.22 $\pm$ 4.61-5.88 mmol/l), and Stage 3 (5.16 $\pm$ 4.55-5.83 mmol/l); the standard deviation also fell as the ride progressed (1.26, 1.11, 1.03).

Discussion: Glucose control in people with type 1 diabetes undertaking an endurance event is improved, then remains stable. This may be due to peer-support and the use of CGM. In people without diabetes glucose and glucose variability fell suggesting physiological change.

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MOLECULAR AND IMMUNOHISTOCHEMICAL STUDIES ON METFORMIN IN TREATMENT OF TYPE 2 DIABETIC RATS

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Type 2 diabetes mellitus (T2DM) is a serious worldwide disease. It is associated with insulin resistance. During insulin resistance, dyslipidemia and alterations in some genes occurred. Metformin is the drug of choice for treatment of type 2 diabetes. The exact mechanism of metformin regulation is still incompletely explained. In this study, the effect of metformin on serum lipid profiles, new identified genes that are related to insulin resistance and histopathology of liver and pancreas was examined. T2DM was induced by feeding rats with a high fat diet for 4 weeks plus medium dose of streptozotocin (STZ, 35 mg/kg BW). Incidence of T2DM was confirmed and metformin was administered orally in a dose of 400 mg/kg BW for 4 weeks. Results showed that metformin improved insulin resistance by normalizing serum lipid profiles in diabetic rats. Metformin up-regulated the expression of both insulin receptors and genes related to lipid metabolism (acyl CoA oxidase ACO; carnitine palmitoyl transferase-1, CPT-1; and peroxisome proliferator activated receptor alpha, PPAR-a). Metformin administration down-regulated fetuin-A and retinol binding protein-4 (RBP-4) expression; moreover, normalization of perilipin expression that was decreased in T2DM rats was reported. Metformin administration induced regenerative changes in hepatocytes cytoplasm and parenchyma. In pancreas, metformin administration showed positive signaling for insulin and regeneration of pancreatic b cells. In conclusion, metformin ameliorated the changes associated with T2DM through controlling fetuin-A, RBP-4 and perilipin together with genes of lipid metabolism with regenerative changes in liver and pancreatic cells.

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CHARACTERIZATION OF DISEASE PROGRESSION OF A NONHUMAN PRIMATE MODEL WITH OBESITY, DYSMETABOLISM AND DIABETES: A POWERFUL TRANSLATIONAL TOOL FOR PHARMACEUTICAL RESEARCH

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It has long been recognized in both academia and the pharmaceutical industry that rodent models of diabetes and metabolic disorders are notoriously unpredictable in clinical outcomes in response to certain therapeutics. Nonhuman primate (NHP) models of obesity, dysmetabolism and diabetes are proven to be the most translatable animal models not only in basic research to understand pathophysiogenic mechanisms of the diseases, but also in testing novel therapies. In over 100 cynomolgus monkeys with naturally occurring obesity, dysmetabolism and diabetes, we have detected different levels of hyperglycemia, hyperinsulinemia, dyslipidemia, obesity with increased fat composition, insulin resistance measured by fasting index as well as insulin tolerance test (ITT) and hyperglycemic and/or hyperinsulinemic/euglycemic clamp test, impaired glucose tolerance (IGT) and insulin response measured by intravenous (ivGTT) and oral glucose (oGTT) or mixed meal (MMTT) load, impaired pancreatic insulin secretion function measured by graded glucose infusion (GGI), etc. Furthermore, this NHP model of dysmetabolism also exhibits micro/macrovascular impairment-related organ injury with some complications such as diabetic nephropathy. Both the obese, dysmetabolism and diabetic phenotypes, as well as diabetic complications, respond similarly as in human patients to some standard therapies, such as rosiglitazone, GLP-1 agonists, metformin, Losartan/Ibersartan, etc. Therefore, this NHP model of obesity, dysmetabolism and diabetes has been used extensively in testing novel small molecule and biologics (protein, peptide and antibodies) drugs with predictable outcomes.

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ASSOCIATION BETWEEN RED BLOOD CELL DEFORMABILITY AND MICROVASCULAR COMPLICATIONS IN PATIENTS WITH TYPE 2 DIABETES

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Background: Red blood cell (RBC) deformability is an ability of RBC to change shape under stress. RBC deformability has been known to be decreased in atherosclerosis and diabetes. But, little is known about the association between impaired RBC deformability and type 2 diabetes (T2D). The aim of this study was to determine the influence of RBC deformability on T2D.

Method: From March to October 2014, a cross-sectional study was conducted with 304 T2D patients who visited in our university hospital. Patients with end stage renal disease (n = 11) and who are taking a pentoxifylline or ginkgo biloba (n = 7) were excluded. RBC deformability was measured by using a Rheoscan-D® (Rheo-Meditech, Seoul, Korea), and expressed as elongation index at 3 Pa (EI@3P). We divided into quartile from lowest (Q1) to highest EI@3P (Q4).

Result: 286 patients (mean age 59.3 years, male = 148) were finally included. EI@3P showed inverse correlation with the glycated hemoglobin, and positive correlation with HOMA-B% ($\beta - 25.09$, $p = 0.006$ and β 439.45, $p = 0.019$, respectively). The level of EI@3P was lower in patients with microvascular complications than the others without complications (0.303623 vs. 0.310637, $p = 0.01$). Of them, subjects who had each retinopathy and neuropathy had significantly lower EI@3P ($p < 0.05$). After adjustment for age, sex, hypertension, smoking, lipid profiles, and disease duration, EI@3P remained significantly associated with the presence of diabetic retinopathy (Odd ratio for Q1 compared with Q4, 5.43; 95% CI, 1.69–17.68).

Conclusion: In patients with T2D, lower EI@3P was related with poor glycemic control, insulin secretary function and presence of diabetic retinopathy. These results suggest that decreased RBC deformability is a useful indicator for predicting diabetic retinopathy.

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IMPACT OF INSULIN PUMP THERAPY ON ERECTILE DYSFUNCTION IN TYPE 2 DIABETES

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Erectile dysfunction (ED) is common in men with T2DM. We investigated the effect of continuous subcutaneous insulin infusion (CSII) in men with T2DM and ED. 20 men were recruited for this pilot study. All patients were put on insulin +/− OHAs and a statin, with CSII in trial arm and multiple daily injections (MDI)/biphasic/basal insulin regimens in control arm. Antihypertensives were used as required. The study was a 6-month, parallel arm, open label, non-randomized, single-blind (outcomes assessor) study. The primary endpoint was change in International Index of Erectile Function (IIEF) score. All subjects also answered Patient Health Questionnaire-9 (PHQ-9) for depression, a global assessment question of whether erections improved, and a neuropathic pain scale for peripheral neuropathy at the end of the study. Other assessments included vibration perception threshold (VPT), HbA1c, free testosterone, lipid profile, & TSH. Baseline measurements were compared using independent sample t-test. Linear regression for final IIEF score corrected for age and baseline IIEF score. All patients had normal testosterone and TSH levels. Age, A1c, PHQ-9 score, and IEEF scores were not statistically significantly different between groups at baseline (CSII: mean age 52.8 years, mean A1c 8.1; Control: 50.8 yrs,7.8 A1c). Patients in CSII arm showed statistically significant improvement in total IEEF score, t(14) = 5.89, p < 0.0001, and in the five subdomains of IEEF. More men in the CSII arm answered 'yes' to the global assessment question at the end of the study (7 vs 3). This is the first study to report improvement of erectile dysfunction with CSII. (NCT01468519)

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RECENT PHARMACOTHERAPEUTIC ADVANCES IN THE TREATMENT OF DIABETIC MACULAR EDEMA

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Diabetic macular edema (DME) is the leading cause of moderate vision loss among working aged individuals in

industrialized nations. Laser photocoagulation of the macula stabilizes visual acuity in many eyes but fewer eyes experience significant improvement. The optimum treatment of DME has recently changed as drugs (pegaptanib, bevacizumab, ranibizumab and aflibercept) that prevent binding of vascular endothelial growth factor (VEGF) to its trans-membrane receptors significantly improve macular edema in most eyes. Not only does VEGF blockade restore the blood-retinal barrier but it also favorably disrupts the underlying pathophysiologic mechanisms and improves the diabetic retinopathy severity score. Patients receive intravitreal injections every 4–8 weeks but this regimen incurs significant direct and indirect costs, challenges patients' compliance, and fills physicians' offices with frequently returning patients. To lessen the impact of these factors on the healthcare system, longer acting drugs and refillable, extended release reservoirs are being developed. Corticosteroid injections for DME have been disappointing, but a biodegradable, sustained release dexamethasone insert and a non-biodegradable, sustained release fluocinolone insert have been approved in the United States and some European countries for the treatment of DME. These devices elute drug for 3–6 (dexamethasone) and 30–36 (fluocinolone) months causing a reduction in macular edema and improvement in visual acuity. Prolonged intraocular corticosteroid therapy causes cataracts and glaucoma so these devices are generally not considered first-line therapy. Combination therapy with anti-VEGF drugs and corticosteroids improves edema more than monotherapy but does not appear to further improve vision.

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OPTICALLY BASED NONINVASIVE GLUCOMETER DEMONSTRATES CLINICAL TREND ACCURACY DURABILITY 24 HOURS AFTER CALIBRATION

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A clinical trial with Grove's noninvasive glucometer demonstrated durable calibration on adults with diabetes.

Methods: 10 adult volunteers (6 males, 4 females, ages 29–72, 2 T1D, 8 T2D, 6 using insulin, 8 Caucasians, 2 non-whites) spent 5 hours in Grove's clinical laboratory on 2 consecutive days. Subjects, all fasting, consumed a standard glucose meal (Glucola®). Noninvasive glucose determinations (earlobe, Grove D Plat Optical Bridge®) were obtained every 10 minutes, and fingerstick glucose values every 20 minutes (Hemocue[TM]). Partial least squares patient calibration models were developed from Day 1 data. Day 2 noninvasive glucose determinations were predictions based on Day 1 calibration. Investigators were blinded to all test results.

Results: 63 of 620 data pairs (DPs) were not analyzed due to laser instability. Blood glucose ranged from 61–363 mg/dl. For entire data set (579 DPs) Day 2, prediction only, MARD was 19.7%, Pearson (r) = 0.593, Clark A = 68.7%, A + B = 96.6%, $p < 8 \times 10^{-44}$. For patients (6) with threshold or better perfusion quality MARD was 13.4%, Pearson (r) = 0.699, Clark A = 80.1%, A + B = 98.9%, $p < 1 \times 10^{-41}$. *Post hoc* analysis revealed that a successful durable calibration model can be constructed with 4 DPs at the fasting, high, and 2 intermediate blood values after a standard glucose challenge.

Conclusions: Grove's noninvasive glucometer is capable of producing trend accuracy results (comparable to all marketed CGMs) 24 hours after calibration. Further studies are being undertaken to lengthen the timespan of calibration durability.

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HIGHER EARLY INSULIN EXPOSURE AND GREATER EARLY GLUCOSE-LOWERING EFFECT WITH FASTER-ACTING INSULIN ASPART IN PATIENTS WITH TYPE 1 DIABETES MELLITUS

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Background: Faster-acting insulin aspart (faster aspart) is insulin aspart (IAsp) in a new formulation containing excipients nicotinamide and arginine, resulting in faster initial absorption after s.c. injection.

Methods: Fifty two patients with T1D (mean ± standard deviation age: 40.3 ± 12.0 years; HbA_{1c}: $7.3 \pm 0.7\%$) received a single dose (0.2 U/kg s.c.) of faster aspart or IAsp under glucose clamp conditions (Biostator; blood glucose target 100 mg/dl; duration 12 hours post-dose) in a crossover design.

Results: Faster aspart had a faster onset of appearance (time from drug administration until first time serum insulin aspart concentrations reached lower limit of quantification; mean difference [95% confidence interval (CI)]: -6.33 minutes $[-7.30; -5.36]$), earlier time to 50% C_{max} (median difference [95% CI]: -11.0 minutes $[-13.5; -9.0]$), earlier t_{max} (median difference [95% CI]: -7.5 minutes $[-17.5; 0.0]$), and greater early exposure up to 1.5 hours post-dose (4.5-fold more insulin aspart in the circulation in the first 15 minutes post-dose) versus IAsp; total exposure was similar (Table). Faster aspart had an earlier and higher glucose-lowering effect (indicated by higher glucose infusion rates, GIR) in the first 1.5 hours post-dose versus IAsp (Table) and an earlier time to 50% GIR_{max} (mean difference [95% CI]: -7.81 minutes $[-13.19; -2.44]$). Maximum GIR and total glucose-lowering effect (Table) were similar between faster aspart and IAsp. No safety/tolerability issues were identified, including no injection site reactions.

Conclusions: Faster onset and higher early exposure with faster aspart led to a greater early glucose-lowering effect, indicating its potential to improve postprandial glucose versus IAsp.

Table: PK and PD results for faster-acting insulin aspart versus insulin aspart.

PK endpoints	Insulin exposure[†] Ratio [95% CI]	PD endpoints	Ratio [95% CI]
$AUC_{0-15\ minutes}$	4.53 [3.62; 5.66]	N/A	N/A
$AUC_{0-30\ minutes}$	2.05 [1.76; 2.38]	$AUC_{GIR, 0-30\ minutes}$	1.48 [1.13; 2.02]
$AUC_{0-1\ hour}$	1.28 [1.15; 1.43]	$AUC_{GIR, 0-1\ hour}$	1.31 [1.18; 1.46]
$AUC_{0-1.5\ hours}$[§]	1.11 [1.01; 1.22]	$AUC_{GIR, 0-1.5\ hours}$	1.17 [1.05; 1.30]
$AUC_{0-2\ hours}$	1.04 [0.95; 1.14]	$AUC_{GIR, 0-2\ hours}$[‡]	1.10 [1.00; 1.22]
$AUC_{0-12\ hours}$	0.96 [0.87; 1.06]	$AUC_{GIR, 0-12\ hours}$	0.98 [0.87; 1.11]
C_{max}	0.98 [0.90; 1.07]	GIR_{max}	1.02 [0.93; 1.12]
Onset of appearance	0.43 [0.36; 0.51]	$t50\%GIR_{max}$[§]	0.83 [0.73; 0.94]
$t50\%C_{max}$[§]	0.65 [0.59; 0.72]	$tGIR_{max}$	0.92 [0.84; 1.01]

[†]Based on free serum insulin aspart; [‡]Primary endpoint; [§]*Post hoc* endpoint; Ratio: faster-acting insulin aspart/insulin aspart; AUC=area under the curve; GIR=glucose infusion rate; PD=pharmacodynamics; PK=pharmacokinetics.
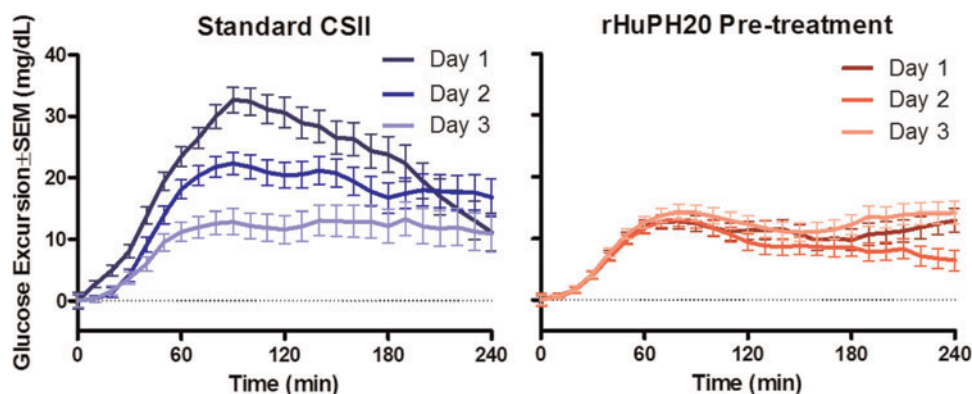
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IMPROVED POSTPRANDIAL GLYCEMIC RESPONSE ACROSS THREE DAYS OF INFUSION SET USE AFTER PRETREATMENT OF INSULIN INFUSION CANNULA SITES WITH RECOMBINANT HUMAN HYALURONIDASE

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Recombinant human hyaluronidase is an FDA-approved adjuvant to increase dispersion and absorption of other injected drugs. Whereas standard continuous subcutaneous insulin infusion (CSII) shows significant acceleration of the time-exposure profile as infusion set wear time increases, pretreatment of the infusion site by injecting 1 mL of commercial *Hylenex* recombinant containing 150 units of enzyme activity through the freshly placed infusion cannula provides a consistent ultrafast insulin profile throughout 3 days of set use. This study evaluated the effect of hyaluronidase pretreatment on the postprandial glucose excursions as determined by continuous glucose monitoring (CGM) compared to standard CSII in 134 subjects with T1DM enrolled in a 6 month ambulatory care study comparing these treatments. CGM postmeal profiles were constructed by merging diary data that contained meal start times. As shown in the figure, postprandial glucose excursions on Day 1 of infusion set use were greatest with standard CSII, with progressive improvement as infusion set wear time increased. In contrast, pretreatment with hyaluronidase provided improved excursions that were unchanged over time. We conclude that preadministration of hyaluronidase at the time of each infusion set change improves postprandial glycemic response to meals during ambulatory care in T1DM subjects using CSII.

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MODELLING ENDOGENOUS INSULIN CONCENTRATION IN TYPE 2 DIABETES WITH OR WITHOUT CLOSED LOOP INSULIN DELIVERY

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Closed-loop insulin delivery is an emerging treatment for type 1 diabetes. Evaluation and testing of insulin dosing algorithms can be accelerated by computer simulations. Efforts to make closed-loop systems available to people with type 2 diabetes (T2D) drive the development of a new type of simulator with a simulation model representing glucose-insulin interactions in T2D at its core, where a model of posthepatic endogenous insulin concentration in T2D is a necessary component. We proposed six competing models to describe the time course of endogenous insulin concentration as a function of the plasma glucose concentration. The models were fitted to clinical data collected in a study involving 11 insulin-naive subjects with T2D. The subjects who underwent two 24-h visits, in a random order, were treated by either closed-loop insulin delivery or glucose-lowering oral agents (control period). Model selection criteria were used to identify the model best describing our clinical data. The model parameters were estimated using a Bayesian approach. The model of choice successfully described endogenous insulin concentration over 24 h in both study periods and provided plausible parameter estimates. Model-derived results were in concordance with the significant clinical finding that revealed increased posthepatic endogenous insulin concentration during the control period ($P < 0.05$). The modelling results further indicated that the excess amount of insulin can be attributed to the glucose-independent effect as the glucose-dependent effect was

Table. Area under the curve (AUC_{ins}) of model-derived endogenous plasma insulin concentration.

|	Closed-loop (n=11)	Control (n=11)	P-value
	AUC_{ins} ($10^3 \cdot min \cdot mU/l$)		
Post-breakfast	6.4 (3.6,7.9)	7.4 (4.9,10.4)	0.006
Post-lunch	7.4 (4.0,10.0)	10.9 (8.2,13.9)	0.026
Post-dinner	6.7 (4.3,10.5)	7.8 (6.9,15.9)	0.048
Fasting	3.1 (2.1,3.8)	4.6 (3.2,7.7)	0.003

Table. Comparison of model derived glucose-dependent, glucose–independent and total AUC_{ins} between visits.

	Closed-loop (n=11)	Control (n=11)	P-value
	AUC_{ins} ($10^3 \cdot min \cdot mU/l$)		
Glucose-dependent	14.8 (12.1,21.0)	15.1 (11.3,19.5)	0.930
Glucose-independent	9.8 (3.7,14.9)	21.3 (8.5,24.5)	0.004
Total	23.5 (15.3,30.0)	35.8 (24.7,49.7)	0.006

Figure. Schematic representation of the six competing models. The models are represented with the (A) glucose-dependent and (B) glucose-independent parameters.
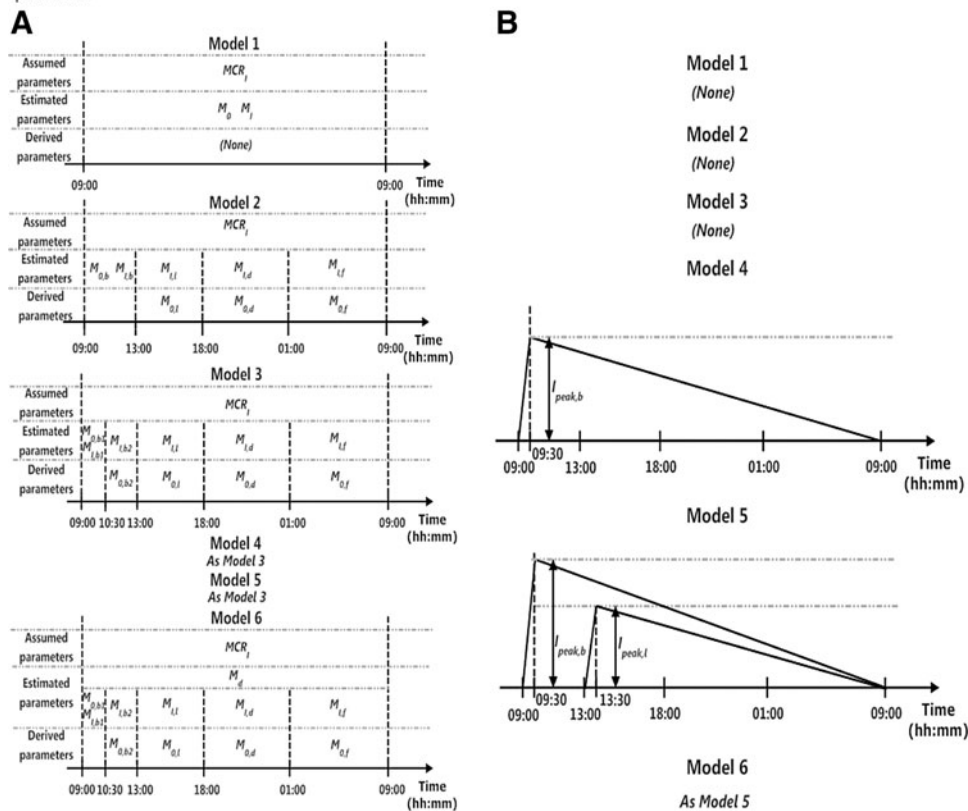
Figure. Sample model fit obtained with subject 7. Model fit (with *Model 5*) to endogenous plasma insulin concentration (upper panel) with plasma glucose excursion (lower panel) during closed-loop (left panel) and control period (right panel); solid line represents model prediction, dashed line 95% intervals, dotted vertical line indicates meal time and dots represent measurements).
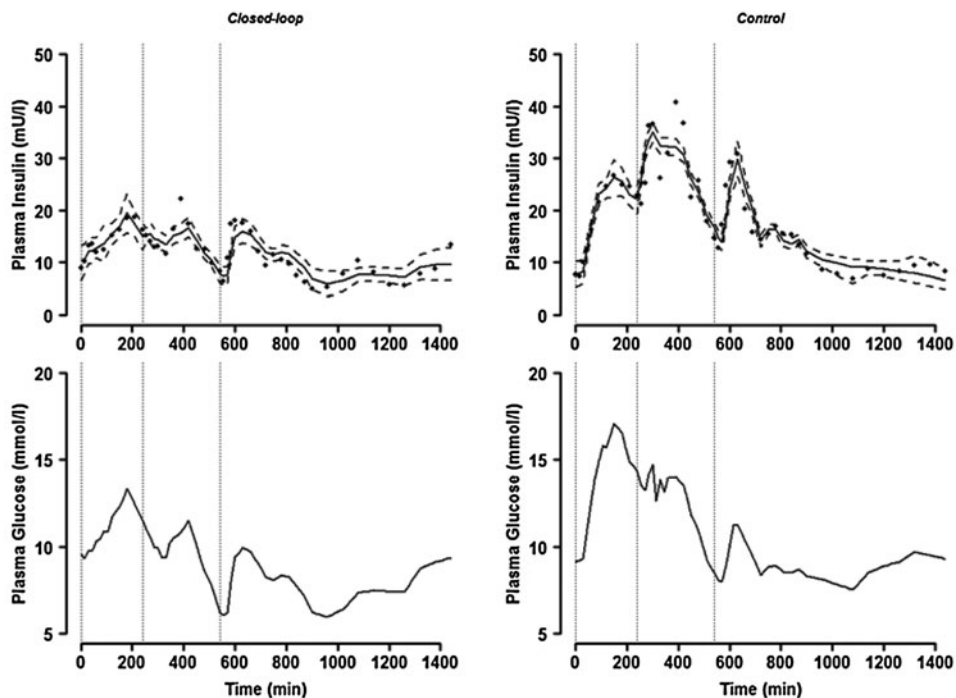
similar between visits ($P > 0.05$). The model shows its applicability in a simulation environment for evaluating closed-loop insulin delivery protocols in T2D.

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REAL-TIME EATING RECOGNITION USING GOOGLE GLASS TO IMPROVE CLOSED-LOOP GLUCOSE CONTROL

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A key gap in closed-loop blood glucose (BG) control is incorporating information on eating. While meals affect BG, current methods either do not use nutrition information or require manual input, precluding a fully automated solution.

Instead, we propose that head-movement data can be used to detect eating and to infer meal start and end times. Automated eating detection can be used as input to a closed-loop controller for BG management and can improve control in both T1 and T2 by reminding individuals to test BG. Our approach uses data continuously collected from sensors in Google Glass, combined with Bayesian online changepoint detection (to detect beginning of a new activity) and a Naïve Bayes classifier (to determine activity type) to find each eating episode. In preliminary studies

with 12 participants, we found eating can be recognized with high ($>80\%$) accuracy with off-the-shelf machine learning methods.

The figure shows results for one subject. The middle scatterplot is inferred likelihood for each class and ground truth (top bar). The bottom figure is likelihood of each time being a changepoint, with red bullets being when a new activity is detected by the algorithm and dashed lines its inferred timing. Both meals are detected shortly after their start. Thus, even with a delay in recognition, we can ultimately recover the actual meal timing and duration.

Ultimately, unobtrusive head mounted accelerometers delivering data wirelessly to a closed-loop system can be used to automatically capture eating information, enabling more precise insulin delivery without patient input.

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CLINICAL EVALUATION OF THE BIO-INSPIRED ARTIFICIAL PANCREAS (BIAP) WITHOUT MEAL ANNOUNCEMENT IN ADULTS WITH TYPE 1 DIABETES

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Objective: To evaluate the safety of the Bio-inspired Artificial Pancreas (BiAP) without meal announcement in adults with type 1 diabetes.

Method: Prospective open-label crossover study with three 24-hour visits to the clinical research facility. At the first visit the BiAP was connected (closed-loop) for 24 hours with three standardized meals (dinner (80 g carbohydrate) at 19:00 h, breakfast (40 g) at 07:00 h and lunch (50 g) at 12:00) announced to the algorithm. At the second visit, participants used standard pump therapy (open-loop). Meal boluses were calculated as per normal practice. The final visit was closed-loop, but the evening meal was not announced, the breakfast was fully announced (100% bolus) and the lunch partially announced (50% bolus). The primary objective was percentage time in target (3.9–10 mmol/l) and secondary outcomes included percentage time in hypoglycaemia (<3.9 mmol) and severe hyperglycaemia (>15 mmol/l).

Results: Eight adults with type 1 diabetes completed the study (62.5% female, mean (SD) age 47(10) years, body mass index 25 (6) kg/m^2, diabetes duration 21(13) years and HbA1c 57(7) mmol/mol. Glycaemic outcome measures for closed-loop with and without meal announcement are outlined in the table.
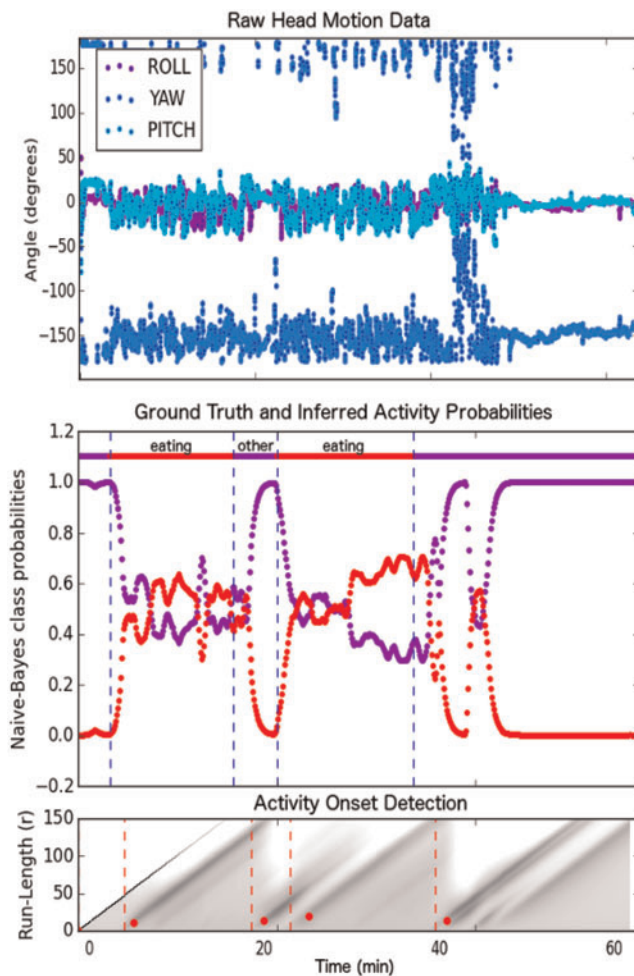
Outcome measure	Closed-loop (n=8)	Closed-loop without meal announcement (n=8)	P-value
Time 18:00 – 18:00 (Total 24 hours)	Sensor glucose Median (IQR)	Sensor glucose Median (IQR)	
% time in target range 3.9-10.0mmol/l	65.7 (53.6 -80.5)	45.5 (38.2 – 68.3)	0.12
% time in hypoglycaemia <3.9mmol/l	5.8 (0.8 – 8.0)	0.4 (0.0 – 1.3)	0.03
% time in hyperglycaemia >15mmol/l	1.4 (0.0 – 6.1)	4.4 (0.0 – 12.0)	0.73
Glucose (mmol/l) Mean (SD)	8.4 (1.3)	9.8 (1.3)	0.06

Mean glucose was non-significantly lower with meal announcement. Time in target range did not statistically differ between closed-loop with and without meal announcement.

Conclusion: We have shown that the BiAP is safe if meal announcement is omitted or if carbohydrate content is underestimated.

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THE ACCURACY AND PRECISION OF CONTOUR PLUS IN CHINESE DIABETES PATIENTS

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Background: The CONTOUR PLUS® (C-PLUS)Blood Glucose Monitoring System was developed and introduced in 2013 following the new ISO standards published in 2013. This prospective clinical research study is to evaluate the accuracy and precision of C-PLUS in Chinese Diabetes patients.

Design: A total of 363 subjects were screened. Subjects included 121 subjects from Peking University People's Hospital (Center 1), 120 subjects from Beijing Hospital of the Ministry of Health (Center 2), and 122 subjects from Fujian Medical University Union Hospital (Center 3).

Result: The calculated accuracy rates of C-PLUS fingertip and venous blood tests were 98.1% (96.06% to 99.22%) and 98.1% (96.02% to 99.21%), respectively. For the Clarkes Error grid analysis (EGA), the C-PLUS fingertip test results demonstrated that 361 (99.7%) subjects fall into CEG Region A, and 1 (0.3%) subject falls into CEG Region B. For C-PLUS venous blood test, 357 (99.4%) subjects fall into CEG Region A, and 2 (0.6%) subjects fall into CEG Region B. For results of Parks EGA, the C-PLUS fingertip and venous blood tests, 360 (99.4%) and 356 (99.2%) subjects, respectively, fall into Region A, and 2 (0.6%) and 3 (0.8%) subjects, respectively, fall into Region B.

Conclusions: The CONTOUR PLUS Blood Glucose Monitoring System provides accurate and precision results for both fingertip blood and venous blood for blood glucose self-monitoring. All results met or exceeded the ISO 15197:2013 criteria, indicating that this system has acceptable accuracy and precision for self-monitoring of blood glucose levels by diabetes patients.

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METAL METALLOPROTEINASES 2 AND 9 ARE DIFFERENTIALLY REGULATED BY THE INTERPLAY BETWEEN INTERLEUKIN-4 AND INSULIN

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Pre-adipocytes are the precursors with the potential to make new fat cells during adipose tissue expansion. Nevertheless, the pre-adipocytes behaviors, and their possible roles in energy homeostasis have long been overlooked. Our previous study implicates that interleukin-4 (IL-4) plays a positive metabolic role by promoting insulin sensitivity and inhibiting lipid accumulation.

Besides, abundant evidence shows the involvement of matrix metalloproteinase-2 (MMP-2) and MMP-9 in the process of adipose tissue expansion. The present study aimed at examining the cross talk between insulin and IL-4 on regulating MMP-2/9 expression and activity in 3T3-L1 pre-adipocytes. Effects of insulin and/or IL-4 on MMP-2/9 expression and activity were examined in pre-adipocytes under euglycemic or hyperglycemic environment by RT-PCR and gelatin zymography, respectively. Our results revealed that glucose level is a pre-requisite for pre-adipocytes taking responses to insulin and/or IL-4 treatment. In high glucose-containing environment, short-term acute insulin treatment (AI) and long-term chronic insulin exposure (CI) showed differential regulation capacity to MMP-2/9 expression and activity. Interestingly, the dominant MMPs regulatory role of CI overriding IL-4 under euglycemic condition were abolished in cells exposed to high glucose concentration. The above results suggest pre-adipocytes may participate in the process of increasing adiposity, diabetic onset and ultimately the diabetic complications through ECM alterations resulted from the changes of MMP-2/9 expression/activity caused by insulin and/or IL-4. The present study uncovers novel observations regarding pre-adipocytes behaviors and suggests their roles in the process of increased adiposity and diabetic complications which have never been examined.

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USING CGM DATA TO TEST THE HYPOTHESIS THAT HIGHER LEVELS OF FEAR OF HYPO- AND HYPERGLYCEMIA ARE RELATED TO LOW AND HIGH BG RISK

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Fear of hypoglycemia (FoHypo) is recognized as a major potential barrier to optimal diabetes control and can increase the risk of poorer glucose control. In contrast, fear of hyperglycemia (FoHyper) can increase risk for hypoglycemia. The purpose of this exploratory study was to test the hypothesis that scores on FoHypo and FoHyper questionnaires would be related in the expected manner to glucose profile variables computed from continuous glucose monitoring (CGM) data. 60 patients (58% female) participated in the study. Mean/SD for age was 40.4 ± 13.6 and for diabetes duration was 23.9 ± 10.8 years (see Table 1). All participants were insulin pump users, and for this study, used CGM devices for one-month (mean CGM readings = 7,586). After CGM data collection, participants completed questionnaires including FoHypo and FoHyper surveys. Table 2 presents correlational analyses showing that higher scores on specific FoHypo subscales were positively related to indices of high BG risk including higher mean BG and BG variability (r's = .29 and .31 respectively, p's < .05). In contrast, higher scores on FoHyper subscales were positively related to indices of low BG risk

Table 1. Participant Demographics

	% (N)
Female	58.3 (35)
Non-Hispanic White	96.6 (57)
	Mean (SD)
Age (years)	40. 4 (13.6)
Diabetes Duration (years)	23.9 (10.8)
HbA1c (%)	7.7 (1.1)
Pump Usage Duration (years)	9.5 (5.7)
Number of BG readings	7,586 (972)

Table 2. Correlations between CGM variables and FoHypo and FoHyper Questionnaire Subscales

	FoHypo Maintain High	FoHypo Avoidance	FoHypo Worry	FoHyper Behavior	FoHyper Worry
HbA1c	.23	-.13	-.02	-.51***	-.15
Sum Low	-.08	.39**	.35*	.39**	.22
Sum High	.26	-.19	-.12	-.51***	-.22
Average BG	.29*	-.17	-.07	-.49***	-.17
LBGI	-.05	.38**	.37**	.31*	.28*
HBGI	.28	-.19	-.01	-.45**	-.16
BGRI	.28*	-.02	.09	-.40**	-.10
ADRR	.31*	.19	.30*	-.30*	.03
** Correlation is significant at the 0.01 level (2-tailed).					
* Correlation is significant at the 0.05 level (2-tailed).					

including hypoglycemia frequency and the low BG risk index (r's = .39 and .31 respectively, p's < .01,) and negatively related to high BG risk variables. This is the first study to investigate the relationship between FoHypo and FoHyper on glucose profiles using CGM data. These preliminary findings support the hypothesis that patient anxiety about hypo- and hyperglycemia may influence diabetes management behaviors and control.

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CORRELATION BETWEEN METHODS OF EVALUATING HYPOGLYCEMIA AWARENESS IN PATIENTS WITH DIABETES

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Background and aims: To evaluate the concordance between two validated methods, Gold score (GS) and Clarke score (CS), used to assess hypoglycemia awareness in patients with diabetes on continuous subcutaneous insulin infusion (CSII) therapy and to analyse the association of these methods with the frequency of hypoglycemia and hypoglycemia symptoms.

Methods: Retrospective evaluation of questionnaires completed by patients at the clinic before the start of CSII and after 2.5 ± 1.1 (1–4) years on CSII. The questionnaires included GS, CS and Edinburg Hypoglycaemia Score (ES), which evaluates hypoglycemia symptoms.

Results: A total of 87 patients, 62% female, age 43 ± 14 (mean ± SD), duration of diabetes 24 ± 13 years, 98% type 1 diabetes, HbA1c 8.7 ± 1.7%, completed the questionnaires. 32% of patients were hypoglycemia unaware (HU) according to GS ≥ 4 and 28% according to CS ≥ 4. A strong association was found between GS and CS at the start of CSII therapy (r = 0.728) and at the end of follow-up (r = 0.820), (both p < 0.005). No significant differences in age or duration of diabetes were found between the HU and the hypoglycemia aware patients. The frequency of mild–moderate hypoglycemia episodes per week and of severe hypoglycemia in the past six months were higher in the HU group, according to both GS and CS (all p < 0.05). The ES for neuroglycopenic symptoms was higher in the HU group according to CS (p < 0.0005), but there were no differences between groups according to GS.

Conclusion: GS and CS show a good correlation in the assessment of hypoglycemia awareness and a good concordance with the frequency of hypoglycemia.

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EVALUATION OF GLYCEMIC CONTROL AND HYPOGLYCEMIC EVENTS IN PATIENTS WITH TYPE 1 DIABETES TREATED WITH BOLUS CALCULATOR. PROSPECTIVE RANDOMIZED CONTROLLED TRIAL. RESULTS AT 4 MONTHS

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Introduction: Bolus calculator (BC) is a device that measures glucose level and, with prior programming, recommends an appropriate quick action insulin dose for DM1 in treatment with multiple daily injections (MDI).

Aim: To show that DM1 patients on MDI therapy, with the help of a BC, can improve glycemic control further than when treated intensively, including carbohydrate counting.

Materials and Methods: Randomized, controlled, two-arms parallel, crossover study. Inclusion criteria: 18–65 years, HbA1c > 7%, basal bolus therapy. For a first phase (4 months) they were assigned either to BC use, or to control group (CT). In the second phase (4 additonal months) all patients were allocated to BC. Variables: age, evolution of diabetes, HbA1c, glycemia, hypoglycemic events, Low Blood Glucose index(LBGI). Surveys on treatment adherence and fear of hypoglycemia (FH-15) questionnaire were administered.

Results: Baseline characteristics (age, evolution of DM, HbA1c) were the same for both groups. First phase: 70 patients, BC 42 (60%), CT 28 (40%).

HbA1c significantly decreased in both groups at 4 months, although there were no differences between both groups. Hypoglycemic events, LBGI and FH-15 were analyzed (Table 1 and 2).

Adherence assessment: 94.6% considered easy the management of BC, 94.6% used it routinely and 91.9% considered it useful in the management of the DM.

Conclusions: Using BC produces an improvement in the glycemic control similar to the obtained with an intensive

Table 1: First phase: HbA1C, descrease in HbA1c, glycemia (total, pre and postprandial).

	HbA1c (%)		Decrease in HbA1c (%)	Overall glycemia (mg/dL)		Preprandial glycemia (mg/dL)		Postprandial glycemia (mg/dL)	
	basal	4m	basal-4m	basal	4m	basal	4m	basal	4m
BC (n=42)	8,37* (SD 0,88)	7,7* (SD 0,59)	-0,66 (SD 0,76)	165,98 (SD 27,42)	166,43 (SD 34,96)	161,66 (SD 27,39)	163,63 (SD 31,14)	176,14 (SD 37,35)	172,5 (SD 47,45)
CT (n=28)	8,28$^\&$ (SD 0,83)	7,94$^\&$ (SD 0,87)	-0,39 (SD 0,65)	169,22 (SD 30,86)	175,95 (SD 37,12)	162,51$^\Omega$ (SD 35,18)	173,98$^\Omega$ (SD 36,68)	176,22 (SD 28,46)	176,65 (SD 40,17)

*, $^\&$, $^\Omega$ p<0,05.

Table 2: First phase: Hypoglycemia , LBGI and FH-15.

	Number of hypoglycemic events (<70 mg/dL/2 weeks)		LBGI			Severe hypoglycemia	Fear of hypoglycemia scores (FH-15)	
	basal	4m		basal	4m	basal-4m	basal	4m
BC (n=42)	8,14* (SD 4,8)	6,57* (SD 4,3)	Minimum Low	18 (43%)	26 (62%)	3 (7,1%)	28,31 (SD 7,98)	27,02 (SD 8,9)
			Moderate High	24 (57%)	16 (38%)			
CT (n=28)	6,86 (SD 4,56)	6 (SD 4,35)	Minimum Low	19 (68%)	22 (78,6%)	1 (3,6%)	27,54 (SD 7,47)	27,61 (SD 10,15)
			Moderate High	9 (32%)	6 (21,4%)			

* P≤ 0,05

treatment without BC. Unlike other intensive treatments, it is associated with a significantly decrease of hypoglycemia. There was a good acceptance of the BC.

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EFFECT OF SOY FLOUR ENRICHED BREAD ON INFLAMMATORY MARKERS AMONG TYPE 2 DIABETIC WOMEN: A CROSS-OVER RANDOMISED CONTROLED CLINICAL TRIAL

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Background: To determine the effects of soy bean flour enriched bread on inflammatory markers, achieved by substituting some soy bean flour for wheat flour in bread.

Methods: This randomized, cross-over, controlled clinical trial was carried out in 30 type 2 diabetic women. After a 2-week run-in period, participants were randomly assigned to either intervention or control groups, each one for 6 weeks. Participants in the intervention group were asked to replacing 120 grams of soy bean flour enriched bread with the same amount of their usual bread intake or other cereal products. After a 4 week washout period, Participants were crossed over for another 6 weeks. This study was approved by Ethical Committee of Isfahan University of Medical Sciences, Isfahan, Iran.

Results: Mean (±SD) age, weight, BMI and waist circumference of study participants was 45.7±3.8 years, 73.8 ± 10.7 kg, 29.5±3.9 kg/m^2, and 87.4±6.7 cm, respectively. No significant effect of soy bean flour enriched bread intake on weight, waist circumference, hip circumference and body mass index (BMI) was seen compared with the control group. We found a slight, but not significant, reduction in hs-CRP (change difference: −0.04, P=0.6), TNF-α (change difference: −14.2, P=0.27) and IL-6 (change difference: −0.06, P=0.15) among women in the intervention group compared with the control group. No significant effects of soy bean flour enriched bread on serum levels of sVCAM1 were seen.

Conclusions: Daily consumption of soy bean flour enriched bread for 6 weeks dose not substantially affect markers of inflammation in type 2 diabetic women.

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TYPE-2 DIABETES PATIENTS ON METFORMIN AND WELL-CONTROLLED BASAL INSULIN WITH PERSISTENT UNCONTROLLED HBA1C: CAN SUPPLEMENTARY VILDAGLIPTIN CONTROL RESIDUAL PRANDIAL HYPERGLYCAEMIA? PRELIMINARY VIBE STUDY RESULTS

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In patients with type-2 diabetes (DT2) unresponsive to oral anti-diabetics (OAD) treated with metformin and well-titrated basal insulin, but whose diabetes remains poorly controlled, high HbA1c levels are associated principally with uncontrolled postprandial glycaemia (PPG). Can supplementary vildagliptin reduce HbA1c to target levels (<7.0%) vs. placebo?

In the study, 34 DT2 patients receiving metformin at the maximum tolerated dose together with well-titrated insulin glargine (fasting blood glucose: <1.20 g/l), but with HbA1c persistently between 7 and 9%, were randomised to double-blind cross-over treatment with either vildagliptin (50 mg b.i.d.) or

placebo, with the 3-month treatment periods being separated by a 3-month wash-out period. Immediately prior to the end of these two periods, patients wore a continuous glucose monitoring device for 5 days.

34 patients were randomised. Baseline data were as follows: HbA1c: $7.65 \pm 0.9\%$; length of diabetes: 18 ± 7.6 years; age: 62.38 ± 7.09 years; BMI: 28.28 ± 4.17; insulin glargine dose: 31.50 ± 21.59 u/d; metformin (glucophage) dose: 2.72 ± 0.56 g/d. HbA1c fell to below 7% in 5 times more patients on vildagliptin vs. placebo, and glycaemic excursions as assessed by AUC were lower for vildagliptin vs. placebo. Predictors for patient response to treatment were also studied.

Treatment with vildagliptin resulted in improved glycaemic control resulting in HbA1c reduction to $< 7\%$ in a greater number of patients on well-titrated metformin + glargine. This improved response involved better control of post-prandial glycaemia, as attested by the glucose monitoring data.

This study received an unrestricted grant from Novartis.

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OSTEOCALCIN ABLATES TNF-ALPHA-INDUCED INHIBITION OF SLC2A4 EXPRESSION IN ADIPOCYTES

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The role of osteocalcin, a protein synthesized by osteoblasts, is beyond the maintenance of bone homeostasis. Recent studies has demonstrated that uncarboxylated osteocalcin (uOCN) acts as an hormone, with positive effects on insulin secretion, insulin sensitivity and fat metabolism. However, very little is known about the molecular mechanisms behind the fascinating discovery of the skeleton as an endocrine organ. Considering that obese and diabetic subjects has reduced circulating uOCN levels and that obesity and diabetes is an inflammatory and insulin resistant state, with reduced insulin-responsive glucose transporter (GLUT4), the aim of the present study is to investigate if uOCN modulates GLUT4 expression in 3T3-L1 adipocytes. For this, adipocytes were incubated with or without TNF-alpha alone for 22 hours or pretreated with uOCN for 6 hours and then treated with TNF-alpha for 16 hours. The expression of *Slc2a4* gene which encodes GLUT4 protein was analyzed by Real Time PCR. Our data shows that chronic TNF-alpha treatment completely inhibited *Slc2a4* expression in 3T3-L1 cells. Interestingly, uOCN pretreatment was able to not only ablateTNF-alpha-induced inhibition of *Slc2a4* but also greatly enhance *Slc2a4* expression in comparison to non-treated cells (5.5-fold vs control). In conclusion, uOCN acts as an hormone increasing *Slc2a4* expression in adipocytes. Although more investigation has to be addressed, our data suggests that uOCN could be an excellent candidate for the treatment of inflammatory and insulin resistant states, such as obesity and diabetes.

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LACTATE IN TYPE 1 DIABETES AS A MARKER OF ETHNIC METABOLISM

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Lactate is both fast and significant prognostic indicator of hypoxia in various diseases, and is using as marker of diabetes severity.

The study included 17 Caucasian race girls with diabetes mellitus type 1 (T1DM) (mean age $- 14.5 \pm 0.3$ years, duration of T1DM was - 5.4 ± 1.0 years) and 11 Mongoloid race girls with T1DM (mean age - 14.1 ± 0.9 years, duration of T1DM - 6.8 ± 1.7 years). Control groups were 19 Caucasian (mean age $- 14.5 \pm 0.2$ years) and 15 Mongoloid girls (mean age - 14.8 ± 0.5 years). The T1DM diagnosis was confirmed by clinical and laboratory studies, the average level of glycated hemoglobin in Caucasians were - $9.58 \pm 2.22\%$, in Mongoloids - $8.65 \pm 1.39\%$. All patients received insulin. Lactate was determined with enzymatic colorimetric Lactat set (LOX-PAP, Biocon, Germany). Pyruvate was evaluated by Pyruvate kit (''Roche Diagnostics'', Germany).

In Caucasians girls with T1DM increased lactate level (2.26 times higher; $p < 0.0001$) and attitudes lactate/pyruvate (2.23 fold, $p < 0.0001$) compared to the control group has been found. Mongoloid girls with T1DM characterized by decreased pyruvate level (1.27 times ($p = 0.0117$), but increased lactate level (1.22 times; $p = 0.0038$), and lactate/pyruvate ratio (1.54 times higher; $p = 0.0008$) compared to control. A comparison of these parameters between ethnic groups showed higher values of lactate (1.37 times higher, $p = 0.0032$), lower values of pyruvate (1.29 times lower, $p = 0.0245$) and increased lactate/pyruvate ratio (1.89 times higer, $p = 0.0026$) in Caucasians patients.

Consequently, Caucasians girls with T1DM demonstrated more intensive development of hypoxia, which should be considered in the treatment of this disease.

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CONTROLLING DIABETES MELLITUS TYPE 2 WITH HERBAL MEDICINES: A TRIPLE BLIND, RANDOMIZED CLINICAL TRIAL OF EFFICACY AND SAFETY

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Background: Alternative medicine is common in patients with diabetes mellitus. The primary objective of the study was to determine the effects of cinnamon and whortleberry on blood glucose control and lipid profile in type 2 diabetes (T2DM) patients.

Methods: In this randomized, triple–blinded clinical trial 105 patients with type 2 diabetes were recruited and randomly divided into 3 groups: placebo, cinnamon and whortleberry supplementations (1 g daily for 90 days). Some biochemical indexes including, fasting blood glucose, serum insulin, lipid profiles and HbA1c were measured before and after the study as Primary outcome.

Result: There was no significant difference in baseline characteristics between three groups. Fasting blood glucose, two hour blood glucose and Homeostasis Model assessment (HOMA) score were significantly reduced in patients in whortleberry group, whereas they were not changed in placebo group. There was a significant difference between cinnamon and control groups in body mass index (P = 0.02). In cinnamon and whortleberry groups there was no significant difference in any variables (P > 0.05). Although all glucose control indexes decreased after intervention (P < 0.05).

Conclusion: There was no significant difference in blood glucose level, insulin sensitivity and lipid profile between 3 groups. However, using cinnamon and whortleberry is recommended for adjusting weight and blood glucose respecting along with medical treatment.

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SITE-SPECIFIC OPTOGENETIC PROTECTION OF BETA CELLS

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Most forms of diabetes are associated with a deficiency in functional pancreatic beta cell mass. As a consequence, there is an increasing interest in identifying molecules and means to support beta cell survival and to increase beta cell proliferation. Growth factors, such as hepatocyte growth factor, fibroblast growth factor 21 or betacellulin, their cognate receptors and associated signaling pathways play a crucial role in the regulation of beta cell survival, function and growth. While many growth factors that are efficacious for the protection and proliferation of beta cells, such as hepatocyte growth factor, these molecules exhibit limited half-life in the circulation and may lead to proliferation of non-beta cells and thus an increased risk of cancer. We have developed growth factor receptors (GFRs) that are activated by light and that offer the ability of cell type-specific or site specific control of cell signaling. Optical control of GFRs was achieved by supplementing mammalian GFRs with light-sensing protein domains from phototropic organisms. These optogenetic growth factor receptors (Opto-GFRs) allow substituting ligand induced signaling activation by light induced signaling activation. We are applying this advanced technology for site-specific and controlled manipulation of beta cell protection and proliferation. In first experiments, we demonstrate the activation of major pro-survival signaling pathways, as MAPK pathway and PI3K/Akt pathway, by light.

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EXENATIDE VERSUS INSULIN GLARGINE IN TYPE 2 DIABETES INADEQUATELY TREATED WITH METFORMIN

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Introduction: Addition of basal insulin or GLP-1 agonist to pre-existing treatment when glycemic control is not achieved

with metformin monotherapy are options addressing either fasting or prandial glucose regulation.

Aim: Compare efficacy and safety of exenatide (E) versus insulin Glargine (G) added after metformin monotherapy.

Patients and Method: Our study was open labeled, non-randomized, retrospective and included 48 patients, 17 men/ 31 women, mean age 61.98 ± 8.8 years, mean duration of DM 11.8 ± 7.25 years, and mean HbA1c 8.34 ± 1.63 at baseline. All patients were on metformin (1700 mg/day) for at least 3 months when E or G was added. Body mass index (BMI), systolic (SBP) and diastolic (DBP) pressure, frequency and severity of hypoglycemic episodes, gastrointestinal side effects, HbA1c and lipid profile were determined at baseline and after 24 weeks.

Results: HbA1c reduction was similar in both groups (E: p = 0.006 vs G: p = 0,010). G group had more hypoglycemias (p = 0.039). E group had greater BMI reduction than G (-2.5 ± 1.8 vs $0.1 \pm 1.4 \, \text{kg/m}^2$; p = 0.002). GI side effects and changes in SBP/DBP were insignificant in both groups. Total cholesterol was reduced (E: p = 0.010 vs G: p = 0.014). E group had higher HDL p = 0.021, lower LDL (p = 0.012) and triglycerides (p = 0.016) at the end of the study.

Conclusion: Exenatide equals Glargine in glycemic control with fewer hypoglycemias and better metabolic parameters. In order to form selection criteria between the two strategies further testing is needed with randomized studies, longer observation period and greater numbers of patients.

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HIRTAFLAVONOSIDE A, A NOVEL COMPETITIVE DPP IV INHIBITOR FROM EUPHORBIA HIRTA L.

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Objective: DPP IV inhibitors are expected to become useful antidiabetic agents. The aim of this study is to characterize the *in vitro* and *in vivo* profile of hirtaflavonoside A (HFA), a prenylated flavonoid isolated from the *Euphorbia hirta* L., for its potential DPP IV inhibitory activity.

Methods: Enzyme inhibition assay of HFA was performed *in vitro*, using rat plasma as DPP IV enzyme source and H-Gly-Pro-*para*-Nitroanilide as chromogenic substrate. Further, a 4 week study was performed on high fat diet + streptozotocin (HFD + STZ) induced diabetic rats.

Results: HFA inhibited DPP IV enzyme in a concentration dependent, competitive manner (IC_{50} - 59.97 nM), which was comparable to sitagliptin (IC_{50} - 11.42 nM). HFA prevented onset of overt diabetes by dose-dependently reducing fasting glucose and HbA_{1C} levels, and increasing liver glycogen contents of HFD + STZ diabetic rats. Furthermore, plasma insulin levels were augmented with HFA treatment which led to improved insulin resistance (HOMA-IR) and β-cell functioning (HOMA-β). Glucagon-like peptide-1 were increased and plasma DPP IV levels were decreased to that of normal rats with HFA treatments. Additionally, HFA treatments were diminished the progressive deterioration of lipid profile such as TC, TG's, LDL and VLDL in HFD-STZ diabetic rats. Ultimately, HFA significantly reduced glucose excursion during the oral glucose tolerance test at the end of 4 week treatments.

Conclusion: Present study indicated that HFA is a novel DPP IV inhibitor. The results also suggested the effectiveness of HFA

Hirtaflavonoside A
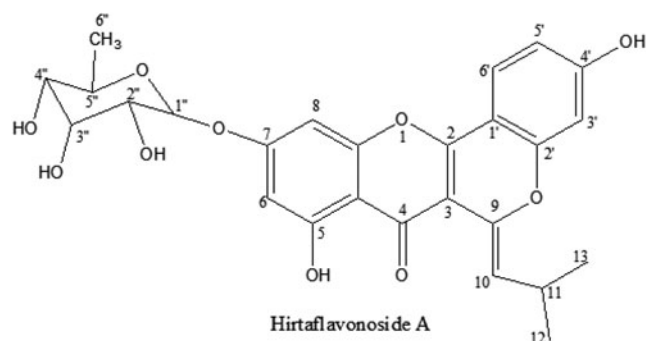
for its further development as a therapeutic agent in type 2 for type 2 diabetes.

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ANALYSIS OF THE EFFICACY, SAFETY AND COST- EFFECTIVENESS OF DULOXETINE AND TRAZODONE TO TREAT NEUROPATHIC DIABETIC PAIN

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Objective: The aim of this study is to analyse the scientific evidence on the use of duloxetine and trazodone in the treatment of diabetic neuropathic pain, and present the comparative costs of existing alternatives in the brazilian public health system.

Methodology: We researched and selected publications with the highest level of evidence in The Cochrane Library, Medline (via PubMed), LILACS and Centre for Reviews and Dissemination (CRD). Likewise, sought for health technology evaluations in foreign agencies websites and evaluated the evidence quality and strength of the recommendation according to the Grade system.

To evaluate the data of the comparative costs, we used the list prices regulated by the Brazilian government (Table 1).

Results: In accordance with the flowchart of Figure 1, the revisions include showed results in favor of duloxetine; but in most cases, the drug is compared to placebo. Direct comparison with other drugs have not been conclusive. International agencies indicate duloxetine, amitriptyline, gabapentin and pregabalin for neuropathic pain. The publication that evaluated the efficacy and safety of trazodone showed results in favor of this drug, but this was just a cases series. Studies of cost-effectiveness of duloxetine have been the only ones found, which, although good results, was not the most cost-effective option.

Conclusions: There is a lack of scientific evidence to support the nationwide use of duloxetine and trazodone to replace tricyclic antidepressants and gabapentin, indicated by the public health system in Brazil.

Figure 1 - Diagram showing the flow of search and selection of studies
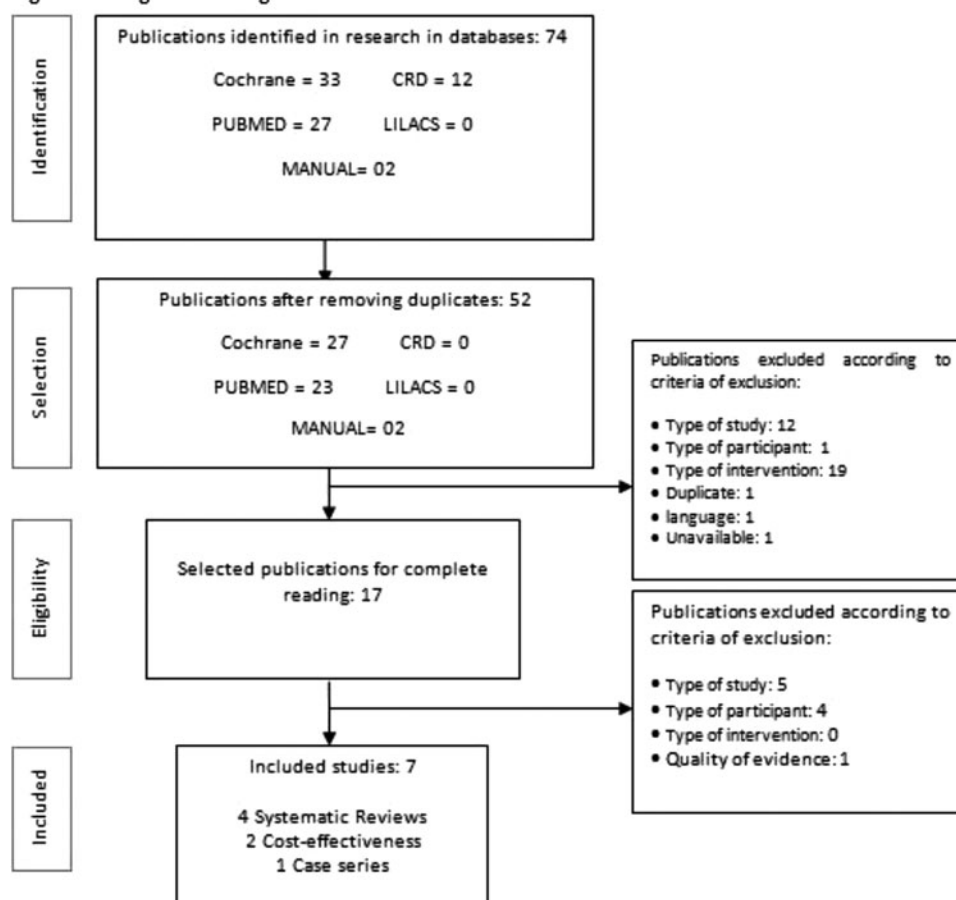
Table 1 - Cost comparison of therapeutic alternatives

Therapeutic Group	Drug name	Presentation	Brand_name*	Laboratory Manufacturer	Daily dose (Bull)	Price unit (R$)	Daily dose cost (R$)**	Monthly cost*** (R$)
Antidepressants	Duloxetine	Cap. 60 mg	CYMBALTA®	ELI LILLY	60	7,14	7,14	214,28
		Cap. 60 mg	DULOXETINE HYDROCHLORIDE	LIBBS	60	4,64	4,64	139,28
Antidepressants	Trazodone	Cap. 100 mg	DONAREN®1	APSEN	900	1,31	11,79	353,70
		Cap. 50mg	DONAREN®1	APSEN	900	0,66	11,79	353,70
Antidepressants	Amitriptyline[2]	Cap. 25 mg	TRYPTANOL®	MERCK SHARP & DOHME	75	0,59	1,78	17,81
		Cap. 25 mg	AMITRIPTYLINE	TEUTO	75	0,23	0,69	6,88
Antiepileptic	Gabapentin[2]	Cap. 300mg	NEURONTIN®	PFIZER	1800	2,44	14,65	73,25
		Cap. 300mg	GABAPENTIN	RANBAXY	1800	1,18	7,05	35,27

R$: Real; Cap: capsule. * The reference drug;** daily cost of treatment; *** Estimated cost for 30 days of treatment; [1] Drug without generic presentation, [2] Drugs incorporated in the list of the Brazilian health system. Source: BRASIL, 2014

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INCORPORATION OF INTRA-DAY VARIABILITY INTO THE UVA/PADOVA TYPE 1 DIABETES SIMULATOR

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The UVA/Padova Type 1 diabetes (T1DM) simulator has accelerated the development of closed-loop control algorithms for artificial pancreas. However, since its domain of validity was limited to a single-meal scenario, the simulator cannot be used to test algorithm robustness for long term trials, e.g. providing a test bed for adaptive algorithms.
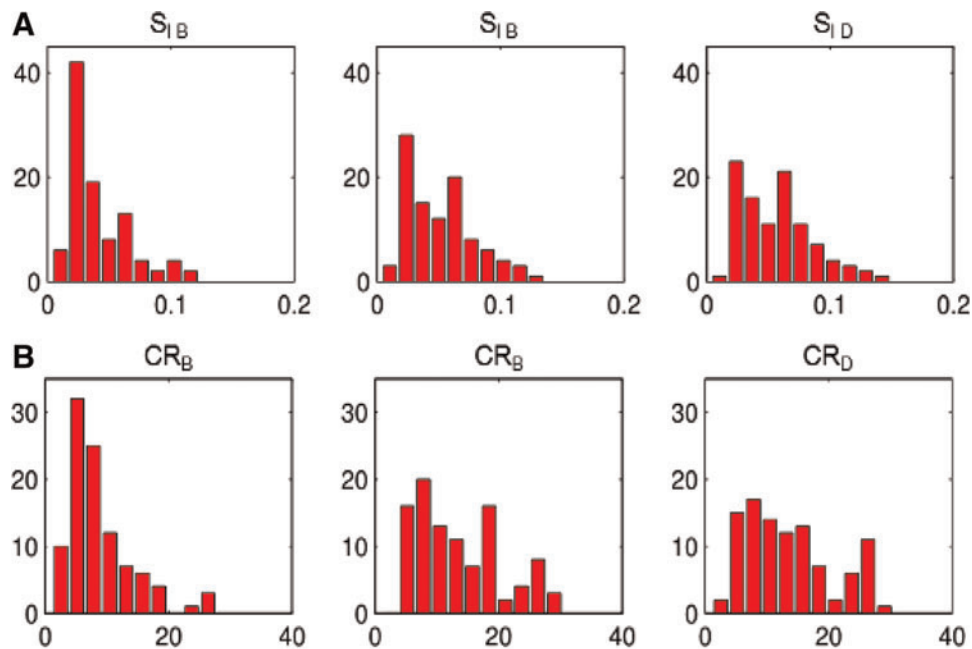

Figure 1. A: distributions of S_I at Breakfast (*left*), Lunch (*middle*), and Dinner (*right*). B: distributions of CR at Breakfast (*left*), Lunch (*middle*), and Dinner (*right*).

Here, we present an update of the T1DM simulator which incorporates intra-day variability of key parameters, i.e. insulin sensitivity (S_I) and carbohydrate-to-insulin ratio (CR), thus making it suitable to perform longer realistic *in-silico* trials.

A recent study in T1DM (Hinshaw et al., Diabetes 2013) revealed the existence of diurnal patterns of S_I, with, on average, S_I lower at breakfast (B) than lunch (L) and dinner. Thanks to this information, a model of intra-day variability of S_I has been incorporated into the simulator. In particular, each *in-silico* subject is associated to a certain S_I variability pattern. Then, time-varying S_I profile is generated by randomly modulating the nominal pattern. Consequently, three CR values (for B, L and D, respectively) have been calculated for each *in-silico* subject. Finally, also the total daily insulin (TDI) and the correction factor (CF) have been recalculated, to account for intra-day variability.

The distributions of *in-silico* S_I reflect those observed in T1DM subjects. The values of CR distribute among B, L, and D consistently with the S_I variations.

The use of the new T1DM simulator will enhance closed-loop control design, e.g. testing self-adaptive control algorithms which aim at day-to-day optimal tuning of subject-specific parameters.

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PHARMACOKINETICS MODELING OF GLUCAGON AND A NOVEL GLUCAGON ANALOGUE AFTER SUBCUTANEOUS ADMINISTRATION IN DOGS

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Objective: Currently available hypoglycemic glucagon rescue kits are difficult to handle and need reconstitution of glucagon immediately before use due to the instability in solution. A novel Zealand Pharma invented glucagon analogue (ZP-GA-1) with increased stability in liquid formulation has potential for application in a ready-to-use rescue pen. Pharmacokinetic (PK) characteristics similar to native glucagon and fast on-set of action are critical for success.

Research Design and Methods: SC bolus injections of 20 nmol/kg and 120 nmol/kg native glucagon or ZP-GA-1 were administered to five dogs at four dosing occasions. The Institutional Animal Care and Use Committee approved the study and all procedures carried out on the dogs were in accordance with the Animals (Scientific Procedures) Act 1986. Data was fitted to a one-compartment PK model with extravascular input using a weighted least-squares method with the measurements inverse as the weights. T_{max}, a surrogate marker of on-set of action, and C_{max} was obtained from the fit.

Results: Based on visual inspection of log-lin plots the model fitted data satisfactory. ANOVAs of model parameters and T_{max} showed no differences between dose level and compound (p-values = N.S.). However, C_{max} was different between both dose levels and compounds (p-values < 0.05). Furthermore, a significant interaction was found between dose level and compound (p-value < 0.05).

Conclusions: The novel glucagon analogue showed many similar PK characteristics (absorption, elimination, volume of distribution, time to maximum concentration) to native glucagon. However, ZP-GA-1 has lower maximum concentration than native glucagon after same level of dose administration.

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STATUS OF CHILDREN BORN IN TIME DEPENDING ON THE MODE OF INTRODUCTION OF INSULIN MOTHER

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Aims: to assess the condition of infants born in the period in patients with type 1 diabetes, according to the method of insulin in the mother.

Materials and methods: in 48 children evaluated birth weight, Apgar score, need for resuscitation in children, the incidence of hypoglycemia in infants born at 38–40 weeks of the term of the mothers of patients with type 1 diabetes. Depending on the method of insulin administration in the mother have been allocated to two groups: with multiple subcutaneous insulin injections (MSII) (28 children) and with constant subcutaneous insulin infusion (CSII) (20 infants). By mother's age, duration of diabetes, the degree of compensation and the stage of diabetic nephropathy groups were comparable (p > 0.05).

Results: In the group of MSII birth weight was 3610.0 (3212.0; 3942.5) grams, which was significantly higher than in the group with CSII - 3160.0 (2980.0; 3607.5) grams (p = 0.01). Apgar score: 7.5 (7.5; 8.0) points in the group at MSII and 7.8 (7.5; 8.5) points in the CSII group (p = 0.4) The need for neonatal resuscitation in a group at MSII met in 18% of cases. In the CSII group at resuscitation did not need. Hypoglycemia in children born to mothers who used MSII - 65.4%, in the grupp with CSII 23.2% (p = 0.04).

Conclusions: Status of children born in the period in patients with type 1 diabetes, the use of GSII versus MSII is improved: less common manifestations of diabetic fetopathy as macrosomia, hypoglycemia at birth, there is no need for resuscitation.

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ECONOMIC EVALUATION OF CONTINUOUS SUBCUTANEOUS INSULIN INFUSION VERSUS CONVENTIONAL THERAPY IN PATIENTS WITH T1DM

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Treatment of T1DM with continuous subcutaneous insulin infusion (CSII) is the most physiological, but it presents economic constraints. Our study evaluates its economic impact to the Spanish public health system.

Patients: 64 T1DM (42 females and 22 males) with an average age of 35.9 ± 10.5 years and a duration of diabetes of 18.5 ± 9.3 years were studied. Recent data were compared with those prior to the CSII. Material and insulin consumption, excluding correction doses, and amount of wasted insulin used by both devices were analysed.

Results: Previous monthly consumption was of 2.8 and 2 pens of basal and rapid insulin respectively, which has a cost of € 61.03. Instead, CSII consumes 1636 IU (€ 35.1). The cost of needles with conventional treatment was € 20 every month,

versus € 192.1 of material for CSII. Thus, CSII implies an average cost increase of € 146.17 per month.

We found no difference in overall glycaemic control (HbA1c 7.68 ± 1.44 pre, 7.59 ± 1.16 post), though it was significant in the subgroup of patients with prior poor control (8.34 ± 1.34 pre, 7.91 ± 1.16 post, p = 0.015).

Conclusions: CSII represents an increase in cost, not offset by an improved metabolic control in our study population. However, several studies have shown it involves less hypoglycaemic events and a better quality of life. More research should be done to evaluate the profitability of CSII regarding altogether metabolic control, reduction of hypoglycaemic events and influence in patients' satisfaction.

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SELF-MONITORING OF BLOOD GLUCOSE AT LEAST SIX TIMES DAILY IS CRUCIAL FOR ACHIEVIENG OPTIMAL GLUCOSE CONTROL DURING PUMP THERAPY

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Due to economical reasons sensor-augmented pumps are not in common use among Polish patients. Subsequently, the subjects on continuous subcutaneous insulin infusion (CSII) therapy are strongly advised to measure blood glucose (self-monitoring of blood glucose, SMBG) at least four times a day. However, the minimal frequency of SMBG required for having optimal glucose control remains unknown. For type 1 subjects Diabetes Poland recommends HbA1c < 6.5% ie. average blood glucose (BG) < 140 mg/dl [7.8 mmol/l]. We conducted a study aiming at identifying minimal frequency of SMBG which would allow type 1 diabetes patients achieving good metabolic control. All subjects were treated with CSII at least for 6 months, thus they had obtained sufficient knowledge about this kind of therapy. The pump settings (basal rate, bolus wizard) were assessed with standard tests. The group comprised 40 type 1 diabetes patients (mean age 27 ± 8 years, diabetes duration 9 ± 8 years, CSII duration 3.1 ± 2.5 years, body weight 70 ± 12 kg, BMI 24.2 ± 3.7 kg/m2, HbA1c 7.7 ± 1.9%, average BG 155 ± 56 mg/dl, number of SMBG 5.7 ± 3.7/day). Data from 2 last weeks before the study visit were analysed. A negative correlation between the frequency of SMBG and the average number of capillary BG measurements (figure) was revealed (r = −0.37; p < 0.05); the recommended target of metabolic control was obtained in sub-

jects who had performed SMBG at least six times a day. In conclusion, CSII therapy may lead to good metabolic control, but the acceptance and willingness of a patient to measure blood glucose more than six times a day is crucial.
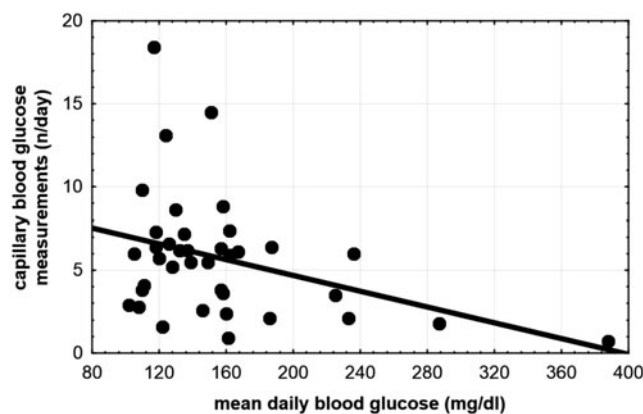
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THE EARLIER THE BETTER: EFFECTIVENESS AND DURABILITY OF INSULIN PUMPS IN CHILDREN AND ADOLESCENTS SOON AFTER DIABETES ONSET

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Aim: to evaluate the predictors of effectiveness and durability of insulin pump therapy in children and adolescents who have initiated this therapy within 2 years after the diagnosis of type 1 diabetes mellitus (T1DM).

Subjects and Methods: the charts of 684 individuals with T1DM using insulin pumps were reviewed, and were included in the study 113 subjects with age at onset of 1 year. The primary end point was the mean glycosylated hemoglobin (HbA1c) value (MHbA1c) throughout the follow-up.

Results: A significant reduction of HbA1c from baseline throughout the 8-years follow-up was observed ($p^2 = 0.089$). Categorizing the sample into four quartiles on the basis of an increasing interval onset—commencement resulted in levels of MHbA1c significantly lower in the 1st and 2nd quartiles in comparison with the 4th quartile (7.6 ± 0.8% and 7.8 ± 1.0%, respectively, versus 8.5 ± 0.8%; p < 0.001 and p = 0.004, respectively). Moreover, only 1st and 2nd quartiles mantained a trend toward reduction of HbA1c from baseline until the 4th year of follow-up, with a less variability of HbA1c.

Conclusions: The present study suggests that early pump commencement (< 6 months from the onset of diabetes) in children and adolescents with T1DM provides lower and more durable HbA1c values than a late commencement, maybe through a prolongation of the honeymoon phase.

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PRECISION, ACCURACY AND DELIVERY SPEED OF DURABLE AND PATCH INSULIN INFUSION PUMPS

J. Capurro[1], R. Venugopalan[1], B. Levy[2]

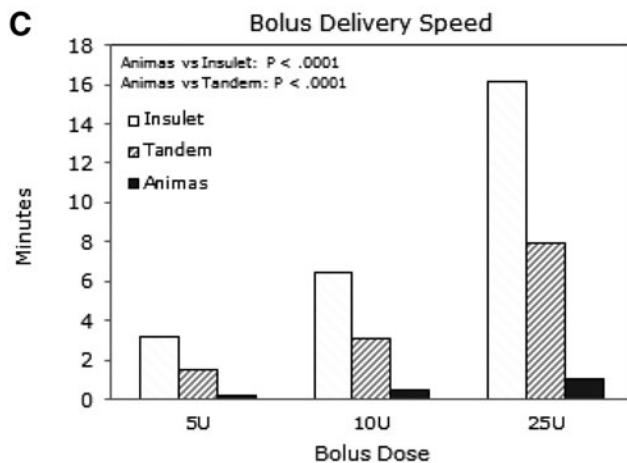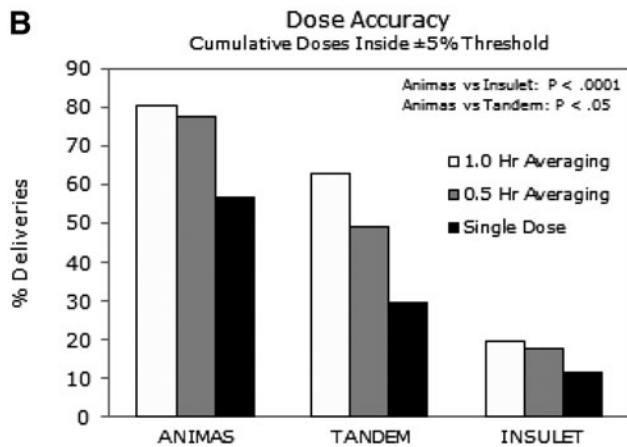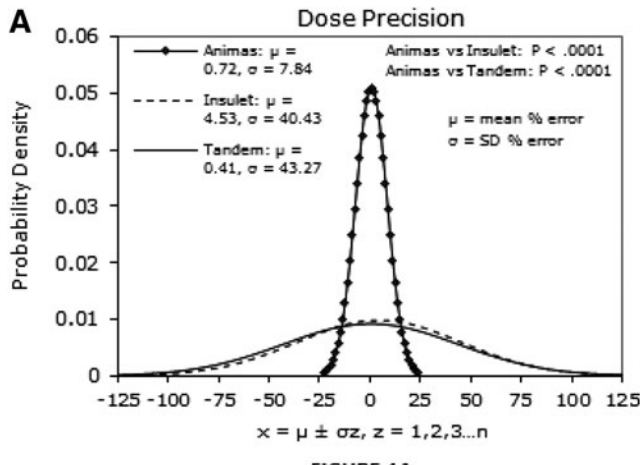*[1]Research & Development, Animas Corporation, Wayne, USA*
[2]Clinical Affairs, Animas Corporation, Wayne, USA

Background: Precision, accuracy and delivery speed of pump insulin infusion may affect PK duration and resulting glycemic control.

Method: For each pump model (Animas OneTouch® Ping®, Tandem® t:slim®, Insulet OmniPod® 2nd Gen), basal (0.5 U/hr over 20 hours) and bolus (5 U, 10 U, 25 U) discrete deliveries were measured using a time-stamped micro-gravimetric system. Dose precision was assessed using the mean percent error and standard deviation percent error of the cumulative deliveries. Dose accuracy was analyzed by comparing single doses and time-averaged doses to percent error thresholds. Bolus speed was determined as the time taken to deliver 95% of the dose.

Results: Animas showed higher dose precision and higher 1-hour averaged dose accuracy with 80% of doses within a ±5% threshold (Figure-1A-1B). Dose precision and 1-hour averaged accuracy for other pump manufacturers ranged broadly, with Insulet and Tandem having 19.5% and 63% of doses within the same threshold respectively. Animas bolus delivery was at least 7 times faster than Insulet or Tandem (Figure-1C).

Conclusions: Animas demonstrated better dose precision and accuracy, and faster bolus delivery than Insulet and Tandem. Large dosing variations and delays in meal bolus delivery may impact clinical outcomes. Further research on the clinical relevance of these findings is warranted.

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### METHODS FOR MEASURING CONTINUOUS DELIVERIES OF DURABLE AND PATCH INSULIN INFUSION PUMPS

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Background: Animas has conducted extensive delivery performance studies following the test methods established in the IEC60601-2-24 international standard [1]. Adjustments to the IEC60601-2-24 setup were performed to adapt different pump designs and to mitigate environmental effects influencing the accuracy of the measurement system. In this study, durable and patch insulin infusion pump doses were measured using two configurations to address any impact in delivery performance.

Method: A time-stamped micro-gravimetric system housed in a vented enclosure was used to measure discrete basal deliveries at 0.5 U/hr for 20 hours. Durable (Animas OneTouch® Ping®) and patch (Insulet OmniPod® 2nd-Gen) pumps were tested using two setup configurations to compare possible variations in delivery performance: (1) pumps in proximity to the weighing pan or "inside enclosure" and (2) using the IEC60601-2-24 setup or "outside enclosure". Normal distribution plots and one-way ANOVA analysis were generated using the cumulative percent error per delivery to determine differences between the methods implemented and pump performance variability.

Results: Figure 1A-B show the delivery normal distribution for Animas ($P < 0.231$) and Insulet ($P < 0.258$) pumps when tested using both methods.
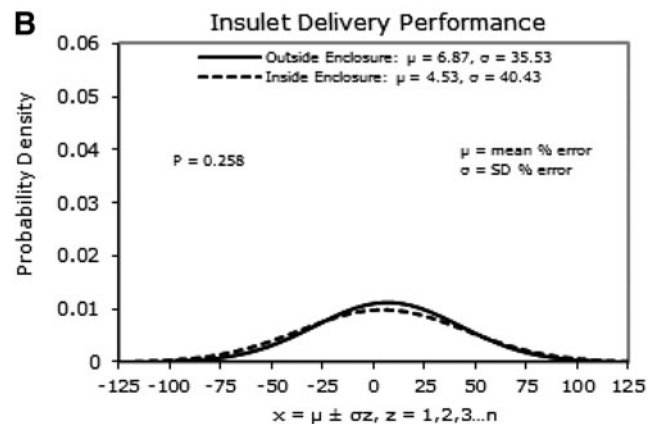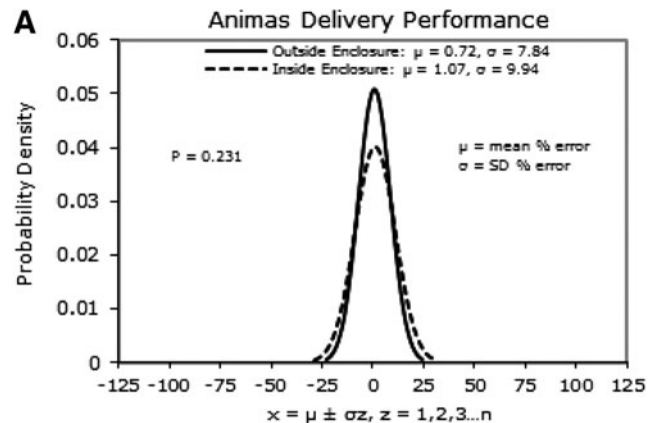
Conclusions: No difference in pump delivery performance due to testing setup was demonstrated.

[1] Jahn L, Capurro J, Levy B. Comparative Dose Accuracy of Durable and Patch Insulin Infusion Pumps. J Diabetes Sci Technol. 2013;7(4)1011–1020.

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BASAL AND BOLUS RATES IN INSULIN ACCU-CHEK COMBO PUMP TYPE 1 DIABETES PATIENTS AND ITS CORRELATION WITH AGE, FREQUENCY OF SELF-MONITORING AND METABOLIC CONTROL

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Introduction: Type 1 Diabetes involves health, economics and social issues. Insulin pumps are the gold standard and must be handled by a specialized teem.

Objetives: to evaluate basal and bolus rates and its correlation with age, frequency of self-monitoring and metabolic control.

Methods: cross sectional from 2014 July-August. Smart pix 3 last month data and 6th month average A1C were collected. Both gender with one year of pump used were included. Protocol was approved by Ethics committee. Graph Pad Prism 5 and $p < 0.05$ were used.

Results: 25 males and 40 females. (Age: female 32 ± 17 male 34 ± 15 years; A1C% female 7.6 ± 1.2 male 7.4 ± 1.4; Self-monitoring/d female 4 ± 1.5 male 4 ± 1.5; % basal female 59 ± 14 male 62 ± 16; % bolus female 41 ± 14 male 38 ± 16; High index female 12 ± 5 male 11 ± 5.9). Low index female 2.1 ± 1.6 male 1.7 ± 1.1 ANOVA $p < .0001$; Correlation test in both AGE/self-monitoring and % bolus -0.2 and -0.4 $p < 0.05$. % BASAL / A1c female 0.38 male 0.28 $p < 0.05$. Low index / self-monitoring in both, female -0.8 $p < 0.02$; male -0.6 and $p < 0.05$. Self-monitoring frequency ≥ 4/d/ low index female -0.29 $p < 0.01$ male -0.34 $p < 0.05$. %bolus / high index female -0.34 male -0.64 $p < 0.05$. A1C/ % basal and %bolus female 0.39 and -0.46 males 0.67 and -0.17 $p < 0.02$. In both A1C/ high index female 0.31 male 0.65 $p < 0.05$ and with low index female -0.42 male -0.19 $p < 0.01$.

Conclusions: Often bolus, higher self-monitoring frequency and low high index were correlated with better metabolic control. Increasing bolus and self-monitoring frequency could reduce hypoglycemia.

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INSULIN PUMPS, MULTIPLE DAILY INSULIN INJECTIONS AND PERINATAL OUTCOMES IN PREGNANT WOMEN WITH TYPE 1 DIABETES

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[2]*neonatology, Ural Research Institute of Maternity and Infancy Welfare, Yekaterinburg, Russia*

Background: Now in the Yekaterinburg region delivery at women with type 1 diabetes is 0.1% of all deliveries in a year.

Objective: to compare the perinatal outcomes wiht insulin pumps and multiple daily insulin injections in pregnant women with type 1 diabetes.

Methods: Prospective study of 57 pregnancy and perinatal outcomes in pregnant women with type 1 in 2013. Insulin pump was used in 21.1%.

Results: Age of women at delivery - 27.8 ± 4.55 years (range 19 to 41 years), diabetes duration prior to pregnancy - 8 [4; 13] years (from 0 to 28 years). Different diabetic complications were detected in 94.7%, complications of pregnancy - in 71.9% of patients. Delivery was 36.1 ± 2.0 weeks with multiple daily insulin injections (MDI) and 36.9 ± 1.5 weeks with insulin pump. Perinatal death was not. Diabetic fetopathy was determined at 71.1% (MDI) and 33% (insulin pump), hypoglycemia - at 60% of newborns (MDI) and 41.7% (insulin pump). Respiratory distress syndrome was detected in 46.5% (MDI) and 25% (insulin pump).

Conclusions: Today perinatal complications in diabetic patients are still higher than population level. Important cause of this is the absence of pregnancy planning in most patients with type 1 diabetes, poor glycemic control during pregnancy. The insulin pump helps to achieve blood glucose as close to normal.

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HOLDING THE HORSES OF INSULIN PUMP INFUSION: USAGE AND EFFECTIVENESS OF THE LOW GLUCOSE SUSPEND FEATURE DURING FASTING IN RAMADAN AMONG TYPE 1 DIABETES ADOLESCENTS

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Background: Severe hypoglycemic episodes during the daytime of Ramadan fasting is the most feared complication. Low Glucose Suspend(LGS) feature can be used to reduce it. We investigated the effect of the LGS algorithm on the frequency of hypoglycemia in adolescents with T1DM who wished to fast Ramadan.

Subjects and Methods: thirty-seven patients (23 males and 14 females, 15.6 ± 3.3 years, duration of diabetes 4.9 ± 4.2 years, pump therapy for 1.8 ± 1.1 years, used the Paradigm(®) Veo(™) system (Medtronic) and were divided into two groups: First (n = 21): those who wished to wear the sensor and use LGS feature. Second (n = 16): those who did not want to wear sensor and measured their BG level regularly.

Results: A total of 2,314 LGS alerts occurred, and 70% began in the afternoon between 2pm - 5pm. The mean duration of LGS events was 26.55 min, 38% lasted for < 5 min, and 7% lasted for 120 min. Among these episodes, the mean sensor glucose was 61.3 ± 9.4 mg/dl at LGS activation, rose to 110.7 ± 34.6 mg/dl by the end of the LGS episode (when insulin delivery was automatically resumed), and was 163.33 ± 42.1 mg/dl at 240 min. LGS usage significantly reduced the number of BG readings < 70 mg/dl ($p = 0.001$) and > 250 mg/dl ($p = 0.03$). None of the LGS group broke their fast vs. 8 in the second group ($p = 0.02$). No episodes of severe hyperglycemia in both.

Conclusions: Use of the LGS significantly reduced exposure to hypoglycemia without compromising safety.

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PHYSICAL ACTIVITY IMMEDIATELY AFTER MEALS: CAN HYPOGLYCAEMIC RISK IN PATIENTS ON PUMP THERAPY BE BEST REDUCED BY RESTRICTION OF BASAL RATE OR OF BOLUS?

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For type-1 diabetes patients on insulin pump therapy, no precise recommendations exist concerning insulin-dose adjustment in the event of physical activity (PA) immediately after meals: is basal rate reduction (BRR) or bolus reduction preferable?

Twenty DT1 patients on pump therapy (HbA1c < 9%, performing CHO counting and recreational PA) underwent determination of V02max and then performed 2 PA sessions at 50%V02max (30 min/bicycle ergometer) 90 min after lunch; bolus reduction (− 30/–50%) was compared with BRR (− 50/–80% for PA + 2 h) (randomised order). Blood glucose and insulin were measured throughout AP + 2 h. The main criterion was the number of hypoglycaemic events on the CGM curve (iPro2).

Data for 37 PA sessions showed a single hypoglycaemic event. Hypoglycaemic events tended to be fewer for bolus vs. BRR in the afternoon (p = 0.0689) with no difference at night. With bolus reduction, blood glucose levels, comparable preprandially, were higher immediately before PA [p = 0.033] but comparable after PA (bolus reduction in: − 71 mg/dL vs BRR: − 77 mg/dL, p = 0.19). With bolus reduction, CGM curves remained stable in the afternoon, with slightly higher blood glucose (168 ± 46 vs. 129 ± 47 mg/dL, p = 0.054). Time at the target range was comparable [70;180 mg/dL], lower at < 80 mg/dL (6.3% vs 20%, p = 0.04) and greater at > 180 mg/dl (42% vs. 16%, p = 0.057). Dinner-time and bed-time blood glucose levels were comparable, with CGM curves remaining flat throughout the night.

For post-prandial PA, reducing the preceding food bolus tended to reduce hypoglycaemic episodes vs. BRR at the expense of higher glucose levels in the afternoon. Where PA is envisaged, bolus reduction thus appears the safest option.

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ANALYSIS OF A COHORT OF PEDIATRIC PATIENTS TREATED WITH CONTINUOUS SUBCUTANEOUS INSULIN INFUSION

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Objective: to evaluate children with type 1 diabetes mellitus treated with insulin pump (CSII).

Carbohydrate Counting

P= 0.014

Cannula Type

P= 0.0006
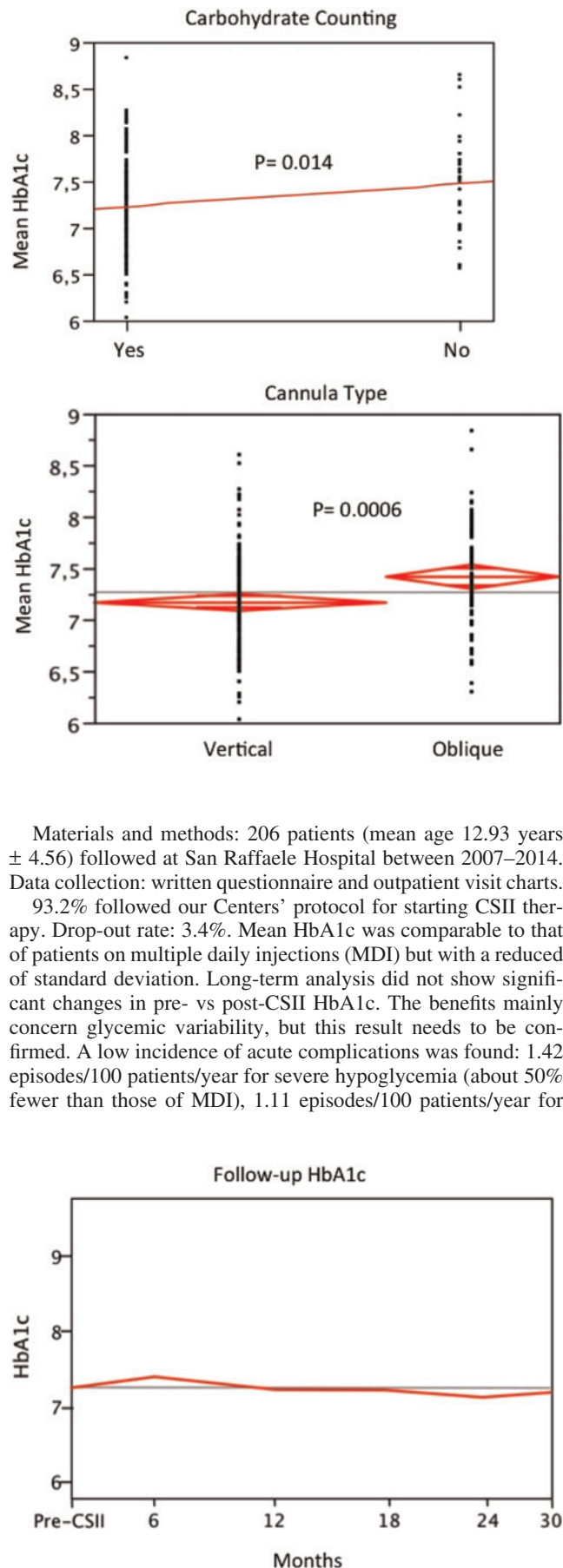
Materials and methods: 206 patients (mean age 12.93 years ± 4.56) followed at San Raffaele Hospital between 2007–2014. Data collection: written questionnaire and outpatient visit charts.

93.2% followed our Centers' protocol for starting CSII therapy. Drop-out rate: 3.4%. Mean HbA1c was comparable to that of patients on multiple daily injections (MDI) but with a reduced of standard deviation. Long-term analysis did not show significant changes in pre- vs post-CSII HbA1c. The benefits mainly concern glycemic variability, but this result needs to be confirmed. A low incidence of acute complications was found: 1.42 episodes/100 patients/year for severe hypoglycemia (about 50% fewer than those of MDI), 1.11 episodes/100 patients/year for

Follow-up HbA1c

diabetic ketoacidosis. CSII is not associated with weight gain. We found a significant association between follow-up BMI and HbA1c. An association between vertical cannula use and HbA1c reduction was found: this result needs to be confirmed. Most patients use advanced functions (bolus calculator, temporary basal rates), telemedicine and carbohydrate counting. Only carbohydrate counting was associated with HbA1c improvement. 60.2% use continuous glucose monitoring (CGM) but no association with reduced HbA1c was found due to short-term CGM use. 53.4% replaced the pump at least once and 41.7% had malfunctions (no adverse events). CSII is a safe and effective. Most studies do not show a significant HbA1c improvement, but it decreases the incidence of acute complications and improves quality of life. Further studies assessing long-term cost and benefits are mandatory.

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IS IT USEFUL TO PROPOSE INSULIN PUMP AT THE ONSET OF TYPE 1 DIABETES MELLITUS (T1DM)?

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Most of type 1 diabetes guidelines suggest the introduction of continuous subcutaneous insulin infusion (CSII) only after onset and in other conditions (poor metabolic control with good compliance, recurrent hypoglycaemia, etc). We postulate that onset ('imprinting' time) is perfect to learn every concepts of CSII 'way', but is the precocious pump use helpful for metabolic control at short term?

We selected 21 pre-pubertal children at T1DM onset, divided in two groups, evaluatating different metabolic control, beta cells reserve and nocturnal hypoglycemia fear. 11 (6M, 5F), after one month of MDI, started with CSII therapy (group A), and 10 (4M, 6F) continued with MDI (group B). HbA1c (in 2nd day of hospital admission, after 12 and 18 months of treatment), C peptide (one month, 12 and 18 months after disease onset) and number of nocturnal glycaemia measurements (as stress index) and severe hypoglycemia episodes during treatment were measured. At 12 and 18 months of therapy everyone had continuous glucose monitor for six days, in order to calculate themean amplitude glycemic excursions index (MAGEi).

At onset HbA1c was statistically better in group A, but no difference in C peptide. After 12 and 18 months nocturnal controls were superior in group B, with no difference for HbA1c and C peptide. MAGEi was better in group A. One severe hypoglycemic episode was detected in group B.

CSII since diabetes onset didn't seem to improve the glycemic control and the beta cells reserve, but seemed better for microvascular damage and hypoglycemia apprehension reduction.

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LIPOHYPERTROPHY - PREVALENCE, RISK FACTORS, AND CLINICAL CHARACTERISTICS OF INSULIN-REQUIRING PATIENTS IN CHINA

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	Group A (11)	Group B (10)	p
HbA1c (mmol/mol) at onset – mean/DS	99,33 / 26,26	121.72 / 20,32	0.03
HbA1c after 12 m m/DS	63.03 / 22,87	63.91/ 11,92	> 0.05
HbA1c 12 vs 18 m m/DS	62,33 / 20,59	63,27 / 12,21	> 0,05
C peptide (ng/ml) at onset – mean/DS	0.32/0.18	0.22/0.10	> 0.05
C peptide after 12 m – m/DS	0.27/0.15	0.33/0.29	> 0.05
C peptide 12 vs 18 m – m/DS	0,24/0,12	0,30/0,27	> 0,05
MAGE index after 12 m (mg/dl) – m/DS	157.25/26.26	183.63/24.79	0.01
MAGE index after 18 m (mg/dl) – m/DS	156,58/17,55	181,27/21,35	0,01
Nocturnal glycaemia measurements (1-12 m) – m/DS	141.58/46.01	194.50/58.39	0.03
Nocturnal glycaemia measurements (1-18 m)- m/DS	185.72/65.18	245.45/73.72	0.04

Characteristic	With LH (n=213)	Without LH (n=188)	P
HbA1c	8.2 (1.8)%	7.7 (1.5)%	0.003
Daily insulin dose (Units)	38.1 (20.1)	27.1 (14.3)	<0.001
Daily insulin dose (U/kg)	0.54 (0.28)	0.41 (0.21)	<0.001
BMI (kg/m²)	26.0 (3.3)	24.8 (3.0)	<0.001
Needle reuse, median # times	13.0	7.5	0.003
Daily injections, #	2.3 (1.0)	1.9 (0.9)	<0.001
Lack of site rotation, patients	4.7%	1.6%	0.080
Needle reimbursement, patients	27.8%	44.1%	<0.001
Injection training, patients	92.5%	87.2%	0.080

Lipohypertrophy (LH) is a poorly-studied complication of insulin injection/infusion therapy that impairs insulin absorption/glycemic control. We evaluated LH prevalence, risk factors and clinical features of LH patients in 4 Chinese cities. Adult patients injecting insulin by pen ≥ 1 year provided detailed information on diabetes/injection history, injection technique/training, pen needle (PN) reimbursement and insulin doses, followed by physical exam and HbA1c testing. Differences from those without LH were evaluated by Student's t-test or Wilcoxon rank sum test. The 401 patients were mean(SD) 59.6(11.5) yrs; BMI 25.4(3.2) kg/m²; 50% male; 93.5% T2DM. HbA1c = 8.0(1.7)%; total daily insulin dose = 33.0(18.4) U with 2.1(1.0) injections daily. Durations of diabetes and of insulin therapy = 11.8(7.3) and 5.8(4.5) yrs, respectively; 95% of patients reused PNs, median 10 (max 360) times; 35.5% had PN reimbursement. LH prevalence was 53% overall (range 38–76%), most commonly abdominal. Compared to those without LH, patients with LH had higher BMI and HbA1c, took 11 U (0.13 U/kg or 31.7%) more insulin daily, took more injections, reused PNs more times and had less PN reimbursement (all $p \leq 0.003$). LH patients rotated injection sites less and had slightly more injection training, of marginal significance (see Table). BMI, insulin dose/kg and needle reuse frequency remained significantly associated with LH prevalence by stepwise logistic regression ($p \leq 0.02$). LH is common in China and associated with worse glycemic control despite higher insulin consumption. Needle reuse frequency, insulin dose/weight, BMI and lack of PN reimbursement are risk factors, suggesting local tissue trauma and/or insulin exposure as important contributors to LH development.

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CHANGE IN HBA1C ONE YEAR AFTER CONTINUOUS SUBCUTANEOUS INSULIN INFUSION INITIATION IN ADULTS WITH TYPE 1 DIABETES: THE JOSLIN AND STENO EXPERIENCES

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Aims: We performed a retrospective analysis of adults ≥ 18 years with T1D seen at the Joslin Diabetes Center (JDC) and Steno Diabetes Center (SDC) since 2002 to assess change in HbA1c (ΔHbA1c) one year after CSII start.

Methods: All JDC and SDC patients were analyzed for age, T1D duration, weight (kg), and HbA1c (IFCC mmol/mol and DCCT %) before and one year after CSII initiation to identify independent variables explaining ΔHbA1c at one year. Data are mean $\pm$ standard deviation. A p-value below 0.05 was considered statistically significant.

Results: Data: 871 patients (271 JDC, 49% male; 600 SDC, 38% male). Mean age and T1D duration at CSII initiation were 46 ± 15 years ; 19 ± 13 years (JDC), and 40 ± 14 years ; 22 ± 13

years (SDC). Baseline HbA1c was 62 ± 12 mmo/mol / 7.8 ± 1.1/ (JDC) and 68 ± 13 mmol/mol / $8.4 \pm 1.6\%$ (SDC). Overall, ΔHbA1c was -1.9 mmol/mol / -0.2% (JDC) and -6.8 mmol/mol / -0.6% (SDC). ΔHbA1c was inversely correlated with ΔWt at SDC ($r = -0.12$, $p < 0.0001$), but not JDC. At JDC, higher baseline HbA1c ($p < 0.05$) was the only independent predictor of ΔHbA1c at one year. At SDC, higher baseline HbA1c, older age, and female sex were independent predictors ($p < 0.0001$ for all) of ΔHbA1c at one year. Both models explained 26% of the variability of ΔHbA1c.

Conclusion: CSII initiation resulted in lower HbA1c, most notably in those with the highest baseline HbA1c; greater HbA1c reduction at SDC may reflect the higher baseline HbA1c observed in this group. Modest weight gain was observed in adults with A1c $\geq 9\%$ prior to CSII initiation.

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EVALUATION OF HBA1C IN THE ADOLESCENCE WITH T1D TRANSFERRED FROM PAEDIATRIC DEPARTMENT 2002 UNTIL 2014 WITH AND WITHOUT INSULIN PUMP

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Aim: Evaluation of Hba1c in the adolescence with T1D transferred from paediatric department 2002 until 2014 with or without insulin pump (CSII).

Methods and results: We studied the adolescence transferred from paediatric department to our clinic from 2002 until 2014 (n = 480; 253 males and 227 females, age (mean SD): 18.6 ± 1.5 vs. 18.8 ± 1.6 years, diabetes duration 6.6 ± 4.8 vs. 7.9 ± 5.0 years.

We divided the cohort into three groups; CSII at transfer (C; n = 96), receiving CSII during follow-up (R; n = 53), and MDI (M; n = 331). Baseline HbA1c was significantly lower in the C compared to the R and M groups (66.1 ± 2.2, 74.9 ± 2.9, and 75.9 ± 1.2, respectively; p = 0.001). Patients already on CSII were older at transfer (19.3 ± 0.2, 18.8 ± 0.2, and 18.5 ± 0.1, respectively; p < 0.0001), and had a significantly longer duration of diabetes (9.8 ± 0.5, 8.4 ± 0.7, and 6.3 ± 0.3 years, respectively; p < 0.0001). The 53 patients receiving CSII during follow-up were characterized by a significant decrease in Hb1Ac between year one and five (from 78.5 ± 22.9 to 72.8 ± 22.4; p = 0.04 [n = 27].
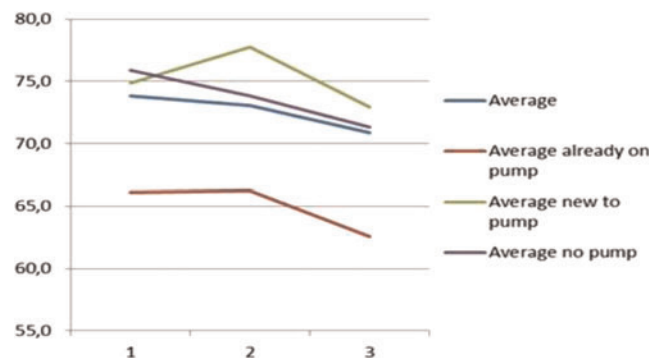
1 = baseline; 2 = 1 year ; 3 = 5 year
C = red; R = green; M = purple

Conclusion: Adolescence patients on CSII transitioning from paediatric to adult diabetes care appear to have a lower HbA1c compared to MDI. This difference persist over time but so far there is insufficient data to make this claim. CSII users trended towards being female and had a longer duration of diabetes. Post-transition put on CSII also experience benefit in terms of HbA1c lowering.

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EXENATIDE ADD-ON FOR PATIENTS WITH UNCONTROLLED TYPE 2 DIABETES DESPITE INTENSIVE INSULIN THERAPY: PHASE-2 RESULTS OF THE RANDOMIZED EXEPUMP TRIAL

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Introduction: Intensified insulin therapy (IIT), with multiple daily injection or insulin pump, represents the ultimate step of type 2 diabetes (T2D) treatment strategy. However, even with IIT, some patients remain uncontrolled with HbA1c above target. Our aim was to assess the impact of exenatide as an add-on therapy to IIT.

Material and methods: EXEPUMP is a phase 2/3 (go/no go) multicentric, double blind, placebo controlled, 6 month, randomized trial. Patients with T2D were enrolled if HbA1c was over 7.5% despite ≥6-month well conducted IIT. They were randomized 2:1 for exenatide (EXE) : placebo (control - CTL) 10 μg BID as an add on to their usual insulin treatment which was titrated to target throughout the study. As scheduled in the analysis plan, we report the results of the pilot phase 2.

Results: 38 patients were enrolled (EXE:CTL n = 26/12). Their baseline (BL) characteristics are reported table 1. In EXE group, HbA1c decreased from 8.8 ± 0.8 (BL) to $8.2 \pm 1.4\%$ at month 6 (M6) (p < 0.002). Weight, BMI and insulin daily dose results for each group are reported table 1. No severe hypoglycemia nor keto-acidosis occured during the study. Gastrointestinal disorders (especially nausea) and headache were reported in 50/16.7% and 15.4/8.3% patients from EXE/CTL group, respectively. No unexpected adverse event was observed.

Conclusion: These pilot phase 2 results suggest a good add-on efficacy and safety of exenatide 10 μg BID in T2D patients with uncontrolled HbA1c despite IIT. These promising results have triggered the decision « go » for the phase 3 of this trial.

	Overall	EXE	CTL	Inter group comparison
Baseline characteristics				
n	38	26	12	
Male (%)	17 (47%)	10 (38%)	7 (58%)	0.307
Age (years)	59.8±7.6	60.2±7.1	59.1±8.7	0.714
Diabetes duration (years)	17.9±7.1	18.6±7.0	16.6±7.5	0.446
HbA1c (%)	8.9±0.9	8.8±0.8	8.9±1.0	0.749
Weight (Kg)	99.0±16.7	95.8±17.0	106.7±13.7	0.096
BMI	36.1±4.0	35.8±4.3	36.9±3.5	0.372
Insulin daily dose (UI)	114.9±67.1	113.7±74.2	117.4±51.2	0.860
6 month outcome measures				
HbA1c (%)	ND	8.2±1.4*	ND	ND
Weight (Kg)	97.4±17.8	93.0±17.7*	107.6±13.7	0.012
BMI	35.5±4.5	34.7±4.7*	37.3±3.7	0.086
Insulin daily dose (UI)	107.6±65.5	101.7±70.0	121.5±53.8	0.358

Table 1: Baseline and outcome measures of the phase 2 EXEPUMP trial. EXE = exenatide group. CTL = placebo control group. ND : not done as pre-specified by the analysis plan. *p<0.05 from baseline.

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CELLULAR PHONE AND WEB-BASED INDIVIDUAL EDUCATION IN POST-MENOPAUSAL WOMEN WITH IMPAIRED FASTING GLUCOSE AND ABDOMINAL OBESITY FOR 12 MONTHS

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Purpose: This study was purposed to examine the effects of an intervention using a short message service (SMS) by cellular phone and Internet in post-menopausal women with impaired fasting glucose and abdominal obesity.

Methods: Thirty subjects completed the entire study, 14 in the intervention group and 16 controls. The goal of intervention was to bring fasting blood sugar (FBS), waist circumference (WC), and blood pressure (BP) close to normal ranges. Patients in the intervention group were requested to record their FBS, WC, BW, and BP in a weekly web based diary through the Internet or by cellular phones. The researchers sent optimal recommendations as an intervention to each patient, by both cellular phone and Internet weekly.

Results: FPG level was no significant change at 12 months compared with baseline in both groups. BW and WC significantly decreased by 3.7 kg and 6.2 cm respectively compared with baseline in the intervention group. The mean change in the control group was, however, not significant in both WC and BW. Systolic BP (SBP) and diastolic BP (DBP) significantly decreased by 15.4 and 13.6 mmHg in the intervention group at 12 months in the intervention group respectively. The mean change in the control group was, however, not significant in both SBP and DBP. Total cholesterol (TC) and Triglyceride (TG) decreased in the intervention group in the intervention group respectively.

Conclusion: Cellular phone and Web-based health education improved WC, BW, BP, TC, and TG in post-menopausal women with abdominal obesity and impaired fasting glucose for 12 months.

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INDIVIDUALIZING DIABETES TECHNOLOGY USE BY BETTER UNDERSTANDING OF HUMAN FACTORS

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HbA1c and glucose variability continues to be sub-optimal in patients with type 1 diabetes mellitus (T1D) even with the expanded use of insulin pumps (IP), continuous glucose monitors (CGM) and CGM augmented IP (CGMIP). Improving glucose variability will require providers to have a better understanding of human factors associated with device use, and control algorithms. Furthermore, this understanding must bridge expectations and the level of understanding in both a provider and user perspective. To better understand our users, we utilized human factors and ethnographic methods to interview 16 subjects using IP and CGMIP. Our intent was to (i)

Gather information on device utility, (ii) Identify barriers to taking full advantage of the device functionality (iii) identify opportunities for the device data to be absorbed and used meaningfully (iv) Discern variance in patients' responses, behaviors, preferences and learning styles. Qualitative analysis of the interviews revealed five potential patient types: minimizer, dutiful and fearful, ashamed and unsupported, curious and excited, and confident in life. This analysis also unveiled six major themes (i)Life with T1D is life interrupted. (ii) Good 'control' has different meanings across users. (iii) Living with T1D requires on-going education and adaptions. (iv) Living with T1D can be cognitively tiring, and people want opportunities where they *don't* have to think about diabetes. (v) The concept of fresh start helps people stay engaged in self-management behaviors. (vi) T1D can be depressing; patients need to feel understood. We conclude that these themes require further investigation to fully optimize the efficacy of diabetes technology.

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ACCU-CHEK® FLEXLINK PLUS AND ITS PREDECESSOR DEVICE CAUSE LOW PAIN PERCEPTIONS IN A CLINICAL RANDOMIZED CROSSOVER TRIAL

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Objective: As pain perception can influence therapy adherence, two infusion sets with soft cannulas were compared in a randomized controlled crossover trial.

Method: 73 patients with type 1 diabetes on pump therapy completed this open label, randomized crossover trial. Two infusion sets Accu-Chek® FlexLink Plus (FLP) and Accu-Chek® FlexLink (FL) (Roche Diagnostics) were investigated. Every patient used each type of infusion set during a period of 4 weeks, respectively. The sequence of the infusion type was randomized. Pain perception was recorded on a visual analog scale (no pain: 0 to maximum pain 10) in a patient diary after each insertion. Also, patients recorded if sets were changed after 3 days according to the study instructions or had to be replaced earlier. During this study, a total of 1771 infusion sets were used by the patients.

Results: Average pain values per patient were calculated and compared:

Pain perception on a visual analog scale (no pain: 0 to maximum pain 10) did not differ between the two sets used: 0.577 ± 0.635 FLP vs. 0.596 ± 0.647 FL ($p = 0.7210$, two-sided t-test).

Conclusion: Very low pain perceptions were demonstrated for the two infusion set types evaluated in this study. This is an indication that insertion pain caused by the novel infusion set Accu-Chek® FlexLink Plus will not influence therapy adherence negatively.

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ARE INSULIN PUMPS A VIABLE TREATMENT OPTION IN TYPE 2 DIABETES?

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Objectives: To evaluate the long-term efficacy of CSII in T2DM patients and to try to recognize which patient would be more likely to succeed.

Methods: Eighteen (12 men and 6 women) T2DM patients who began CSII between January 2000 and August 2012 were included in a study. All patients were previously treated by insulin (mean duration - 58.4 months).

Results: The median duration of follow-up on CSII therapy was 42.2 months.

Near-significant changes were seen in HbA1c in total cohort ($8.4 \pm 1.6\%$ before CSII and $7.8 \pm 1.2\%$ on CSII, $p = 0.064$). Fasting plasma glucose was reduced from 189.7 ± 51.6 mg % to 136.8 ± 34.8 mg%, $p = 0.007$. No weight gain in total cohort was observed: 89.3 ± 15.8 kg before vs.89.9 ± 15.7 kg during CSII, $p = NS$. No severe hypoglycemia was detected.

Patients were divided to three groups: Successful (5 patients), those who failed (8 patients), and those whose treatment achievements were equivocal (5 patients). Hence, CSII was successful only in 27.8% of cases.

There was a tendency to reduction of body weight in Success-group patients: 88.0 ± 21.1 kg before and 83.7 ± 19.2 kg during CSII, $p = 0.08$, while the 'Failure' group showed a significant body weight elevation on CSII (94.6 ± 15.1 kg vs. 98.6 ± 14.1 kg, $p = 0.017$).

Conclusions: The long-term use of CSII in T2DM is safe, but effective only in minority of diabetes patients. Weight reduction may play a key role.

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MULTIPLE INSULIN INJECTIONS VERSUS INSULIN PUMP THERAPY TO DIABETES MELLITUS TYPE 1 IN THE SAME PATIENT: WHICH ONE IS BETTER? CROSS SECTIONAL STUDY–BRAZILIAN EXPERIENCE

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Aims: To compare multiple insulin doses (MID) and continuous insulin infusion therapy (CIIT) as treatment for type 1 diabetes.

Methods: 40 patients with type 1 diabetes (21 female) with ages between 10 to 20 years (mean = 14.2) and mean time of diabetes of 7 years used MID for at least 6 months and after that, CIIT for at least 6 months. Each one of the patients have used MID and CIIT. For analysis of HbA1c, mean glycated hemoglobin (mGH) was obtained during each treatment period (MDI and CIIT).

Results: Although mGH levels were lower during CIIT the difference was not statistically significant. During MDI, 14.2% had mGH values below 7.5%, versus 35.71% CIIT demonstrating better glycemic control with the use of CIIT. During MDI, 15/40 patients have severe hypoglycemic events versus 5/40 CIIT. No ketoacidosis were recorded.

Conclusions: As we know, this is the first study with this design comparing MDI and CIIT showing better metabolic control and reduction of severe hypoglycemic events with CIIT.

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DURATION OF INFUSION SET SURVIVAL IN LIPOHYPERTROPHY VERSUS NONLIPOHYPERTROPHIED TISSUE IN PATIENTS WITH TYPE 1 DIABETES

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Infusion set survival in patients with type 1 diabetes is highly variable. The objective of this study was to determine the effect of lipohypertrophy on infusion set survival. To this end, we recruited subjects with type 1 diabetes with lipohypertrophy in an area of prolonged insulin infusion, measuring ≥ 3 cm. Subjects alternated on a weekly basis wearing a Teflon infusion set for up to 7 days in an area of lipohypertrophy or nonlipohypertrophy. Each subject participated for 4 weeks.

We enrolled 26 subjects giving rise to 104 weeks of infusion set wear. Mean $\pm$ SD age was 29 ± 9 y, duration of diabetes was 16.7 ± 9.2 y, insulin dose was 0.7 ± 0.3 u/kg/day and A1C was $7.6 \pm 0.8\%$.

The median (IQR) duration of infusion set survival was 6.0 days (3.7, 6.9) in lipohypertrophied tissue and 6.0 days (3.4, 7.0) in nonlipohypertrophied tissue (p = 0.484). In 42% of weeks, the infusion set lasted 7 days prior to removal per protocol. In the remaining 58%, sets were removed prior to the 7 day endpoint for the following reasons: hyperglycemia with failure of correction dose to reduce glucose by 50 mg/dL/h (28%); mechanical cause such as site pulled out, leaking insulin or adhesive failure (15%); pain, irritation or suspected infection (5%); and unknown (11%). There was no difference in causes of failure between the conditions. There were two localized site infections in two subjects occurring in both lipohypertrophy and nonlipohypertrophied areas which resolved with oral cephalexin. Lipohypertrophy does not appear to affect duration of infusion set survival in patients with type 1 diabetes.

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ASSESSMENT OF EFFECTIVENESS OF CONTINUOUS SUBCUTANEOUS INSULIN INFUSION IN A SPECIALIZED CENTER IN KUWAIT

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Introduction: It is important that patients at pubertal and prepubertal stages be targeted for strict glycemic control to prevent long-term complications. Continuous subcutaneous insulin infusion (CSII) has increasingly become an appealing treatment alternative for Multiple daily injection (MDI) regimen since its introduction about four decades ago.

Objectives: The aim of this study is to assess the effectiveness and safety of CSII in type 1 diabetic patients attending Dasman Pediatric diabetic clinics.

Methods: A retrospective cohort study was carried out for all patients with type 1 diabetes (T1D) who have initiated CSII between 1st of January 2012 till 31st of December 2013 in Dasman Diabetes Institute (DDI). Inclusion criteria included age less than 20 years, attending at least 3 clinic visits every year and having at least two Hb_{A1C} test in DDI lab every year. Data was collected from patients' electronic health records.

Results: 92 patients were enrolled in the study with a mean age of 10.2 ± 4. Male to female ratio was 1.14. Although, there

was a drop of baseline HbA_{1C} of the cohort from 8.63% to 8.51%, it did not reach statistical significance. Males started with a higher baseline HbA_{1C}; 8.93% vs 8.32% for females, but reached 8.97% vs 8.04% for females. Improvement was evident in the younger age group. There was a significant reduction in total daily dose, more evident in females. Reduction in BMI was not statistically significant.

Conclusion: CSII reduced HbA_{1C} and TDD in our cohort, improvement were evident in females and in younger patients.

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EVALUATION OF THE OUTCOMES OF TREATMENT OF T1DM PATIENTS WITH CONTINUOUS SUBCUTANEOUS INSULIN INFUSION THERAPY (CSII) AFTER 3, 6 AND 12 MONTHS OF ITS INITIATION

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Background and Aims: CSII is the most phiysiological way of delivering insulin in type 1 diabetes (T1DM). The aim of this study is to assess the outcomes of CSII treatment in terms of metabolic control, required insulin dose, hypoglycemic events and patient satisfaction.

Materials and Methods: Observational retrospective study of the data of 45 adults with T1DM started on CSII in 2012–2013. We assessed HBA1c and basal insulin required dose (UI/kg/day) at the beginning and 3, 6 and 12 months after, overall hypoglycemias and satisfaction.

Results: 47% were women and 53% men, mean age of 36 years old. The mean duration of the disease was 21 years. The reasons for the initiation of CSII were: 47% bad metabolic control, 42% hypoglycemias, 9% pregnancies and 2% dawn phenomenom. 40% had chronic complications at the initiation of CSII, 15.5% retinopathy, 9% nefropathy and 2% gastroparesis, 9% retinopathy and nephropathy, 4% retinopathy, nephropathy and neuropathy and 2% neuropathy and gastroparesis. The mean HbA1c at baseline was 8% and after 3, 6 and 12 months the it was 7.3%, 7.2% and 7.4% respectively, overall mean reduction 0.7%. During the first year of CSII there was one DKA episode. In terms of basal insulin needs we observed 10% and 10.5% reduction after 6 and 12 months, respectively. There was a reduction in the number and severity of hypoglycemias and an improvement in satisfaction with the treatment.

Conclusion: CSII therapy has proven to be an effective and safe treatment in our group of patients with T1DM.

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SELF-ADJUST OF BASAL INSULIN ON CONTINUOUS SUBCUTANEOUS INSULIN INFUSION (CSII) PATIENTS: DOES IT SUPPOSE A BETTER GLYCEMIC CONTROL?

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N	53	Patients who made modifications in the basal rate	Patients who did not make modifications in the basal rate	p value
		53	25	28	
Age (years)	39,6 ± 10,2	37,2 ± 5,9	41,9 ± 12,7	0,085
CSII Duration (years)	4,2 ± 1,7	4,2 ± 1,6	4,3 ± 1,7	0,978
Mean glucose (mg /dl)	171,3 ± 24,1	166,2 ± 21,3	175,9 ± 25,7	0,273
Standard Desviation (mg /dl)	76,5 ± 13,4	70,9 ±10,6	81,5 ± 13,8	0,006
HbA1c (%)	7,8 ± 1,0	7,4 ± 0,76	8,1 ± 1,1	0,013
Self Blood Glucose Monitoring (n)	126,7 ± 42,2	136,8 ± 44,4	117,7 ± 38,7	0,105
Hypoglycemic values (%)	8,3 ± 5,4	7,3 ± 5,3	9,2 ± 5,4	0,159

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Objectives: To study whether patients on CSII who modify the basal rate present a have better control than those who do not make any changes.

To evaluate if the use of tools that assist in the analysis of capillary glucose, such as trends detector glucose-meter, enables the patient to make basal rate adjustments.

Material and methods: Retrospective observational study. 53 patients (33 women) with CSII treatment were included.

During the follow-up visits, as a part of the structured educational program, patients were instructed on how to change the basal insulin.

We evaluated if patients who perform modifications in the basal rate have better glycemic control than those who do not. Furthermore, in subjects who have a trends detector glucose meter, we studied if its use can help them to modify the pattern of basal insulin. We defined the need to make changes when the hyperglycemia values (>180 mg/dl) were over 50% of the total capillary blood glucose and/or when the values of hypoglycemia (<70 mg/dl) exceed 10%.

Results: The results are showed in Table 1.

47.2% (n=25) of patients made changes in basal insulin. 71.4% (n=20) of participants who did not make changes in basal rate had to do it. 90% (n=9) of patients who had trends detector glucose-meter modified the basal rate.

Conclusions: The educational support and the use of tools that analyze capillary blood glucose trends help the patient in adjusting the basal rate.

Patients who perform self-adjustment of basal insulin rate have a better glycemic control.

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FUNCTIONAL INSULIN THERAPY

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Introduction: Functional insulin therapy is the leading treatment of Type 1 Diabetes Mellitus. Multiple Daily Injections (MDI) and Continuous Subcutaneous Insulin Infusion (CSII) are the options available, and they allow dose adjustment according to capilarglycemia and the percentage of carbohydrates on meals.

Objective: To evaluate the efficiency of multiple daily injections (MDI) and continuous subcutaneous insulin infusion (CSII) in the treatment of Type 1 Diabetes Mellitus.

Methods: This is a longitudinal and retrospective study in 43 patients, 16 treated with CSII and 27 with MDI, the mean age was 34 ± 11 years, and the duration of the disease was 16 ± 8 years. A1c values, fasting plasma glucose (FPG) levels, lipid profile, data from continuous glucose monitoring and from a questionnaire applied to the patients were recorded.

Results: There was a 0.5% decrease on hemoglobin A1c values ($p < 0.05$) 12 months after pump introduction in the CSII group, and this reduction was sustained for at least another two years ($p < 0.001$). Those patients registered fewer episodes of hypoglycemia and hyperglycemia per week with this treatment.

Conclusion: CSII offers benefits over MDI with improvement in HbA1c and FPG levels over a long period of time.

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HIGHER FREQUENCY OF BLOOD GLUCOSE TESTING AND BOLUS NUMBERS IS ASSOCIATED WITH LOWER GLYCEMIC VARIABILITY: POST-HOC ANALYSIS RESULTS FROM THE REAL WORLD PROACT-STUDY

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Tansition from older pump systems to the Accu-Chek®–Combo system in a large patient population resulted in stable glycemic control with significant improvements in HbA1c (ProAct Study). In this post-hoc analysis, we investigated the glycemic control and glycemic variability at baseline by determination of several established proposed glycemic variability scores in patients with different daily bolus numbers and different blood glucose measurement frequencies (<3/day, 3–5/day, and >5/day, in both cases).

The data was derived from 299 patients (172 female, 127 male, age (mean$\pm$SD): 39.4 ± 15.2 yrs., CSII duration: 7.0 ± 5.2 yrs.) enrolled by 61 European sites. Patients with frequent daily blood glucose readings (>5/day) were better controlled than patients with few blood glucose readings (<3/day; HbA1c: $7.2 \pm 1.1\%$ vs.$8.0 \pm 0.9\%$; mean daily blood glucose: 151 ± 22 mg/dL vs. 176 ± 30 mg/dL, % readings/month >300 mg/dL: 10 ± 4 vs. 14 ± 5; % readings in euglycemia (80–180 mg/dL): 59% vs. 48% $p < 0.05$ in all cases, % readings/month <70 mg/dL: 4 ± 2 vs. 4 ± 3, n.s.) and had a lower glycemic variability (J-score: 49 ± 13 vs. 71 ± 25, hyperglycemia index: 0.9 ± 0.5 vs. 1.9 ± 1.2, index of glycemic control: 1.9 ± 0.8 vs. 3.1 ± 1.6; $p < 0.05$ in all cases, hypoglycemia index: 0.9 ± 0.8 vs. 1.2 ± 1.3, n.s.). Frequent testing was associated with a higher number of bolus applications (6.1 ± 2.2 boli/day vs. 4.5 ± 2.0 boli/day, $p < 0.05$). Therefore, a similar but less pronounced effect on glycemic variability in favor of more daily bolus applications was observed.

CSII patients, who perform frequent daily blood glucose readings have a better glycemic control associated lower glycemic variability as assessed by a variety of glycemic variability indices.

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CROSS-OVER STUDY ON USAGE TIME FOR INSULIN PUMP INFUSION SYSTEMS

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Infusion sets for use with insulin pumps shouldbe used for two to three days, e.g. to avoid local skin reactions to the insulin formulation and preservatives (e.g. meta-cresol). However, many patients use the catheters longer for economical reasons. We performed this study to investigate the tolerability of two day use in comparison to four day use in a real world setting.

This prospective randomized controlled crossover study with 2×3 months observation periods was performed with 24 type 1 patients. At baseline, patients were trained on the use of the infusion System (Medtronic /Mio® or inset™ II) and randomized to any of the two treatment sequences. Observation parameters included frequency andnature of device-related and procedure-related adverse events and patient preference.

The per protocol analysis was performed with 22 patients (5 men, 17 women, age 39 ± 11 years, BMI: $27.0 \pm 3.5 \, \text{kg/m}^2$). The number of catheter related adverse events was 290 with 2-day use vs. 495 with 4-day use ($p < 0.05$). The overall number of treatment related events was 750 with 2-day use vs. 934 with 4-day use ($p < 0.001$). Treatment satisfaction was higher with 2-day use (very high/high satisfaction: 90.4% vs. 4-day use: 77.3%, $p < 0.05$).

Our results demonstrate that using the infusion sets for a longer usage period of 2–3 days resulted in a clinically relevant increase in treatment-related tolerability problems. Patients should be encouraged not to use insulin pump infusion sets for a longer than the recommended time period.

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USE OF INSULIN PUMP THERAPY (CSII) DURING PREGNANCY IN WOMEN WITH TYPE 1 DIABETES (DM-1) OVER A DECADE

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Objective: Women with DM-1 should be offered CSII if they are planning pregnancy and adequate glycaemic control is not achieved by multiple daily injections (MDI). The main objective of our study is to assess if the use of CSII have changed during the last decade.

Materials And Methods: We have collected data of 133 pregnancies between 2004 and 2013. Age: 29.91 ± 5.2 years old, duration of diabetes:14.0 ± 7.9 years, 14.3% had retinopathy and 4.0% had microalbuminuria. HbA1c prior to pregnancy: $7.44 \pm 1.45\%$. 48.9% of patients planned their pregnancy (n = 65). Concerning the type of basal insulin, 41.4% (55) used NPH insulin, 30.9% (41) used a long acting insulin analog (Lantus or Levemir). 27.8% (37) were already receiving treatment with CSII before pregnancy.

Results: No difference between groups (CSII/MDI) was found regarding age, duration of diabetes and presence of chronic complications. HbA1c levels were similar before pregnancy as well as at the end of each trimester. (tables 1–2). No difference in terms of perinatal outcomes (neonatal hipoglucemia, ICU admission or shoulder dystocia) was found. There were also no differences in the percentage of women who planned their pregnancy. The use of NPH insulin has decreased over the years with an increase of long acting insulin utilization. Nevertheless, CSII treatment remains stable though out the years.

Conclusions: Although the extended use of long acting insulin analogs in the treatment of pregnant type 1 diabetes women because of their usefulness and safety, the CSII treatment is still required in those patients where good glycemic control cannot be achieved.

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A SINGLE TEAM APPROACH FOR TRANSITIONING TEENS TREATED WITH INSULIN PUMPS

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At our Center, the transition from childhood to adulthood of the subjects treated with insulin pumps is managed by the same health care providers, in a single team approach. Aims of this study are to assess: 1) if our approach is helpful to face some transition related issues such as increase of HBA1c, risk of loss to follow-up (LTFU) and diabetic ketoacidosis (DKA); 2) if insulin pumps implanted during transition are effective and durable. From 684 subjects treated with insulin pumps, we selected 208 subjects aged 10–22 years and with a follow-up duration ≥ 2 years: the cross-sectional evaluation of their yearly mean HBA1c did not show any significant difference by age group, with the only exception of HBA1c at 10 versus 15 years of age (8.0%, 95%CI 7.7–8.5 versus 8.7%, 95%CI 8.2–9.3; p = 0.0487; Fig. 1); the yearly incidences of LTFU and DKA were not different from the mean values obtained when the same subjects were 6–10 years old. A longitudinal assessment of the yearly mean HBA1c of 96 subjects implanted in the age range 10–18 years and a

Figure 1 . Cross sectional evaluation of mean yearly HBA1c

Figure 2. HBA1c values until four years from implant
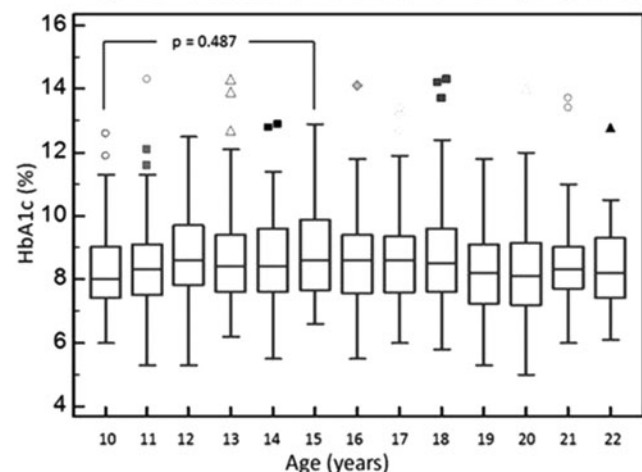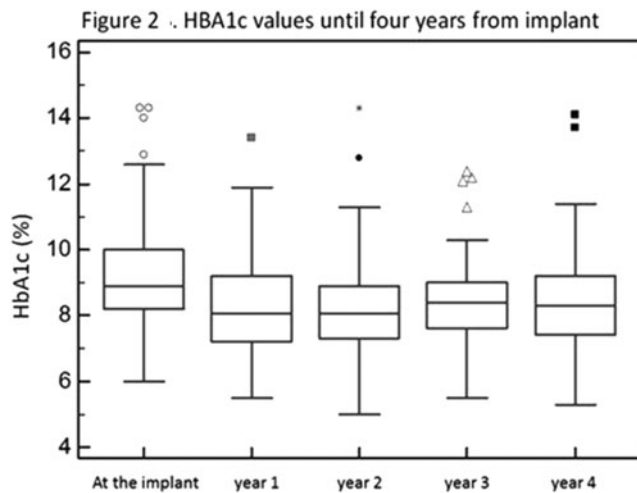
follow-up duration ≥ 4 years showed an effective and durable effect of the pumps (HBA1c at the implant = 8.9% IQR 8.2–10.0%; HBA1c after 4 years = 8.3% IQR 7.4–9.2%; p < 0.001; Fig. 2). Our approach provide stable HBA1c levels and a durable lowering effect on HBA1c to transitioning teens, without an increased incidence of LTFU nor of DKA.

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RESOLUTION OF THE MAIN INDICATION AND SUSTAINABILITY OF LONG-TERM GLYCEMIC CONTROL IN T1D WITH CONTINUOUS SUBCUTANEOUS INSULIN INFUSION

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Objective: The effectiveness of continuous subcutaneous insulin infusion (CSII) in Type 1 diabetes (T1D) has been established in the short-term. However, less information is available regarding the impact on solving main indications for initiating CSII and whether good control can be maintained over several years. Our objective was to assess the resolution of the main indication and sustainability of long-term glycaemic control in T1D using CSII.

Methods: Retrospective observational study including 178 T1D patients who started CSII treatment in our Center (2003–2008). All patients were followed in our CSII program for outpatients for at least 5 years. Data on annually HbA_{1c} was collected and the resolution of the main indication for starting CSII was analysed.

Results: 27 out of 178 patients were excluded because of loss of follow-up or withdrawal from CSII. 151 patients (37.4 $\pm$ 10.5 years, 64% women) were analysed. The main indications to start CSII were suboptimal metabolic control (SMC-group, 62.9%), severe hypoglycaemia/hypoglycaemia unawareness (H-group, 27.2%) and other (9.9%). HbA_{1c} at the start of CSII was 8.0 $\pm$ 1.2 and 7.8 $\pm$ 1.2 after 5 years in the total cohort (p < 0.05). In the SMC-group HbA_{1c} dropped from 8.3 $\pm$ 1.2% to 8.0 $\pm$ 1.3% (p < 0.05) and 38% of patients in this group had an HbA_{1c} $\leq$ 7.5% after 5 years. The resolution of the main indication was obtained in 64% of the SMC-group and 93% in H-group.

Conclusions: CSII therapy maintains long term glycaemic benefits after 5 years of follow up. In addition, the main indication for this treatment can be resolved in two thirds of T1D patients.

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PERCEPTIONS OF PATIENTS AND SIGNIFCIANT OTHERS REGARDING CSII AND MDII ON LIFESTYLE AND DIABETES MANAGEMENT

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Purpose: To investigate the impact of continuous subcutaneous insulin infusion (CSII) (insulin pumps) and multiple daily insulin injection (MDII) on patient lifestyle and diabetes management as perceived by the patient and a ''significant other''.

Methodology: In Phase I, developed, tested and validated detailed parallel questionnaires for four groups of patients and corresponding ''significant others'': CSIIpt/CSIIso) and MDIIpt/MDIIPso). Phase I yielded results from 261 pairs. In Phase II, using results from Phase I, all four instruments were revised, and validity & reliability established (n = 354 pairs). Cronbach's α = .901 (CSIIpt); α = .940 (CSIIso); α = .912 (MDIIpt); α = .940 (MDIIso). For participants > 50 yrs α = .901 (CSIIpt); α = .940 (CSIIso); α = .912 (MDIIpt); α = .940 (MDIIso). Sociotechnical Systems Theory and the Life Patterns Model framed the study.

Instruments: 20 demographic items; 43 perception items (5-pt Likert Scale); 10 True/False items; and 2 items (4-pt Likert Scale) on overall satisfaction with diabetes management and impact on lifestyle.

Findings: A substantial number of SO's did not know how to suspend the pump in case of severe hypoglycemia (< or = 40 yrs, 41.86%; 41–60 yrs, 43.88%; > 60 yrs, 41.30%). Although management improves with either intensive therapy, fear of hypoglycemia is not reduced. Factor analyses yielded themes for overall satisfaction, changes in relationships and roles, and impact on the use of support groups. CSII patients and significant others were more satisfied with impact on diabetes management and lifestyle than were MDIIs. Education needed for significant others on insulin pumps and symptoms of hypoglycemia.

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THE EFFECT OF 4 YEARS INSULIN PUMP TREATMENT ON ALBUMINURIA IN TYPE 1 DIABETES

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Aim: We investigated the effect of 4 years insulin pump (CSII) treatment on $HbA_{1c,}$ albuminuria and kidney function compared to multiple daily injections (MDI) in a single center clinical setting.

Methods: We conducted a case-control study of all patients initiating CSII from 2004-10 and followed for at least 4 years:

193 patients with type 1 diabetes matched (1:2) to 386 patients treated with MDI in the same period. Matching was based on diabetes duration, sex, HbA$_{1c}$ and normo-, micro- or macro-albuminuria at baseline. Urinary albumin creatinine ratio (UACR) was measured yearly and annual change assessed from linear regression. Unpaired t-test compared groups and multiple regression adjusted associations.

Results: Group were comparable at baseline. After 4 years HbA$_{1c}$ was 62 ± 11 *vs.* 69 ± 11 mmol/mol ($p < 0.001$). Annual change in UACR in CSII *vs.* MDI treated patients was (mean (CI95%)) $-11.3(-14.6; -8.0)\%$ *vs.* $-1.1(-3.3;1.1)\%$, ($p < 0.001$). Reduction in UACR was significantly associated to CSII treatment after adjustment for age, sex, diabetes duration, eGFR, UACR, MAP, HbA$_{1c}$, cholesterol, RAASi, AHT and smoking ($p < 0.001$). In adjusted analyses of patients on stable RAASi during follow up (n = 465) CSII treatment remained significantly associated to a reduction in UACR ($p < 0.001$).

Conclusion: CSII treatment over 4 years independently reduced HbA$_{1c}$ and UACR compared to MDI, but eGFR remained unchanged. Reduced UACR may be due to less glycaemic variability as the well-known effect of CSII on HbA$_{1c}$ could only partially explain the effect. This cannot be assessed from our data. The effect of CSII treatment on UACR needs confirmation in randomized controlled trials.

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PROJECTION OF HEALTH-ECONOMIC BENEFITS OF SENSOR AUGMENTED PUMP (SAP) VERSUS PUMP THERAPY ALONE (CSII) IN T1DM, A UK PERSPECTIVE

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Aims: The objective of this study was to estimate the health-economic impact of sensor augmented pump (SAP) compared to pump therapy alone (CSII) of type 1 diabetes (T1DM) in the UK.

Material and methods: The Core Diabetes Model was used to project the incidence of diabetes-related complications over a lifetime horizon, based on A) a published meta-analysis comparing SAP versus CSII, and B) a real life observational study. The cohort characteristics are presented in Table 1. SAP effects also included a decrease in the annual rate of major hypoglycaemic events from 2.2 events per 100 patients' month for CSII to 0. The quality of life was adjusted for a reduced fear of hypoglycaemic event in the SAP arm. Sensitivity analyses were carried out on several key parameters.

Results: The incremental cost-effectiveness ratio (ICER) was 16,986 GBP (£) per Quality Adjusted Life Year gained (QALY). The improvement in discounted QALY was 3.1 years in favour of SAP. Additional SAP related costs were partially offset by the savings due to the reduction in diabetes related complications and the lower frequency of SMBG tests. Remaining extra costs due to SAP were on average 1,143£ per year. When a societal perspective was considered, ICER was reduced to 8,462 £ per QALY.

Conclusions: Projection of the improvement in HbA1c of SAP versus CSII translated into cost-effective ratio, generally considered as very good value for money in the UK. Extensive

Table 1: Cohort and intervention characteristics	
Mean baseline age	27 years
Proportion of male	48.5 %
Diabetes duration	13 years
Mean baseline HbA1c	10 %
HbA1c reduction SAP	-1.49 %
HbA1c reduction CSII	-0.62 %

sensitivity analysis on key drivers confirmed the robustness of results under a wide range of assumptions.

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AN AUDIT OF INSULIN PUMP THERAPY IN TWO LARGE DIABETES CENTRES IN THE UNITED ARAB EMIRATES (UAE)

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Introduction: There are few published data on use and outcomes of insulin pump therapy (IPT) in the UAE. We have conducted an audit of IPT in two large Diabetes Centres Abu Dhabi and Al Ain.

Method: Electronic patients records were accessed to retrieve relevant information on patients with type 1 diabetes including those currently on IPT.

Results: 149 patients were on IPT (94 from patients in ICLDC Abu Dhabi and 55 from patients in ICLDC Al Ain, age 21.2 ± 13.4 years, 42.3% male and 57.7% female, HbA1c ($8.5 \pm 1.7\%$). No significant difference was seen in HbA1c between patients followed up in the two centres ($8.6 \pm 1.8\%$ vs $8.5 \pm 1.6\%$ respectively, P = 0.7). Among IPT patients, glycaemic control was worse ($p < 0.001$) among paediatric patients (n = 78, age 11.8 ± 3.6 years, HbA1c $9.1 \pm 1.6\%$) compared to adult patients (n = 71, age 31.5 ± 12.7 years, HbA1c $7.9 \pm 1.7\%$). Corresponding figures for paediatric and adult patients with type 1 diabetes and NOT on IPT were $9.6 \pm 2.2\%$ (age 11.3 ± 4.5 years) and $8.7 \pm 2.1\%$ (age 32.2 ± 10.7 years) respectively. HbA1c was above 8.0% in 55.7% of patients on IPT.

Conclusion: Amongst Emirati patients, IPT therapy does not appear to achieve better glycaemic targets compared to standard insulin therapy. Better patient education and an improved clinic set-up with trained diabetes educators is needed to help improve outcomes among these patients.

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OPTIMIZATION OF CSII THERAPY BY PERSONALIZED KNOWLEDGE-BASED DECISION SUPPORT

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Background and aims: Each patient has his individual changes in daily insulin requirements. Therefore physicians have to adjust the basal rates to the individual insulin sensitivity pattern, if a patient has to be subjected to CSII Therapy. It was the aim of our study to develop and to verify a knowledge-based decision support system for easy, quick, and save personalized basal rate adjustment procedures.

Material and methods: A special version of the well known Karlsburg Diabetes Management System KADIS® was developed (CSII-KADIS®) and a three step CSII adjustment procedure created. At first the individual metabolic situation of a given patient was identified by CSII-KADIS®-supported calculation of the so called 'Metabolic Fingerprint'. At second the individual basal rate requirement was estimated by interactive, CSII-KADIS®-based simulation strategy and finally the CSII-KADIS®-supported individual basal rate adjustment was performed whereas the basal rate profile was divided into 12 one hour segments. To verify and to evaluate the practicability and the effectiveness of the CSII-KADIS®-supported basal rate adjustment procedure, a study with 12 type 1 diabetic patients was performed.

Results: The effort needed by physicians for a sufficient individual basal rate adjustment was remarkably reduced from weeks or months to only about one hour if CSII-KADIS®-based adjustment procedure is applied. Using the CSII-KADIS®-supported basal rate adjustment procedure the HbA1c declined after three and six months the glucose variability was significantly reduced by running KADIS®-supported CSII-therapy.

Conclusion: Individually related basal rate adjustment becomes easier, safer, and is less time consuming by applying CSII-KADIS®-based decision support.

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ANALYSIS OF GLYCEMIC CONTROL USING SPECIAL SOFTWARE IN SUBJECTS WITH CSII

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Background: Several studies have demonstrated a strong correlation between frequency of SMBG and glycemic control. Blood glucose monitoring software helps in the analysis of large amounts of patient data. Some systems are able to download data from both glucometers that the pump system providing a number of useful data for management of patients with diabetes. The relationship between A1C and chronic glycemia has been explored in several studies that have supported the association of A1C with AG levels over the preceding 5–12 weeks.

Tab. 1

Correlation	r	p
between A1C and:		
Average Glucose (AG);	0.702	0.000
percentage of glycemic value within range 70-140 mg/dl;	-0.744	0.000
Frequency of SMBG;	-0.564	0.001
average amount of total daily insulin;	0.394	0.031
frequency of insulin bolus.	-0.218	0.248
Between:		
frequency of SMBG and frequency of insulin bolus	0.637	0.000

Purpose: To assess the relationship between HbA1c and a number of data downloaded by dedicated software in a group of type 1 diabetes CSII users.

Materials and methods: A1C levels (mean ± SD: 7.54 + 0.76) of 30 type 1 diabetes CSII users (M/F 9/21), were correlated with the data shown in tab.1. All of the data both glucometer and pump, were downloaded by diasend, smart pix and carelink software. All data were filtered by date and last 3 months, was the time period set.

Results: The results are shown in tab.1

Conclusions: This study confirm the relationship between A1C and such parameters downloaded by a dedicated software in a group of selected CSII users. Analyzing blood glucose data in a systematic method on a computer allows the inclusion of large amounts of data and improve the management of diabetes.

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OPTIMAL PUMP SETTINGS DIFFER ACCORDING TO AGE AND INSULIN DOSE

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Introduction: Knowledge is scarce about optimal bolus guide settings, but may be important in increasing adherence in young persons with diabetes. Our aim was to estimate the carbohydrate factor (CF) and insulin sensitivity factor (ISF) in well-controlled patients.

Methods and material: Medtronic pumps were uploaded at clinical visits and bolus guide settings were linked to HbA1c. Multiple regression analysis was used to explore data. The CF and ISF were calculated using insulin dose*carbohydrate ratio and *sensitivity ratio respectively.

Optimal control was defined as HbA1c < 59 mmol/mol and no severe hypoglycemic events.

Results: A number of 108 children (58 males) with HbA1c below 59 mmol/mol, mean age 11.6 (+/- 0.5), diabetes duration 5.1 (+/- 0.4) were included. Insulin dose/kg varied from 0.5 (+/- 0.1) to 0.8 (+/- 0.1). CF varied from 268 in the youngest to 436 in the oldest and the ISF from 100 to 121, the highest level in 6–12 years old. Using backward elimination age, insulin dose and number of boluses per day were significantly associated with CF. Age, pump duration, insulin/kg and percentage of insulin as boluses were associated with ISF.

Conclusion: In children with an optimal metabolic control age, pump duration, use of pump and insulin dose all influence the bolus-guide settings. Calculation factors vary with age and total insulin dose, and therefore age and insulin dose dependent calculation factors are needed. There is a lack of intervention studies aiming at optimizing bolus guide settings during child growth.

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PUMP SETTINGS IN DIFFERENT AGE GROUPS

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Introduction: Use of the bolus guide improves metabolic control in insulin pump users. Optimal settings from pump start may increase adherence. It is common to use the 500 (Carbohydrate Factor/CF) and 100 (Insulin Sensitivity Factor/ISF) rules to calculate bolus guide settings. Calculation factors may differ for age and insulin dose.

Methods and material: Pump settings were uploaded at each clinical visits and linked to HbA1c. Multiple regression analysis was used to explore data. CF and ISF were calculated using insulin dose*carbohydrate ratio and *sensitivity ratio respectively.

Results: In total 287 children, (138 males) mean age 12.9 (+/- 0.3), diabetes duration 6.2 (+/- 0.2), were included. There were 38 percent with HbA1c < 59 mmol/l and 27% had HbA1c > 70 mmol/mol. CF varied from 283 in the youngest to 438 in the oldest and the ISF varied from 100 to 120. Using backward elimination gender, age, insulin dose and number of boluses per day were significantly associated with CF. Age, HbA1c, duration on pump, number of daily boluses and percentage of bolus insulin were associated with ISF.

Conclusion: Age, gender, duration of pump treatment, number of boluses, and insulin dose all influence the bolus-guide settings. The 500 rule used to estimate CF does not fit in children, especially not in the youngest, whereas the100 rule correlated closer to the estimated ISF value. Age, the use of the pump and insulin dose need to be taken into account when carbohydrate ratio and insulin correction factor is calculated at pump initiation.

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DERMATOLOGICAL COMPLICATIONS OF CONTINUOUS SUBCUTANEOUS INSULIN INFUSION IN YOUNG ADULTS WITH TYPE 1 DIABETES MELLITUS

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Objective: The aim of this study was to evaluate the problem of dermatological complications during insulin pump therapy in young adult type 1 diabetic patients.

Study group and methods: Cross-sectional study was performed in consecutive patients using insulin pump treatment above 1 year. The mean age of the patients was 23.3 ± 4.3 and diabetes duration 13.6 ± 5.0 years. Insertion sites were investigated and the following dermatological manifestations were documented: scars > 3 and < 3 mm, intracutaneous nodules, erythema, areas of lipohypertrophy and lipoatrophy, and abscesses.

Results: The most common dermatological complications were nodules (in 68 patients 38%), lipohypertrophic areas at the insertion sites (in 49 patients – 27.4%) and erythema (in 22 patients – 12.3%). Local abscesses and scars > 3 mm were found in 2 and in 3 patients – 1.2% and 1.7% respectively). Lipohypotrophic areas at the insertion sites were observed in 3 patients (1.7%). None of dermatological complication led to interruption or stop of CSII. In patients with lipohypotrophy the type of human insulin analog was changed. The patients with nodules or

erythema had worse metabolic control than patients without dermatological side effects (HbA1c: 7.8 vs 7.3% p = 0.002).

Conclusions: Dermatological side effects during CSII are common in young adults. The worse metabolic control can provoke such complications.

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INSULIN PUMP THERAPY AND HEART RATE VARIABILITY IN CHILDREN WITH DIABETES MELLITUS TYPE 1

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Aim: To investigate the possible influence of the mode of administration of insulin on the parameters of heart rate variability (HRV) in patients with diabetes mellitus type 1.

Materials and methods: The study involved 101 children with type 1 diabetes. The study of heart rate variability (HRV) was performed according to the recommendations of the European Society of Cardiology and the North American Electrophysiological Society (1996), using an apparatus ''VNS-spectrum'' corporation ''Neurosoft'' and HRV analysis program ''Poly-Spectrum''.

Results and discussion: The study involved 101 diabetic children (49 girls, 52 boys) from 6 to 17 years, with the disease duration of 1 month to 15 years.

All patients were on the basal-bolus insulin therapy in the mode of multiple subcutaneous injections - MPII (89 patients - 88.1%) or a constant subcutaneous infusion - CSII using wearable insulin pump (12 patients - 11.9%).

Patients on MPII demonstrated a significant increase in the LF/HF coefficient (p = 0.034), indicating that they have autonomic imbalance. Patients on CSII have a statistically significant increase in the total power spectrum (p = 0.033), Valsalva ratio (p = 0.044), amplitude variations (p = 0.030) and stress index (p = 0.016).

Conclusions: Patients receiving insulin in CSII mode, have a more pronounced HRV on the background of lower voltage adaptive systems of the body than patients on multiple subcutaneous insulin injections. Probably, insulin pump therapy can reduce the risk of diabetic damage to the autonomic nervous system which regulates the activity of the heart and blood vessels.

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THE DAILY REQUIREMENT OF BASAL INSULIN IN PREGNANT WOMEN WITH TYPE 1 DIABETES RECEIVING INSULIN BY THE PUMP

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Aim: To calculate the daily requirement of basal insulin depending on the initial state of the kidneys.

We examined 40 pregnant women with type 1 DM (DM1) on the insulin pump therapy. We assessed the need in basal insulin, daily urinary albumin excretion on the 12, 22–24, 30–32 weeks of pregnancy. Patients were divided into two groups: 1- patients without proteinuria, 2- with proteinuria.

Results: In group 1 the need for basal insulin in the first trimester was 0.22 (0.18, 0.25) IU / kg, in the second - 0.34

(0.26, 0.38), the third 0.38 (0.31, 0.49). A significant increase in the need for basal insulin noted from the second trimester (U = 91.00 p < 0.001) and up to the end of pregnancy (U = 75.00 p < 0.001 and U = 149.50 p = 0.22 between the first and the third; the second and third trimesters, respectively). In group 2 the need for basal insulin in the first trimester was 0.23 (0.21, 0.25) IU / kg, in the second - 0.32 (0.29, 0.36), the third - 0.34 (0.33, 0.47). A significant increase detected only in the third trimester (U = 4.00 p = 0.22; U = 0.00 p = 0.03 and U = 0.00 p = 0.03) between the first and the second, the second and third, and the first and third trimesters, respectively.

Conclusion: The increase of basal insulin dosage in pregnant women with type 1 diabetes who are on insulin pump therapy depends on the initial state of the kidneys.

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URINARY EXCRETION OF PROINFLAMMATORY CYTOKINES IL-1β, MCP-1 AND FIBROGENIC GROWTH FACTOR TGF-β1 IN PREGNANT WOMEN WITH TYPE 1 DIABETES (T1DM)

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Objective: To study the dynamics of IL-1β, MCP-1 and TGF-β1 in pregnant women with T1DM with different stages of diabetic nephropathy (DN) depending on the mode of administration of insulin.

Methods: we study 48 pregnant women with T1DM in different trimesters of gestation. They were divided into two groups: on the standard intensified basal-bolus insulin therapy (MPII) and on the insulin pump. Stages of DN was determined by the level of urinary albumin excretion. We assessed HbA1c, daily monitoring of glucose with CGMS MiniMed Medtronic, IL-1β, MCP-1 and TGF-β1 in the daily urine.

Results: Analysis of the urinary excretion of IL-1β, MCP-1 and TGF-β1 showed that in all patients excretion of IL-1β, MCP-1 and TGF-β1 is increased and there is a direct correlation with the level of urinary albumin: in the MPII group (IL-1β = 0.35, MCP-1 = 0.36, TGF-β1 = 0.45) and in the insulin pump group (IL-1β = 0.26, MCP-1 = 0.26, TGF-β1 = 0.35). Also was found a close correlation of MCP-1 with TGF-β1 (r = 0.88), MCP-1 with IL-1β (r = 0.93), TGF-β1 with IL-1β r = 0.9 - all statistically significant) in both groups.

Conclusions: The study showed that the excretion of IL-1β, MCP-1 and TGF-β1 increases with the increase of proteinuria and is not dependent on the mode of administration of insulin. Hyperproduction of IL-1β, MCP-1 and TGF-β1 in pregnant women with T1DM along with a stimulating effect on the synthesis of each other may cause acceleration of development of nephrosclerosis.

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SENSOR-AUGMENTED INSULIN PUMP THERAPY AS BEST METHOD TO SWITCH FROM INSULIN TO SULPHONYLUREA IN INFANT WITH PERMANENT NEONATAL DIABETES MELLITUS

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Introduction: Neonatal diabetes mellitus (NDM) is a rare disease requiring insulin treatment. NDM presents complex management of glycemic control, due to the need of small insulin doses, the lack of subcutaneous fat and the frequency of meals. The availability of sensor-augmented insulin pump therapy (SAP) provides an opportunity to monitor glucose levels more closely and deliver insulin more safely in these patients.

Case report: A male infant was born by caesarean section; on the first day of life blood glucose (BG) concentration was 198 mg/dl (11.0 mmol/L) and intravenous insulin treatment was started. At 33 days of life, intravenous treatment was stopped and sensor-augmented insulin pump therapy was started. The insulin-starting dose was 0.75 IU/Kg of body weight; the insulin was administered as a single basal rate (0.05 IU/h, 40% of the insulin total dose) and meal boluses (0.20 IU every meal, 60% of the insulin total dose). Using SAP the glycemic variability was reduced.

A genetic diagnosis of KIR6.2 V59M mutation was performed and an attempt of switching therapy, from insulin to oral sulfonylurea (glibenclamide), was done. Because of considerable improvement of BG control, insulin therapy was stopped. After a week, there was marked improvement in the glycaemic control.

Conclusions: During neonatal period, use SAP therapy is safe, accurate and easier for the management of insulin administration. Moreover, SAP therapy is considered really useful during the switch of therapy from insulin to glibenclamide.

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INDIVIDUALS WITH TYPE 1 DIABETES PREVIOUSLY TREATED WITH MDI OR EARLIER GENERATION INSULIN PUMPS PREFERED LATEST GENERATION INSULIN PUMP

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Aims: The effects of transition to recently available insulin pumps from multiple daily insulin injections (MDI) or earlier generation insulin pumps have not been well studied. We assessed treatment satisfaction among users of the Animas® Vibe™ insulin pump, a latest generation insulin pump (LGIP) system (continuous glucose monitoring (CGM)-enabled), after switching from MDI or an earlier generation pump.

Methods: Individuals with T1D from 82 centers in five countries participated. We administered a 50-item online

Figure 1. Respondent ratings of LGIP use compared with previous treatment
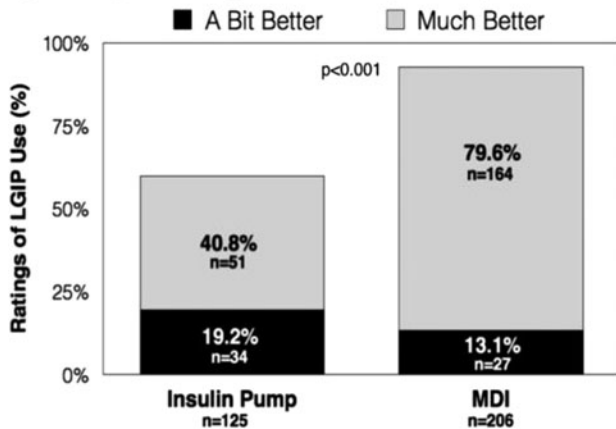
questionnaire that assessed preference for using the LGIP compared with previous treatment and other factors.

Results: A total of 356 individuals, age 12–79 years, responded to the survey: mean (SD) age 38.4(16.1) years; diabetes duration 19.1(13.3) years; and female 59%. Among respondents, 38% (n=135) reported previous treatment with an earlier generation pump, 61% (n=215) reported previous MDI treatment and 1% (n=4) reported no previous treatment. Most (83%) rated the LGIP to be better than their previous insulin delivery system: 65% 'much better', 18% 'a bit better'. A significantly greater percentage of respondents with previous MDI rated the LGIP 'much better' or 'a bit better' compared with prior insulin pump users (p (**Figure 1**). Preference for the LGIP was particularly notable among the youngest and oldest previous MDI users: 83% (12–17 years) and 88% (50–79 years) rated the LGIP 'much better'.

Conclusions: Use of the Animas® Vibe™ was perceived as a better method of insulin delivery among individuals with T1D regardless of previous insulin therapy or age but particularly among previous MDI users.

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PUMP USERS AND INSULIN INFUSION SETS DURING FINANCIAL CRISIS: A MATTER OF CONSIDERATION?

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Continuous Subcutaneous Insulin Infusion (CSII) treatment has been shown to be effective in the improvement of glycaemic control in patients with Type 1 Diabetes Mellitus. However there is evidence that precise insulin delivery could be disrupted if Pump users keep the infusion set in place too long. In Greece, during the culmination of the financial crisis between the years 2012–2013 were reported critical delays in the reimbursement of Insulin Pump consumables. We reviewed retrospectively the medical records of 60 patients on long term Insulin Pump use who were regularly followed up in our Center (35 females-25 males, mean ± SD age = 37.4 ± 11.8 years, BMI = 24.5 ± 3.9 kg/m², diabetes duration = 22.5 ± 8.8 years, Pump use = 6.7 ± 3.2 years). CSII use resulted in impressive decrease in mean HbA1c (9.5 ± 1.9 versus 7.3 ± 0.9%, p < 0.001). However, during the

crisis period it was observed a significant deterioration of HbA1c (7.7 ± 0.9% vs 7.3 ± 0.9%, p < 0.001). It is noticeable that HbA1c was renormalized after the amelioration of the financial situation of the country, which was started in the end of 2013 (7.7 ± 0.9% vs 7.4 ± 0.9%, p = 0.004). In total 32 patients were affected by the crisis. In this group, 24 patients performed less frequent infusion set changes (the average duration of infusion set use was 8.2 ± 10 days vs 3.7 ± 9 before the crisis, p < 0.001) and 8 patients discontinued the Pump. This fact was combined with deterioration of glycaemic control (HbA1c = 7.2 ± 0.8 vs 7.9 ± 0.9, p < 0.001). Moreover, during 2014 these patients exhibited improved HbA1c values (7.2 ± 0.8 vs 7.9 ± 0.9, p < 0.001) which was associated with decreased duration of catheter use (5 ± 10 days vs 8.2 ± 10 p = 0,003).

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EFFECT OF SENSOR AUGMENTED PUMP TREATMENT ON FEAR OF HYPOGLYCEMIA AND QUALITY OF LIFE IN SUBJECTS WITH DYSREGULATED TYPE 1 DIABETES

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Aim: To investigate the effect of one year of sensor augmented pump (SAP) treatment on the quality of life of subjects characterized by dysregulated type 1 diabetes or hypoglycaemia concerns.

Methods: We conducted a one year study in 64 patients (32 male and 32 female) with dysregulated type 1 diabetes (HbA1c > 8.5%), or problematic hypoglycaemia, as they were offered SAP. Quality of life was evaluated by the Hypo Fear Scale (HFS), Problem Areas in Diabetes (PAID), and WHO5. Non-parametric statistical analyses were used to compare responses before and one year after SAP was initiated. Data are expressed as mean ± sem.

Results: Baseline HbA1c was 75.3 ± 1.5 mmol/mol (n = 64), HFS 38 ± 3 (n = 53), PAID 26.6 ± 2.6 (n = 54), and WHO5 302.7 ± 13 (n = 59). After one year 48 patients (75%) were still using SAP. Sensor use was 9.0 ± 0.6 out of 12 months. HbA1c decreased in both SAP users and in those who stopped using SAP (from 73.8 ± 1.6 to 66.1 ± 1.7 [n = 48; p < 0.0001] and 80.3 ± 3.5 to 72.9 ± 3.2 [n = 14; p = 0.001], in users and non-users, respectively). There was no correlation between time on SAP and HbA1c lowering. By 12 months HFS had decreased significantly (from 38.1 ± 3.2 to 28.9 ± 3.4; n = 39, p = 0.001), as had PAID (from 25.2 ± 2.6 to 20.9 ± 2.6; n = 41, p = 0.007), whereas there was no difference in WHO5.

Conclusion: Apart from a significant improvement in HbA1c, SAP seems to offer specific support concerning the fear of hypoglycaemia and diabetes related distress to subjects with type 1 diabetes who are prone to hypoglycaemia with no impact on overall wellbeing of patients.

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USER PERFORMANCE EVALUATION OF THE CONTOUR TS BLOOD GLUCOSE MONITORING SYSTEM WITH AN UPDATED METER ALGORITHM

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Table 1. Summary of BGMS Accuracy Results

		Percent of meter results within specified error limits (glucose values <100 mg/dL [5.6 mmol/L])					Percent of meter results within specified error limits (glucose values ≥100 mg/dL [5.6 mmol/L])			
Test	N	±5 mg/dL (0.3 mmol/L)	±10 mg/dL (0.6 mmol/L)	±15 mg/dL (0.8 mmol/L)*	±20 mg/dL (1.1 mmol/L)	N	±5%	±10%	±15%*	±20%
Fingertip subject self-test	19	52.6%	94.7%	100.0%	100.0%	113	56.6%	84.1%	95.6%	99.1%
Fingertip staff test	19	78.9%	84.2%	100.0%	100.0%	114	58.8%	88.6%	98.3%	99.1%
Palm subject self-test	16	43.8%	87.5%	93.8%	100.0%	113	40.7%	82.3%	93.8%	98.2%
Venous test	24	79.2%	95.8%	100.0%	100.0%	107	82.2%	97.2%	100.0%	100.0%

BGMS, blood glucose monitoring system.
*ISO 15197:2013 Section 8 accuracy criteria.

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Background: This study assessed the accuracy and ease of use of an updated CONTOUR TS blood glucose monitoring system (BGMS) when used by untrained lay users with diabetes and study staff. This CONTOUR TS meter contains an updated algorithm for measuring blood glucose and uses the currently available CONTOUR TS test strips.

Methods: 134 subjects with type 1 (42.5%) or type 2 (57.5%) diabetes were enrolled at 2 clinical sites. Untrained subjects performed fingertip and palm alternative site testing (AST) self-tests. Study staff tested subjects' fingertip and venous blood. BGMS results were compared with YSI reference results. Accuracy was assessed using ISO 15197:2013 Section 8 accuracy criteria ($\geq 95\%$ of results within ± 15 mg/dL [0.8 mmol/L] and $\pm 15\%$ of reference at YSI glucose concentrations < 100 mg/dL [5.6 mmol/L] and ≥ 100 mg/dL [5.6 mmol/L], respectively). Per ISO15197:2013 Section 8, subjects completed a questionnaire about the ease of use of the BGMS and the user instructions (acceptance criterion was $\geq 90\%$ of subjects responding 'strongly agree,' 'agree,' or 'neutral' to each of 6 statements).

Results: BGMS accuracy results are shown in **Table 1**. ISO 15197:2013 accuracy criteria were met by 96.2% of subject fingertip, 98.5% of study staff fingertip, 93.8% of subject palm, and 100% of venous results. Additionally, $\geq 98.5\%$ of subjects responded 'strongly agree,' 'agree,' or 'neutral' to all ease of use questionnaire statements.

Conclusion: The CONTOUR TS BGMS exceeded ISO 15197:2013 Section 8 accuracy criteria for fingertip testing and demonstrated ease of use in the hands of lay users with diabetes.

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RELEVANCE OF CONTINUOUS GLUCOSE MONITORING SYSTEM IN T1D PATIENTS WITH SUBCUTANEOUS INSULIN PUMP AND CORRECT HBA1C.

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Introduction: Continuous Subcutaneous Insulin Infusion (CSII) should provide a therapeutic optimization in unstable T1D patients. In case of correct glycemic equilibrium, can HbA1c show the real level of variability?

Patients and methods: 49 T1D patients with CSII for 4.1 years, HbA1C $7.3 \pm 0.6\%$ (enrolled if HbA1c $\leq 8\%$), 52.4 years old, diabetic for 24.8 years, sex ratio (M/F): 0.96, BMI: 26.8 kg/m^{2}, insulin dose 0.6 U/kg/j, were provided with a continuous glucose monitoring system (glucose sensors) during 32.3 ± 1.6 days. The analysis was performed through 2 groups according to HbA1c levels: Acceptable – Group A $< 7.5\%$ (n = 26) and Poor – Group P $\geq 7.5\%$ $\leq 8\%$ (n = 23).

Results: Both groups (A vs P) are different for HbA1c: $6.9 \pm 0.4\%$ vs $7.8 \pm 0.2\%$ - Δ : 0.9% -p < 0.05 and are compared for average blood glucose levels : 1.44 ± 0.22 vs 1.57 ± 0.25 gr/l - Δ : 0.13 gr/l - p < 0.05, standard deviation : 0.53 vs 0.59 gr/l - NS, average highest blood glucose levels : 2.95 vs 2.91 gr/l - NS and lowest blood glucose levels : 0.51 vs 0.51 gr/l - NS - difference: 2.44 vs 2.40 gr/l. Glycemic variability (standard deviation/average of blood glucose levels $\times 100$) : 36.8% vs 37.6% is not different, while the average number of hypoglycemias (< 0.7 gr/l) : 26 ± 36 vs 41 ± 55 per day: 1.6 ± 2.7 vs 2.6 ± 4 is higher in the group P, but not significantly.

Conclusion: Continuous glucose monitoring system in T1D patients with CSII and HbA1c $< 8\%$, shows the persistence of a sensible glycemic variability, with a visible hypoglycemic tendency in the worst controlled T1D patients (rebound hyperglycemia?).

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A MULTICENTER EVALUATION OF THE ACCURACY OF THE CONTOUR©XT GLUCOSE METER FOLLOWING ISO 15197:2013, FDA AND CLSI ACCURACY CRITERIA

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A multicenter study was carried out in 21 Spanish Hospitals to evaluate the performance of the Contour®XT glucose meter, under routine conditions, compared to the hexokinase method.

Each site measured glucose in 100 venous blood samples (range 33 mg/dL to 562 mg/dL) with a Contour®XT and the laboratory analyzer hexokinase method.

The time between the Contour®XT measurement and the centrifugation to obtain plasma hexokinase measurement was controlled to be $< 10'$.

At each site, the Contour®XT results were compared to the respective hexokinase method, to determine if they fulfilled the following accuracy criteria:

ISO 15197:2013.- $\geq 95\%$ of results must be within either ± 15 mg/dL of the analyzer result, for glucose < 100 mg/dL, or $\pm 15\%$ for glucose ≥ 100 mg/dL.

FDA DRAFT SMBG/OTC 2014 Guidance

a) $\geq 95\%$ of the results must be within $\pm 15\%$ of the analyzer results (entire range).
b) $\geq 99\%$ of the results must be within $\pm 20\%$ (entire range).

Clinical Laboratory Standards Institute (CLSI)

a) $\geq 95\%$ of the results must be within either ± 12 mg/dL of the analyzer result, for samples < 100 mg/dL, or $\pm 12.5\%$ for samples ≥ 100 mg/dL.

b) ≤2% of results present differences >20% when glucose is ≥75 mg/dL or >15 mg/dL when glucose is <75 mg/dL.

Results (table)-

Criteria	Definition	Minimum % Acceptable	% Obtained
ISO	±15 mg/dL (laboratory <100 mg/dL) or ±15% (laboratory ≥ 100 mg/dL)	95,0	99,43
CLSI-a	±12 mg/dL (laboratory <100 mg/dL) or ±12.5% (laboratory ≥ 100 mg/dL)	95,0	98,52
CLSI-b	>15 mg/dL (laboratory <75 mg/dL) or >20% (laboratory ≥75 mg/dL)	≤2	0,43
FDA-a	≤15% (any laboratory value)	95,0	98,91
FDA-b	≤20% (any laboratory value)	99,0	99,52

Discussion.- This is one of the few multicenter studies performed with a glucose meter. Overall results exceed the accuracy requirements of the ISO 15197:2013, FDA and CLSI criteria. In conclusion, Contour XT tested under daily routine conditions was found to be a highly accurate and robust blood glucose monitoring system.

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LOWER HBA1C LEVEL IS ASSOCIATED WITH LOWER BLOOD GLUCOSE VARIABILITY IN TYPE 2, BUT NOT IN TYPE 1 DIABETES

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The risk of vascular complications is elevated also in diabetes patients with good glucose control. Blood glucose variability (BGV) has been shown to be a likely contributor to this risk as it may be increased even in the subjects with optimal HbA1c values. Continuous glucose monitoring (CGM) enables assessment of BGV. We conducted a study aiming to evaluate BGV in patients with type 1 (n = 40) and type 2 (n = 40) diabetes divided into groups with good (HbA1c ~ 7%) and poor (HbA1c ~ 10%) control: DM1 7%; DM1 10%; DM2 7%; and DM2 10% (each group n = 20). Mean age of subjects, duration of diabetes, BMI and HbA1c was 43 ± 14, 40 ± 15, 61 ± 10, 64 ± 7 years; 15 ± 11, 13 ± 7, 10 ± 5, 13 ± 7 years; 23.1 ± 3.1, 25.0 ± 4.2, $30,4 \pm 5.2$, 32.6 ± 5.5 kg/m^2; 7.0 ± 0.7, 10.1 ± 1.0, 7.1 ± 0.7, $9.6 \pm 0.7\%$. Each subject underwent blinded CGM (iPro2, Medtronic) for 5.1 ± 0.7 days (number of glucose values recordings was 688 ± 206) and blood glucose coefficient of variability (= SD/mean*100%) was calculated for (Fig. 1). No statistically significant differences between subjects with good or poor glucose control within each diabetes type was found, with lower BGV in DM2 than in DM1 and higher in the evening than in the morning. The tendency towards greater BGV in DM1 with lower rather than higher HbA1c values was noted, and the opposite trend was found in individuals with DM2. We conclude that BGV is independent of glucose control level and it may contribute to the risk of vascular complications in all patients with diabetes, particularly in individuals with type 1 diabetes and low HbA1c values.

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ENLITE3 CONTINUOUS GLUCOSE SENSOR ACCURACY DURING INPATIENT AND OUTPATIENT HYBRID CLOSED-LOOP CONTROL WITH MEDTRONIC 670G SYSTEM

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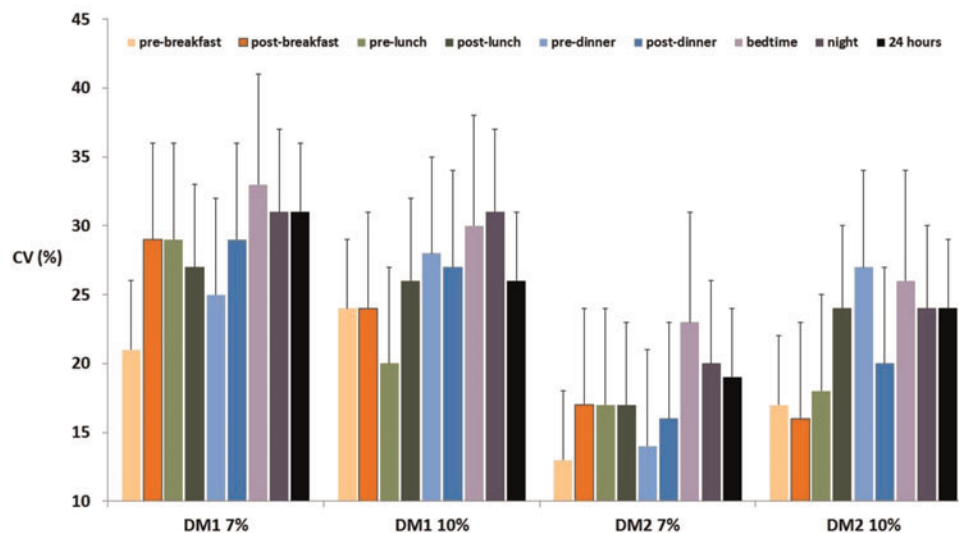
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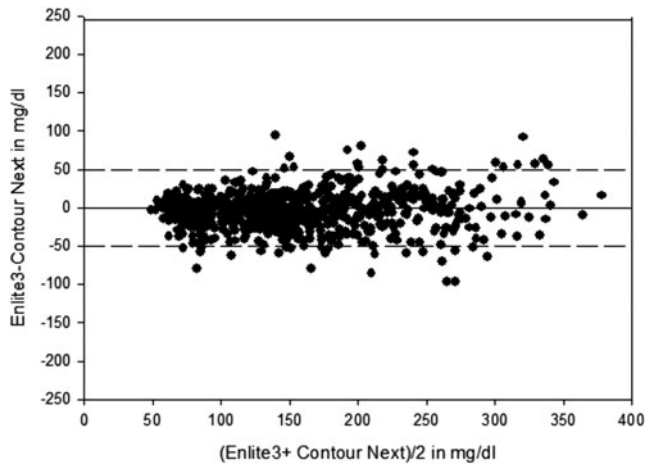[3]Clinical Research, Medtronic Minimed, Northridge, USA

Background: The Medtronic 670G is the first fully integrated hybrid closed-loop system and utilizes the new Enlite3 glucose sensor. While conducting inpatient and diabetes camp closed-loop studies, accuracy of the Enlite3 sensor under these conditions was assessed.

Methods: Enlite3 values were compared to a reference plasma glucose, obtained hourly and measured by YSI over 48 hours during an inpatient admission in 8 subjects, aged 15–18 y. This was followed by a camp study where 10 subjects, aged 15–35 y,

Figure 1. Blood glucose coefficients of variability (CV) for periods of day in each study group.

Precision Analysis

	n = 67,951
Percent ARD	9.8 ± 9.9%
PCV	6.9 ± 7.0%

Accuracy Analysis

	Sensor in normal tissue n = 1,020	Sensor in lipohypertrophy n = 1,029
Mean MARD	15.6 ± 16.5%	14.2 ± 15.5%
Median MARD	11.4% (IQR: 5.6, 20.2%)	10.4% (IQR: 4.4, 18.6%)

wore the Enlite3 over 6 days, and sensor glucose values were compared to Bayer Contour Next meter glucose values. Meter readings used the second drop of blood after cleaning with alcohol or hand washing.

Results: From the inpatient studies, the mean absolute relative difference (ARD) ± SD of the Enlite3 was 10.8 ± 10.2% (range for individuals 8.8–14.3%) and median ARD (IQR) was 8.1% (3.8, 14.7) (range for individuals of 6.2–11.1%), n = 383.

From the camp study, the mean ARD was 12.6 ± 11.0% (range for individuals 9.8–15.1%) and median ARD was 9.7% (4.7, 17.6) (range for individuals 6.5–13.8), n = 742. A Bland-Altman plot for the camp data is given in the figure above.

Conclusion: The Enlite3 sensor did not show a significant bias over the range of glucose values tested and had a median ARD of < 10% in both the inpatient and camp studies.

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EFFECT OF LIPOHYPERTROPHY ON CONTINUOUS GLUCOSE SENSOR PERFORMANCE IN PATIENTS WITH TYPE 1 DIABETES

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Areas of lipohypertrophy are commonly used for continuous glucose monitor (CGM) sensor sites, but the effect on sensor performance is unknown.

We analyzed data from 23 subjects aged 29 ± 9 years with type 1 diabetes (mean A1c 7.5 ± 0.8%) on insulin pump therapy, with at least one area of moderate lipohypertrophy (≥ 3 cm). Subjects wore two Dexcom G4P sensors simultaneously: one in lipohypertrophy, one in normal tissue and this was repeated for an additional week. Precision analysis was performed on matched sensor glucose pairs in lipohypertrophied and normal tissue. Bayer® Contour Next (CN) readings were used as reference values for accuracy analysis.

There were 67,951 matched sensor glucose values available for precision analysis with 1,029 CN readings for accuracy analysis. Overall precision derived by the mean paired sensor coefficient of variation (PCV) was 6.9%, which compares well with published Dexcom G4 PCV of 7% in normal tissue (Christiansen et al. DTT 15:881, 2013). The overall mean

absolute relative difference (MARD) for sensors in lipohypertrophy was 10.4%, (IQR: 4.4, 18.6%) versus normal tissue 11.4%, IQR: 5.6, 20.2% (P = 0.006).

These data suggest that lipohypertrophy may not have a negative impact on CGM sensor performance.

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CLINICIAN'S PERCEPTION OF HYPOGLYCAEMIA IS INCREASED BY CONTINUOUS GLUCOSE MONITORING

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Background: Intensive insulin treatment increases exposure to hypoglycaemia, which can have a significant impact in the patient morbidity and mortality. The ability to better predict and identify the patients at risk of developing hypoglycaemia could reduce its occurrence. Our aim was to assess the concordance of clinician's perception of hypoglycaemia with continuous glucose monitoring (CGM).

Research Design and Methods: We retrospectively analysed 62 CGMs from 61 patients with type 1 diabetes. Patients were stratified in two groups based on the motive pointed out by the clinician to undertake the CGM: suspicion of hypoglycaemia (group A) and without suspicion of hypoglycaemia (group B). iPro™2 CGM device (Medtronic, Northridge, CA) was used in all patients.

Results: A total of 9,392 hours of continuous glucose monitoring were analysed. Patients from group A were more time in hypoglycaemia than the group B (9.6% versus 7.7%) and more prone to hypoglycaemic excursions (16.0% versus 13.4%), though percentage coefficient of variation (%CV) was 46.5% and 46.8%, respectively (p = 0.231). Approximately half of hypoglycaemia time occurred during the weekend. Nocturnal hypoglycaemia was equally prevalent in both groups (9.6% and 8.6% for group A and B, respectively), mean glucose was 158 mg/dL in both groups with a %CV of 45.2% and 48.1% for groups A and B (p = 0.714), respectively.

Conclusions: CGM improves the recognition of hypoglycaemia in subjects without previous suspicion. The precocious identification of these patients allows the development of preventive efforts and close monitoring of those at risk.

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RETROFITTING DEXCOM G4 TRACES ALLOWS BETTER ASSESSMENT OF OUTPATIENT GLUCOSE CONTROL

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Objective: In artificial pancreas outpatient trials glucose-control metrics are calculated using Continuous Glucose Monitoring (CGM) data. However, CGM-based metrics may be under/overestimated because of possible CGM inaccuracy. Recently, we proposed a 'retrofitting' algorithm (Del Favero et al., IEEE TBME 2013) to retrospectively improve CGM accuracy and showed its efficacy on Dexcom SEVEN Plus data (Del Favero et al., ATTD 2013). Here we assess the same method on Dexcom G4 data.

Method: The retrofitting method produces accurate continuous-time blood glucose (BG) profile by simultaneously exploiting a few BG references and the CGM trace. The algorithm was tested in 72 subjects, studied for seven days with the Dexcom G4 Platinum (Christiansen et al., DT&T 2013). In study days 1, 4 and 7, frequent YSI measurements were also collected for 12 hrs. About 5 references/admission were used to feed the algorithm, while the remaining as test set ($>85\%$).

Result: The retrofitted CGM profiles resulted more accurate than the original CGM: MARD was reduced from 17.16% to 12.03% (day 1), from 11.42% to 8.35% (day 4) and from 12.03% to 7.21% (day 7). Use of retrofitted CGM reduces also the error in time-in-target evaluation with respect to the original CGM: from 10.32% to 5.18% (day 1), from 5.95% to 4.66% (day 4) and from 7.29% to 4.78% (day 7).

Conclusion: Retrofitting Dexcom G4 traces increases their accuracy and reduces the errors in assessing glucose-control with respect to the use of the original CGM.

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USE OF INSULIN-BOLUS CALCULATOR FREE STYLE INSULINX® IN DIABETES TYPE-1 PATIENTS TREATED WITH BASAL-BOLUS INSULIN REGIMEN

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Self-monitoring of blood glucose improve diabetes management. However, many patients are unable to use that information for their daily care, especially on insulin-regimen. Now, there are available a new generation glucometers designed to simplify the patient's life and help him making treatments decisions, according to different variables. There are many clinical studies in diabetes type 1 patients treated with continuous subcutaneous insulin infusion but reports with patients on basal-bolus insulin-regimen are scarce. The aim of this study is to evaluate the impact of glucose bolus calculator in metabolic control in real clinical practice in diabetes type 1 patients on basal-bolus-regimen.

We evaluated six-months efficacy of bolus calculator (Free Style Insulinx®, Abbott Laboratories, Illinois, EEUU) on long-term glycemic control in seventy-five type 1 diabetes patients (27 males, 48 females, age 32.7 ± 14.6 years-old, duration of diabetes 10.9 ± 6.4 years) treated with basal-bolus insulin-regimen that started using a bolus calculator. The mean initial HbA1c was 8.3% and the mean final HbA1c was 7.5%. HbA1c decreased significantly after six months with bolus calculator ($-0.53 \pm 0.23\%$, p = 0.03).

82.6% of patients think that bolus calculator facilitates the choice of postprandial insulin. 64% of patients do more glycemic controls after the use of calculator. 46.6% patients reduced the fear to hypoglycemia.

Although our study was only a prospective observation we suggest that insulin bolus calculators help to improve metabolic control adherence to treatment, decrease the fear of hypoglycemia and provides daily patient management.

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EFFECTS ON GLYCEMIC VARIABILITY, GLYCO-METABOLIC CONTROL AND PATIENTS' SATISFACTION OF AN INSULIN PUMP INTEGRATED WITH CONTINUOUS GLUCOSE MONITORING SYSTEM IN TYPE 1 DIABETIC PATIENTS

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Aim: to evaluate the effects of an insulin pump integrated with continuous glucose monitoring system (CGMS) compared to insulin pump alone on glycemic control, and blood glucose variability in type 1 diabetic patients, in a case-control clinical trial. We also evaluated the degree of patients' satisfaction to treatment.

Methods: we enrolled 20 type 1 diabetic subjects, with an inadequate glycemic control (glycated hemoglobin $>7.5\%$), with an insulin pump from at least three months. At baseline, patients were instructed to use a CGMS able to communicate with the insulin pump (Medtronic MiniMed Paradigm Veo) in an integrated system. The function of suspension of insulin delivery, in case of hypoglycemia, was activated. We evaluated: anthropometric measurements, glycemic variability, glycated hemoglobin, fasting plasma glucose (FPG), post-prandial glucose (PPG). These parameters were recorded at baseline, at 3 and 6 months after the placement of the device.

Results: after 6 months since the placement of the integrated system, there was a decrease of glycated hemoglobin. The daily blood glucose variability, expressed as mean amplitude of glycemic excursions, was reduced after the placement of the integrated system. Also the glycemic variability from day to day was reduced compared to insulin pump alone. In addition, we recorded an improvement of the score at the Diabetes Treatment Satisfaction Questionnaire, meaning an increase of patients' satisfaction toward treatment.

Conclusions: the insulin pump integrated with CGMS better improved glycemic control, glycemic variability and patients' satisfaction in type 1 diabetic patients compared to insulin pump alone.

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EFFECTS OF TWO DIALYSIS TECHNIQUES ON GLYCEMIC EXCURSION AND INFLAMMATION IN PATIENTS WITH AND WITHOUT TYPE 2 DIABETES MELLITUS

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Aim: to evaluate the effects on glycemic excursion and on some inflammatory parameters during bicarbonate dialysis (BHD) compared to hemodiafiltration (HDF).

Methods: thirty-six patients (20 affected by type 2 diabetes mellitus, and 16 not diabetic patients) were evaluated and underwent a BHD dialysis, followed by a HDF dialysis two days later. We measured: fasting plasma glucose (FPG), fasting plasma insulin (FPI), HOMA-IR, lipid profile, high sensitivity C-reactive protein (hs-CRP), lipoprotein (a) [Lp(a)], metalloproteinases-2, and -9 (MMP-2 and MMP-9), interleukins 6 (IL-6), and -8 (IL-8), and soluble receptor for advanced glycation end products (sRAGE). All patients underwent a glucose continuous monitoring system, using *i*Pro Continuous Glucose Monitor System (Medtronic MiniMed) starting just before the BHD, and ending five days later, two days after the HDF dialysis.

Results: we observed a decrease of glycemic excursions during HDF dialysis. In particular, in type 2 diabetic patients, standard deviation and mean blood glucose were lower with HDF compared to BHD. Area under the glucose curve > 180 mg/dl was lower during HDF. The mean amplitude of glycemic excursions value was lower with HDF. Regarding inflammatory parameters, we observed a decrease of Hs-CRP, MMP-2 and -9 after HDF, but not after BHD. We observed a decrease of sRAGE with BHD, but not with HDF. Moreover, in type 2 diabetic patients, there was a significant correlation between glycemia and MMP-9, and between glycemia and Lp(a).

Conclusion: HDF seems to greater reduce glycemic excursions during the treatment compared to BHD, and to better decrease some inflammatory markers.

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GLYCATED ALBUMIN AS A MARKER OF GLYCEMIC CONTROL IN HEMODIALYSIS PATIENTS WITH TYPE 2 DIABETES

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Aim: To compare glycated albumin (GA) and HbA1c in the assessment of glycemic control in hemodialysis patients with diabetes mellitus type2 (DM2).

Patients and Methods: We studied 23 hemodialysis patients with DM2 (12 men), age: 60.9 ± 16.7 years, HbA1c: $6.3 \pm 1.3\%$

and GA: $29.7 \pm 9.0\%$. Seven day continuous glucose monitoring system was placed on the patients (iPro2 CGM). The mean (Glu: 158.7 ± 41.1 mg/dl) and the standard deviation of glucose (SDglu: 50.2 ± 19.0 mg/dl) were correlated with HbA1c and GA. ROC analysis was performed to determine which of the two methods detects better average glucose value ≥ 154 mg/dl, which corresponds to a HbA1c value > 7%.

Results: We found a strong positive correlation between HbA1c, and Glu, HbA1c and SDglu GA and Glu, and GA and SDglu ($p < 0.001$, $p < 0.015$, $p < 0.001$, $p < 0.001$ respectively). There were no significant relationships between GA and age, BMI, Hb, Ht, CRP, serum albumin, ferritin, transferrin and transferrin saturation. In ROC analysis, the area under the receiver operating curve was higher with GA than HbA1c (0.964 vs. 0.945) for detecting average glucose values ≥ 154 mg/dl.

Conclusions: In hemodialysis patients with type 2 diabetes, glycated albumin was shown to correlate strongly with the level of glycemic control without being affected by serum albumin, markers of inflammation, and the hematological profile of the patients. Compared with HbA1c, GA appears to detect better uncontrolled diabetic patients.

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### INTENTIONAL LARGE INSULIN OVERDOSE CAPTURED ON A CONTINUOUS GLUCOSE MONITOR: A NOVEL CASE REPORT

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Continuous glucose monitoring (CGM) is an important therapeutic and educational tool in type 1 diabetes management. We
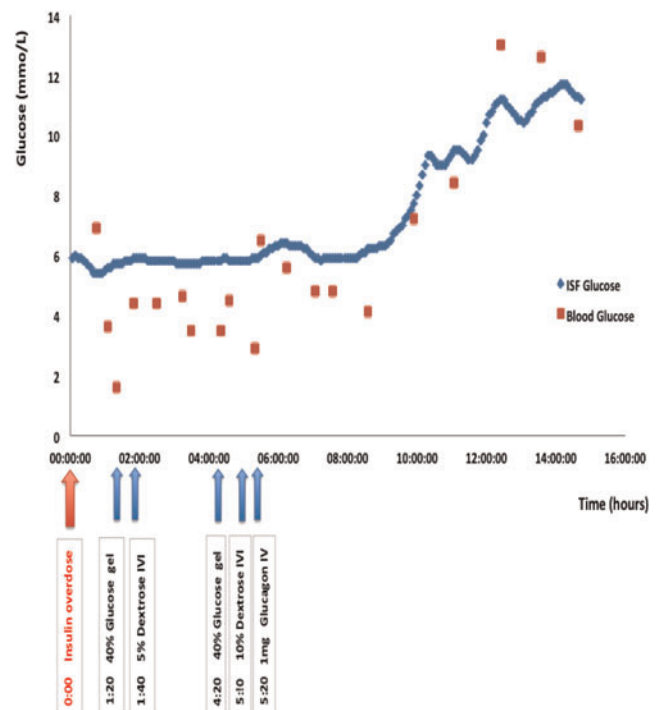
present a case of deliberate insulin overdose in a patient with type 1 diabetes wearing blinded CGM.

A 25-year-old man with type 1 diabetes diagnosed aged 10 complicated by pre-proliferative retinopathy, microalbuminuria, recurrent diabetic ketoacidosis and a personality disorder had multiple previous presentations with deliberate self-harm including an insulin overdose. A period of CGM using a Medtronic iPro2 system was arranged to guide intensification of insulin therapy. On day six of the monitoring period, he presented to the emergency department with a deliberate overdose of 300 units of insulin aspart. His venous blood glucose was 1.6 mmol/L, serum insulin 452.3 mu/L (fasting reference range 3 – 15 mu/L) at admission. He was treated with dextrose infusion, glucagon injection, and 40% glucose gel over 9 hours with in-patient monitoring for 36 hours. At the end of day 7, the CGM was removed and data downloaded. The sensor failed to detect biochemically proven severe hypoglycaemia with sensor glucose reported between 5–6 mmol/L. The mean absolute difference (MAD%) in the 9 hours post insulin overdose was 52%, indicating poor accuracy. Despite clinical benefits, CGM devices remain inaccurate in the hypoglycaemic range. We present the first reported case of deliberate insulin overdose captured on CGM, highlighting an important limitation of existing CGM technology, with the reduced sensor accuracy in the hypoglycaemic range.

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EFFECT OF REAL-TIME CONTINUOUS GLUCOSE MONITORING ON MEASURES OF GLYCEMIC VARIABILITY AND QUALITY OF GLYCEMIC CONTROL IN TYPE 1 DIABETES

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Background & objective: There is evidence supporting a role for glycemic variability (GV) in the pathogenesis of diabetes-
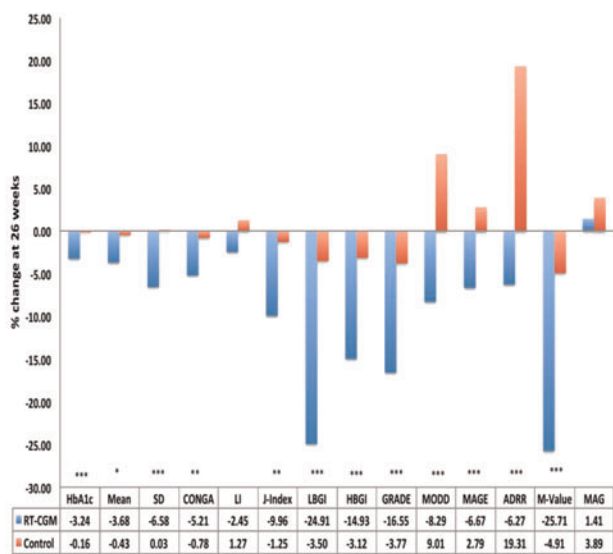

Figure 1 showing the effect of RT-CGM at 26 weeks on % change in the mean of various measures of GV and glycemic control in comparison to control group. *** P<0.001, ** P<0.01, *p<0.05. [SD: standard deviation, CONGA: continuous overall net glycemic action, LI: liability index, LBGI: low Blood glucose Index, HBGI: high blood glucose index, GRADE: glycemic risk assessment diabetes equation, MODD: mean of daily differences, MAGE: mean amplitude of glycemic excursions, ADRR: average daily risk range, MAG: mean absolute glucose].

related complications. Several indices have been described for estimating GV and quality of glycemic control. However, there is a lack of consensus on a gold standard measure. We describe the effect of real time continuous glucose monitoring (RT-CGM) on GV indices in a large cohort of people with type 1 diabetes.

Method: CGM data from subjects with type 1 diabetes in the JDRF CGM randomised control study were processed using EasyGV software (v8.8.2R2). Subjects were randomised to either standard self-monitoring of blood glucose (SMBG) (control, n = 217) or additional use of RT-CGM (intervention, n = 231). At 26 weeks, subjects in the control group underwent 96 hours of blinded-CGM.

Results: At 26 weeks, results available from all subjects in the intervention group and from 214 subjects in the control group showed significant reduction in the majority of measures of GV and quality of glycemic control from baseline in the intervention group. The largest reductions were in M-value, low blood glucose index (LBGI) and glycemic risk assessment diabetes equation (GRADE) with reductions of 25.7%, 24.9% and 16.5% respectively (P < 0.001). In comparison, there was no statistically significant reduction in any of the GV measures in the control group at 26 weeks compared to baseline.

Conclusion: RT-CGM reduces GV and improves measures of glucose risk compared with SMBG in children, adolescents and adults with type 1 diabetes. This may be important in minimising the risk of diabetes complications.

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FACTORS PREDICTIVE OF EFFECT OF REAL-TIME CONTINUOUS GLUCOSE MONITORING ON MEASURES OF GLYCEMIC VARIABILITY AND QUALITY OF GLYCEMIC CONTROL IN TYPE 1 DIABETES

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Background & objective: Glycemic variability (GV) may contribute to the pathogenesis of diabetes-related complications. Several indices have been described to estimate GV with no consensus on a gold standard measure. We evaluated factors predictive of the effect of real time continuous glucose monitoring (RT-CGM) on GV indices in a large cohort of people with type 1 diabetes.

Method: CGM data from subjects with type 1 diabetes in the JDRF CGM randomised control study were processed using EasyGV software (v8.8.2R2). The associations of baseline demographic and clinical factors with change in GV indices from baseline to 6 months were evaluated in the RT-CGM group (intervention, n = 231) using regression models.

Results: Baseline factors found to be associated with greater reduction in measures of GV at 6 months were age [except for mean absolute glucose (MAG) and low blood glucose index (LBGI)] (P < 0.01) and baseline GV (P < 0.001). Treatment with insulin pump predicted a reduction in mean (P = 0.036), J index (P = 0.017), LBGI (P = 0.004), high blood glucose index (P = 0.015), glycemic risk assessment diabetes equation (P = 0.013), M value (P = 0.003) and mean amplitude of glycemic excursions (P = 0.027). Furthermore, frequency of self-reported daily blood glucose monitoring predicted reduction in some measures of GV as seen in table 1.

Conclusion: Older age and higher GV at baseline are associated with greater reduction in GV at 6 month of RT-CGM.

	Significant Predictors	P	Model*	
			R square	P
Δ Mean at 26 weeks	Age	.000	.560	<0.001
	Insulin Modality (Pump)	.036		
	Baseline Mean	.000		
Δ SD at 26 weeks	Age	.000	.470	<0.001
	Daily SMBG readings	.005		
	Baseline SD	.000		
Δ J index at 26 weeks	Age	.000	.533	<0.001
	Insulin Modality (Pump)	.017		
	Daily SMBG readings	.039		
	Baseline J Index	.000		
Δ LBGI at 26 weeks	Insulin Modality (Pump)	.004	.744	<0.001
	Baseline LBGI	.000		
Δ HBGI at 26 weeks	Age	.000	.526	<0.001
	Insulin Modality (Pump)	.015		
	Daily SMBG readings	.024		
	Baseline HBGI	.000		
Δ GRADE at 26 weeks	Age	.000	.568	<0.001
	Insulin Modality (Pump)	.013		
	Baseline GRADE	.000		
Δ MODD at 26 weeks	Age	.000	.514	<0.001
	Daily SMBG readings	.004		
	Baseline MODD	.000		
Δ MAGE at 26 weeks	Age	.000	.672	<0.001
	Insulin Modality (Pump)	.027		
	Daily SMBG readings	.017		
	Baseline MAGE	.000		
Δ ADRR at 26 weeks	Age	.000	.473	<0.001
	Daily SMBG readings	.004		
	Baseline ADRR	.000		

Table 1 showing significant predictors associated with reduction in measures of GV and glycemic control at 6 months in the RT-CGM group. *Predictor variables included in the regression model included : age, gender, race, education level of care giver, insulin modality (pump or MDI), frequency of self-reported blood glucose monitoring per day, frequency of severe hypoglycemia in last 6 months and baseline GV.

Treatment with insulin pump and frequent blood glucose monitoring may also contribute to the long-term benefit of RT-CGM in reducing GV indices.

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THE ADMINISTRATION OF LIGHTENING CREAM CONTAINING HYDROQUINONE PROVOKES FALSELY HIGH RESULTS OF GLUCOSE AND BETAHYDROXYBUTYRATE CAPILLARY MEASUREMENTS

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Background/Objective: In clinical practice the accuracy of capillary glucose and betahydroxybutyrate measurements is essential in the management of hypoglycemic and hyperglycemic disorders. It can be affected by the administration of lightening creams containing hydroquinone.

Case report: A 56-year-old woman originating from Central Africa with a ten-year history of DM-2; presented neurological symptoms such as somnolence, trembling, craving that could evoke the hypoglycemia under treatment by metformin, vildagliptine and detemir. Self-monitoring of blood glucose with One Touch Ultra Easy glucometer showed in the last month persistent hyperglycemia (150–300 mg/dl) in opposite to the hemoglobin A1c which remained at 7%. The glucometer failure was incriminated. At the admission in our unit, capillary glycaemia was high (320 mg/dl) measured by Freestyle Optium glucometer as well as the betahydroxybutyrate value (2.9 mmol/l), there was no acidosis. Despite of continuous insulin infusion those values remained high; however the glycaemia and the betahydroxybutyrate level appeared lower after meticulous hand washing.

We re-interrogated the patient, who admitted using a lightening cream based on hydroquinone. Capillary vs blood level, were tested before and after the cream application. Glucose was measured in capillary at >500 mg/dl (''HI'') and betahydroxybutyrate at 2.8 mmol/l and respectively at 210 mg/dl and 0.4 mmol/l in the blood sample after the cream application.

Conclusions: The administration of lightening cream containing hydroquinone can provoke falsely high results of glucose and betahydroxybutyrate measurements. Physicians should be alerted by the divergence between the results from a self-monitoring of blood glucose with glucometers based on the electrochemical technic and the hemoglobin A1c.

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A NOVEL NON-INVASIVE GLUCOSE MONITOR FOR HOME USE: ASSESSING THE LEARNING CURVE OF USE

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The learning curve, i.e. time required for a layperson to acquire knowledge on proper use and operation of a new device, is an important factor in device acceptance and utilization. GlucoTrack® is a Non-Invasive, CE Mark approved glucose monitoring device for personal use. Assessment of GlucoTrack's acceptance included evaluation of its learning curve of use.

Following individual calibration, measurements' performance using GlucoTrack requires positioning of the sensor-bearing Personal-Ear-Clip (PEC) at the same location as during calibration. When wrongly positioned, the device instructs to adjust location and disables measurement until the PEC is located appropriately. Learning curve of use was assessed in clinical trials, based on the time required to successful positioning of the PEC. Following calibration and training, 42 subjects (variety of demography) conducted measurements by themselves for 3 non-sequential days within a month. The Mean number of Times to Successful PEC Positioning (MTSPP) per measurement (each day) indicates users' proficiency level.

The MTSPP per measurement was found as 1.6 on the first day of use (average proficient users' MTSPP per measurement is 1.2). On second day of use, MTSPP reduced to 1.3 and on the third day to 1.2. No variation was found due to demography.

The results suggest that proficiency in conducting measurements is gained, in average, after about 3 days of use. Furthermore, the most significant increase in PEC positioning skill level is obtained in just one day. Achieving high proficiency level after such short experience should encourage device acceptance among new users.

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ENABLING FREQUENT BLOOD GLUCOSE MONITORING AT HOME USING A TRULY NON-INVASIVE DEVICE

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Blood Glucose (BG) monitor that provides painless, easy and simple use, with acceptable accuracy, may promote frequent self-monitoring. GlucoTrack®, a CE mark approved Non-Invasive BG monitoring device for home-use offers painless way of measurement. It requires individual calibration (once every 6 months), afterwards, enabling virtually unlimited utilization. To evaluate suitability for frequent self-monitoring, GlucoTrack usability, ease of use and accuracy level maintenance (along device's calibration validity period) were assessed.

GlucoTrack usability and accuracy maintenance (throughout 6 months) were evaluated in 198 subjects (12,956 data points). Following calibration, subjects participated in 2–19 non-consecutive full-day sessions. To demonstrate consistency of accuracy, inter-daily performances were analyzed across subjects. Device usability and ease of use were assessed based on users' feedback analysis.

Throughout all trial days, up to 6 months from calibration, results remain similar: $95.9 \pm 3.1\%$ of the points within Clarke Error Grid A + B zones and Mean Absolute Relative Difference of $32.9 \pm 4.2\%$. 86% of the subjects are willing to use the device regularly. 97% declared they will use the device more often than their invasive one. 71% claimed the device is easy to use and 81% found performing measurement easy and simple.

The similar accuracy demonstrated inter-daily during a 6 months period suggests the device accuracy is maintained at any home and home-alike environment, over device's calibration

validity period. The results demonstrate positive user feedback, high satisfaction of use and willingness to increase frequency of self-monitoring. These findings can support frequent use of GlucoTrack for enhanced BG monitoring and tighter glycemic control.

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CARBAWARE, AN ACCELERATED EDUCATION COURSE FOR PEOPLE WITH T1DM USING AN AUTOMATED BOLUS DOSE CALCULATOR

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Introduction: The importance of near normalization of blood glucose (BG) in T1DM is well understood but difficult to achieve. Education programs help achieve these targets but, people may find it difficult to attend prolonged programs. We have designed a short (3 hour) single intense course held at a convenient time for people with T1DM.

Methods: People with sub-optimally controlled T1DM (aged >18 y, duration >1 y, using basal bolus insulin regimen) attended a 3-h group course by skilled diabetes trained dietician covering: food recommendations, self-monitoring of BG techniques, insulin profiles, and appropriate management of hypo- and hyperglycaemia, being taught to estimate the CHO content of foods, and how to calculate insulin-CHO-ratios and insulin sensitivity factors. Patients are shown how to use the bolus calculator function (Aviva Expert, Roche) and provided with this meter.

Results: 45 people (25 male, 39.4 ± 2.3 y) attended the courses. HbA1c fell from **81.5 ± 2.6** at start to **71.0 ± 2.6** mmol/mol at 6 months (p < 0.001). In 7 people there was no change or increase in HbA1c. There were no admissions with DKA or hypoglycaemia. Measures of satisfaction with the course and confidence in use of the meter and bolus dose adjustment function were all high. Patient feedback was universally positive. The unit cost of the course excluding meter and strip costs ranged from £37.50-£60 depending upon group size and attendance rate.

Change in HbA1c following CarbAware
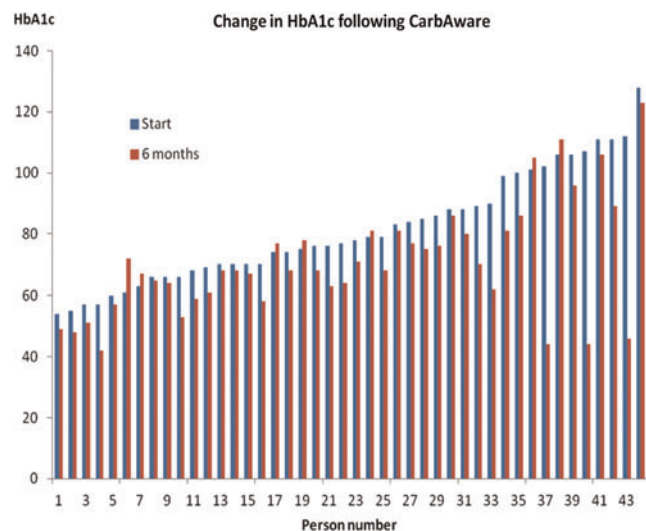
Summary: Use of our 3 h novel carbohydrate counting course (**CarbAware**) combined significantly improves glycaemic control in T1DM, is at low cost and has high patient satisfaction.

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CGMS AND INTENSE EXERCISE IN REAL LIFE

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Aim: was to evaluate the usefulness of CGMS in intense exercise in real life.

Methods: Thirty eight adolescents and young adults, (females/males 20/18), mean age ± SD, 29 ± 11.8 years, mean ± SD disease duration 16.3 ± 9.0 years, participated to a prolonged exercise program, crossing Samaria gorge, covering a distance of 13 km within 5–7 hours. Twenty subjects used Real Time (RT) CGM, 18 blind CGMS (iPRO). The two groups had similar age and HbA1c, but different disease duration. Eighteen subjects were on multiple injections (MDI), 20 on continuous subcutaneous insulin infusion (CSII). Data from RT or iPRO were downloaded the following day after the event.

Results: Subjects with RT had significantly smaller AUC below 70 mg/dl compared with subjects with iPRO during the

whole day of the event p = 0.037. No difference was found for the AUC > 140 mg/dl. No difference was found on the number or duration of hypoglycemic episodes during the event nor time spent > 180 mg/dl. Similarly those on CSII had significantly smaller AUC for blood glucose levels < 70 mg/dl compared with those with MDI (p = 0.025) during the day of the event. Lowering the morning bolus by 30% before the event resulted in high blood glucose levels during the first hour of exercise.

Conclusion: RT was superior to iPro and CSII to MDI in reducing the AUC < 70 mg/dl during a period of intense exercise. Manipulating the basal insulin or the basal rate maybe more preferable to the acute reduction of bolus right before the beginning of prolonged exercise.

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SENSOR-AUGMENTED PUMP THERAPY: ADHERENCE, USAGE AND PATIENTS' SATISFACTION

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The effectiveness of SAP in reducing HbA1c depends on the continuity of the sensor's usage but many patients abandon the sensor.

Aim of this retrospective observational study was to evaluate adherence, way of usage and satisfaction in T1DM patients started SAP in 2008–2012 in our Diabetes Unit.

Methods: A specific questionnaire was administered to 37 patients (16M/21F), 37.13 ± 10.40 yrs; disease duration 19.5 ± 10.12 years; SAP therapy 2.9 ± 1.62 yrs. Ten patients (3M,7F) within one year (4.7 ± 3.8 months) stopped because of SAP complexity (4), ineffectiveness (2), disturbing alarms (1), portability (1) and 1 to return to MDI. The use of sensor was 22.7 ± 7.4 days/month for those who continued (p = 0.001 vs
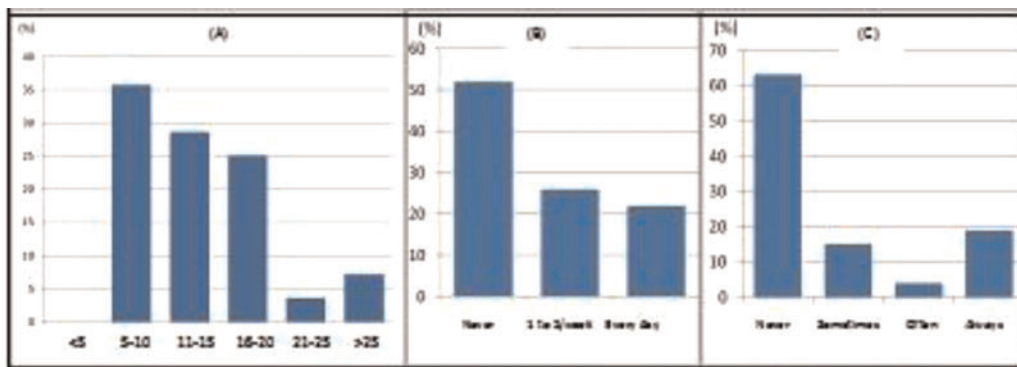

Fig 2. Pts (%) subdivided by number of times/day view of the display (A), the use of silent mode (B) and use of the silent mode for more than 6 hours (C).
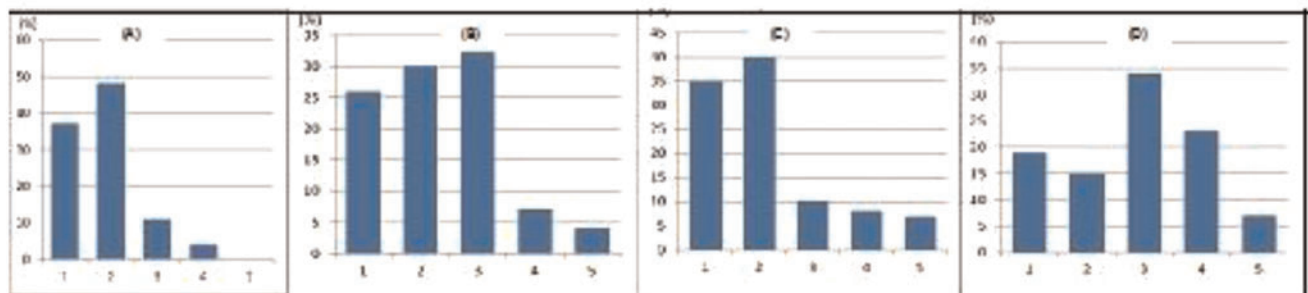

Fig. 3. Pts (%) satisfaction of the sensor's insertion (A), of how to put on the sensor and the transmitter (B), of the use of the uploading system data (C) and of the quality of sleep (D).
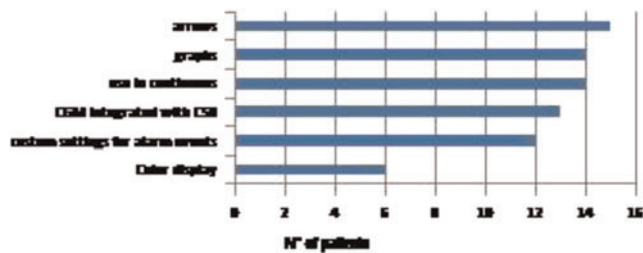
Fig 1. Functions that help the most in improving glycemic control in patients' opinion.

11.1 ± 4,5 days/month of drop out). Predictive factors of stopping were the sensor's usage for less than 50% of the time (p = 0.000) and lower educational level (p = 0.026). In the 27 patients who continued HbA1C reduced at 1 year from 7.9 ± 0.9% to 7.45 ± 0.7% (p < 0.001); higher HbA1C before SAP (p = 0.013), use of calculator bolus (p = 0.025) and older age (p = 0.05) showed a significant predictive value.

Results: Partial data about patients' usage and satisfaction in SAP are shown in Fig 1–3. Patients are aware, in high extent (82%), of the importance of accuracy and calibration, and they tend to use all of the display modes, but especially those from short to medium term (3–6 hours). 82% of patients are able to send data through uploading software analysis.

Conclusions: The analysis reveals that the patients investigated use SAP efficiently, in a qualitatively adequate way and report a good level of satisfaction.

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EVOLUTION OF THE METABOLIC CONTROL AFTER AN INTERVENTION WITH A CGM SENSOR: OUTCOME DURING AND AFTER A PERIOD OF TWO YEARS OF FOLLOW-UP AND MONITORING

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Objective: Assessing the impact of sequential continuous glucose monitoring in a group of unstable and poorly controlled type 1 diabetics, during the intervention period and after the removal of the sensor.

Patients and intervention:

Intervention group: 26 patients with type 1 diabetes, in poor metabolic control (HbA1c > 8%) with 3 determinations,

	BasaL	**12 weeks**	**24 weeks**	**52 weeks**	**104 weeks**
HbA1c (%)					
Intervention	8,81 ±0,86	8,01 ±0,91	8,02 ±0,92	8,08 ±0,93	8,12 ±0,55
Control	8,72 ±0,87	8,24 ±0,72	8,27 ±0,96	8,02 ±0,82	8,32 ±0,43
BMI					
Intervention	25,6 ±3,6	25,9 ±3,7	25,9 ±3,6	26,1 ±3,6	26,3 ±1,7
Control	24,7 ±1,4	24,9 ±1,4	24.9 ±1,6	24,9 ±1,6	25,8 ±1,4
IU					
Insulin/kg					
Intervention	0,62 ±0,1	0,68 ±0,1	0,71 ±0,1	0,74 ±0,1	0,75 ±0,1
Control	0,63 ±0,1	0,63 ±0,1	0,64 ±0,1	0,65 ±0,1	0,64 ±0,1

associated with recurrent hypoglycemia and wide glycemic variability.

Intervention: Changing the overall diabetes treatment based on the results of the continuous glucose monitoring for 7 days with Ipro2 (Medtronic) sensor in the following weeks of the study: basal, 12 and 14.

Control group: 24 similar patients to those in the intervention group, who received conventional medical care in consultations scheduled to happen at the same times that the intervention group.

Results: the table below shows the evolutionary data of metabolic control, BMI and insulin needs of both groups.

Conclusions: After 2 years, the intervention group shows, stable metabolic control, better than before the intervention. The same stability is observed in the evolution of BMI and in increased insulin requirements.

Subjectively, after sequential monitoring, these patients show greater motivation that results in better control and increase in the insulin doses.

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ACCURACY OF BLOOD GLUCOSE DETECTION IN DIABETES ALERT DOGS

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Use of DADs to monitor BG extremes in type 1 diabetes is growing, but there is little data on their accuracy. This study investigated DAD accuracy using owner diaries of daily BG levels and DAD alerts.

Participants were 18 DAD owners (44.4% female; 77.8% children) with T1D, all of whom obtained a DAD from the same training organization. Adults ranged in age from 40-47 yrs ($M = 44.3 \pm 4.4$) and children ranged from 2–15 yrs ($M = 9.1 \pm 4.9$). Participants (or parents) completed diaries, recording all daily BG readings and DAD alerts. Number of days of completed diaries ranged from 5–134 and number of entries ranged from 34–569. For each DAD, % Hits (alert with BG < 5.0 or > 11.1 mmol/L), % Misses (no alert with BG < 5.0 or > 11.1 mmol/L), and % False Alarms (alert with BG > 5.0 and < 11.1 mmol/L) were computed.

Table 1 shows an overview of results. Individual DADs varied greatly in accuracy. For low BG, 50% of DADs hit at rates > 65% and 44.4% hit > 70%. For high BG, 16.7% of DADs hit > 65% and 5.6% hit > 70%.

Table 1. Comparison of Hits to Misses for all out of range, low, and high BG readings

	Average Hit %	Minimum Hit %	Maximum Hit %	Total Number of Entries
Overall	54.4%	39.0%	73.7%	2014
Low BG	65.6%	33.3%	100.0%	584
High BG	52.1%	29.4%	76.9%	1430

Results indicate that DADs may be an effective tool for detecting out of range BG values. However, more research is needed to establish DAD accuracy and identify factors influencing variability of DAD accuracy in BG detection.

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ACCURACY ASSESSMENT OF THE CONTOUR TS BLOOD GLUCOSE MONITORING SYSTEM CONTAINING AN UPDATED METER ALGORITHM

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Background: This study assessed the accuracy of an updated CONTOUR TS blood glucose monitoring system (BGMS) per ISO 15197:2013 Section 6.3 accuracy criteria. This CONTOUR TS BGMS contains an updated meter algorithm and uses currently available CONTOUR TS test strips.

Methods: Using 3 CONTOUR TS test strip lots, fingertip capillary blood samples from 100 subjects were tested. Each sample was tested in duplicate, for a total of 600 results. To obtain reference values for comparison, samples were also tested in parallel on a YSI 2300 STAT Plus glucose analyzer. Evaluation of accuracy was performed according to ISO 15197:2013 Section 6.3 accuracy criteria, which are as follows: ≥95% of results for each test strip lot shall fall within ± 15 mg/dL [0.83 mmol/L] or ± 15% of reference at YSI glucose concentrations.

Results: For test strip lots 1, 2, and 3, 97.0% (194/200), 97.0% (194/200), and 99.0% (198/200) of BGMS results, respectively, fell within ± 15 mg/dL (0.83 mmol/L) or ± 15% of the YSI result (**Table 1**). Thus, all 3 test strip lots met ISO 15197:2013 section 6.3 accuracy criteria. Additionally, 99.7% (598/600) of results fell within Zone A and the remaining 2 results fell in Zone B of the Parkes-Consensus Error Grid.

Conclusion: In this study, the CONTOUR TS BGMS demonstrated accuracy, meeting ISO 15197:2013 Section 6.3 accuracy criteria.

Table 1. Summary of BGMS Accuracy Results

Test strip lot	N	±5 mg/dL (0.28 mmol/L)* or ±5%†	±10 mg/dL (0.56 mmol/L)* or ±10%†	±15 mg/dL (0.83 mmol/L)*‡ or ±15%†‡
		Number of meter results within specified error limits		
Lot 1	200	116 (58.0%)	185 (92.5%)	194 (97.0%)
Lot 2	200	123 (61.5%)	175 (87.5%)	194 (97.0%)
Lot 3	200	135 (67.5%)	184 (92.0%)	198 (99.0%)
Combined	600	374 (62.3%)	544 (90.7%)	586 (97.7%)

BGMS, blood glucose monitoring system.
*For glucose values <100 mg/dL (5.55 mmol/L).
†For glucose values ≥100 mg/dL (5.55 mmol/L).
‡ISO 15197:2013 Section 6.3 accuracy criteria.

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ACCURACY EVALUATION OF THE CONTOUR BLOOD GLUCOSE MONITORING SYSTEM WITH AN UPDATED METER ALGORITHM

B. Harrison[1], D.A. Simmons[1], M.E. Warchal-Windham[1]

[1]Bayer HealthCare LLC, Diabetes Care, Whippany NJ, USA

Background: This study evaluated the accuracy of an updated CONTOUR blood glucose monitoring system (BGMS) containing an updated meter algorithm and using currently available

Table 1. Summary of BGMS Accuracy Results

Test strip lot	N	±5 mg/dL (0.28 mmol/L)* or ±5%†	±10 mg/dL (0.56 mmol/L)* or ±10%†	±15 mg/dL (0.83 mmol/L)*‡ or ±15%†‡
		Number of meter results within specified error limits		
Lot 1	200	139 (69.5%)	186 (93.0%)	197 (98.5%)
Lot 2	200	126 (63.0%)	187 (93.5%)	198 (99.0%)
Lot 3	200	125 (62.5%)	180 (90.0%)	197 (98.5%)
Combined	600	390 (65.0%)	553 (92.2%)	592 (98.7%)

BGMS, blood glucose monitoring system.
*For glucose values <100 mg/dL (5.55 mmol/L).
†For glucose values ≥100 mg/dL (5.55 mmol/L).
‡ISO 15197:2013 Section 6.3 accuracy criteria.

CONTOUR test strips, as assessed per ISO 15197:2013 Section 6.3 accuracy criteria.

Methods: Fingertip capillary blood samples from 100 subjects were evaluated using 3 CONTOUR test strip lots, and each sample was tested in duplicate (N = 600). Samples were also tested in parallel on a YSI 2300 STAT Plus glucose analyzer to obtain reference values for comparison. Accuracy was assessed based on ISO 15197:2013 Section 6.3 accuracy criteria, which are as follows: ≥95% of results for each test strip lot shall fall within ± 15 mg/dL [0.83 mmol/L] or ± 15% of reference at YSI glucose concentrations.

Results: All 3 test strip lots met ISO 15197:2013 section 6.3 accuracy criteria, with 98.5% (197/200), 99.0% (198/200), and 98.5% (197/200) of results falling within ± 15 mg/dL (0.83 mmol/L) or ± 15% of the YSI reference for test strip lots 1, 2, and 3, respectively (**Table 1**). Furthermore, Parkes-Consensus Error Grid analysis showed that 99.8% (599/600) of results were within Zone A, with the remaining result in Zone B.

Conclusion: Study findings showed that the accuracy of the CONTOUR BGMS met ISO 15197:2013 Section 6.3 accuracy criteria.

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EVALUATION OF THE IMPACT OF CGM ANALYTICAL PERFORMANCE DIFFERENCES ON RELEVANT CLINICAL OUTCOMES BY SIMULATION TESTING

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Background: This in-silico study simulates the impact of the analytical performance of real-time continuous glucose monitoring (CGM) systems on clinical outcomes under various conditions similar to daily life.

Materials and methods: A Roche Diagnostics prototype CGM-sensor has already demonstrated improved accuracy in a small clinical study. Here we compare the sensor with two competitor sensors in an in-silico environment of 100 virtual type-1-diabetic (T1DM) patients, using the University of Virginia/Padova T1DM Metabolic Simulator to examine performance under conditions difficult to study clinically. All three sensors were simulated under optimal glucose control (1), hyperglycemia (2), overbolus-induced hypoglycemia (3), exercise (4), insulin stacking and mistimed dosing (5), nocturnal hypoglycemia (6), and rapid BG fluctuations (7).

Results: Lowest average mean absolute relative difference (MARD) and precision absolute relative difference (PARD) were obtained from 5000 simulation runs. Lowest average MARD / PARD in (1) were 6.8% / 6.7% (Roche), 12.3% / 14.8% (CGM1), and 8.4% / 8.6% (CGM2). In (2) MARD / PARD were 8.6% / 7.1% (Roche), 18.5% / 20.5% (CGM1), and 9.8% / 8.8% (CGM2). In (3) MARD was 8.9% (Roche), 35.0% (CGM1), and 13.4% (CGM2). The probability of missing hypoglycemia < 70 mg/dL (< 55 mg/dL) was 0.087 (0.076) (Roche), 0.428 (0.627) (CGM1), and 0.135 (0.157) (CGM2). Average delays in hypoglycemia (< 70 mg/dL) detection were 1.4 min (Roche), 24.6 min (CGM1), and 8.6 min (CGM2).

Conclusion: In this study the Roche prototype sensor showed superior analytical performance across all glycemic ranges of the simulated scenarios, was fastest to detect hypoglycemia and had the lowest probability of missing an event.

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THE EFFECT OF CONTINUOUS GLUCOSE MEASUREMENT ON HBA1C IN ADOLESCENTS WITH TYPE 1 DIABETES TREATED WITH MULTIPLE DAILY INJECTIONS AND WHO DO NOT MEASURE BLOOD GLUCOSE

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Aim: The effect of continuous glucose mesurement (CGM) on HbA1c in adolescents with type 1 diabetes treated with multiple daily injections who do not measure blood glucose in a randomised pilot study.

Material and Methods: Fourteen young patients with T1D and with HbA1c > 64 mmol/mol were randomized to CGM (n = 8) or control (n = 6). Age was 20.6 ± 1.8 vs 20.5 ± 1.4 years and diabetes duration 8.8 ± 2.9 vs 6.7 ± 4.1 years, respectively. Patients were seen every month for 5 months. The patients who were randomised to active sensor group were asked to use the sensor 4 × 3 weeks and the control group were asked to use the sensor 2 × 3 weeks. Soft sensor combined with Guardian was used and the patients were told to calibrate the sensor 3 times a day. All data are mean ± SD and non-parametric tests were performed.

Results: HbA1c was significantly reduced in the active group (baseline vs 5 months) 88 ± 14 vs 77 ± 13 mmol/mol (p = 0.01) but not in the control group; 83 ± 14 vs 82 ± 20 (p = ns). The delta HbA1c was significantly greater in the active sensor group 11 ± 4.7 vs 0.8 ± 7.3 mmol/mol (p < 0.01).

Conclusion: This pilot study showed that CGM can reduce HbA1c significantly in young patients with T1D treated with MDI and who do not measure blood glucose prior to the study.

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CLINICAL USEFULNESS OF CONTINUOUS GLUCOSE MONITORING IN HYPOGLYCEMIA DETECTION

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Introduction and objectives: retrospective continuous glucose monitoring (RCGM) is a diagnostic tool to assess the frequency of hypoglycemia, unawareness hypoglycemia (UH) and nocturnal hypoglycemia (NH). Our objective was to analyse UH and NH through RCGM on type 1 Diabetes (DM1) patients.

Material and Methods: Prospective descriptive study of RCGM conducted on DM1 patients. We consider frequent hypoglycemia (FH) as > 10% of glycemic values ≤ 70 mg/dL, and nocturnal hypoglycemia (NH) when it occurred from 00 to 06 am. RCGM were performed through CGMS-Gold (Medtronic Inc®, IL, EEUU). Statistical analysis was carried out with SPSS v 15.0 software (IBM Inc®, IL, EEUU).

Results: we analysed results from 70 RCGM with an average of 1423.8 ± 244.2 values of glycemia per patient. Frequency of hypoglycemic events: total 0.45 ± 0.48/day, UH 5.2 ± 4.7/total (1.8 ± 2.1/d were also NH), severe hypoglycemia 2.1 ± 2.4/ month. FH patients (37.1%) presented higher glycemic variability (GV), defined as greater between-day SD (57.5 ± 8.1 mg/ dL vs 70.3 ± 20.6 mg/dL) and variation coefficient (VC) (0.31 ± 0.39 vs 0.46 ± 0.15). Patients with severe hypoglycemia showed a higher frequency of UH compared with those who do notice symptoms (1.0 ± 0.0 vs 0.13 ± 0.34, $p = 0.045$). We did not found NH risk factors.

Conclusions: Our results revealed a high rate of FH, UH or severe hypoglycemia. Severe hypoglycemia incidence was higher among UH patients. Patients with FH had greater glycemic variability.

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GLUCOSENSE: PHOTONIC CHIP BASED NON-INVASIVE GLUCOSE MONITOR

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Current cutting edge invasive glucose sensing technologies offer personalized care, however the need for frequent testing combined with the development of tender sampling sites limit their use. We have fabricated a novel non-invasive glucose sensor that relies on an indigenously developed photonic chip. It emits fluorescence in near infrared region (NIR) which specifically interacts with glucose present in the blood. This photonic chip is manufactured with implantation of fluorescent ions into silica glass using a pulsed laser plasma implantation method. The measurement is based on the variation of NIR photoluminescence lifetime of the photonic chip via macroscopic electromagnetic interactions with the skin. This new approach gives a direct real time glucose measurement with high signal to noise ratio. We have tested the device in a pilot clinical study of 12 patients with Type 1 diabetes by measuring glucose in the range of 50 to 400 mg/dl. Ethics approval was obtained from NHS, UK to conduct the clinical trials. The glucose values were measured every 10 mins from the GlucoSense and continuous glucose monitor. Blood glucose values were obtained every hour from handheld glucose monitor. Total 192 data points, 1.008 data were obtained in comparison with glucose handheld meter and continuous glucose monitor respectively. Clarke error grid analysis demonstrates more than 95% clinical acceptability (figure 1) with finger prick measurement and 92% clinical acceptability
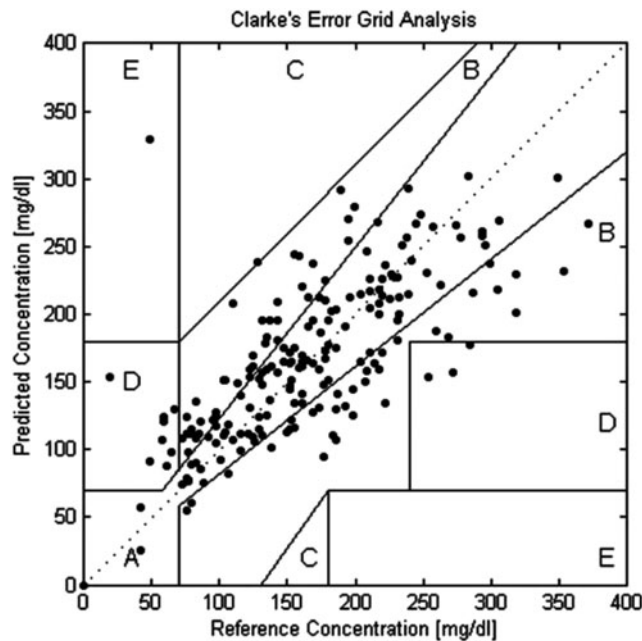
Figure 1 Clarke error grid analysis showing the correlation between GlucoSense compared with reference glucose handheld monitor.

with continuous glucose meter. Next product development phase is underway.

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RAMADAN FASTING IN ADOLESCENTS WITH TYPE 1 DIABETES, CGM STUDY

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Background: Due to the scantiness of data about the effect of fasting on glucose profile in type 1 diabetes (T1DM) children and adolescents, healthcare providers have been giving conflicting recommendations regarding safety of fasting in this group of patients.

This study was done to monitor glucose profile in fasting children and adolescents with T1DM by using CGM.

Method: Children and adolescents with type 1 diabetes who intended to fast Ramadan, 2013 were asked to wear the CGM for a minimum of 3 days, and to report episodes of severe hypoglycemia (required help of others), DKA, or ER visits. Insulin regimens were adjusted according to the eating pattern in Ramadan. 24 h BG averages, duration of hypoglycemia and hyperglycemia were extracted from the CGM downloads.

Result: 21 patients were enrolled, age (mean ± SD) 15 ± 5 years, duration of diabetes 6 ± 3 years, and HbA1C 8.6 ± 1%. 18 patients were on CSII, and 3 on MDI.

All subjects could fast 15 or more days. There was no reported episodes of severe hypoglycemia, DKA or ER visit throughout the whole month for any of the subjects.

24 h average BG was 182 ± 17 mg/dL. Hypoglycemia and hyperglycemia were encountered in 14% and 10% of the CGM time, respectively.

Conclusion: The majority of children and adolescents with type 1 DM could fast safely during Ramadan. There were no episodes of DKA or severe hypoglycemia despite evident BG fluctuation. Proper insulin regimen should be established to minimize BG fluctuation during day time fasting and night time eating.

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FUNDAMENTAL DIFFERENCES IN GLUCOSE STABILITY IN PATIENTS ON INSULIN COMPARED TO DIET/METFORMIN TREATED PATIENTS DURING RAMADAN FASTING: INSIGHTS FROM POINCARÉ PLOT

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Introduction: The Poincaré plot (PCP) is a valuable tool for describing glucose variability from continuous glucose monitoring (CGM). We used this plot to study the temporal glucose variability derived from CGM in patients fasting during Ramadan.

Methods: Fifteen patients with diabetes (8 on insulin; 7 on metformin or diet alone) had CGM performed before and during Ramadan fasting. PCPs were constructed with a fixed Δt value of 30 minutes. A comparison of the two groups was made.

Results: Different patterns in PCP were seen in the diet/metformin v insulin groups (figure 1). Diet/metformin group showed a more concentrated plot with less scatter and greater stability which changed little during Ramadan fasting. In contrast, in the insulin treated group greater scatter was seen which was exaggerated during the Ramadan fast.
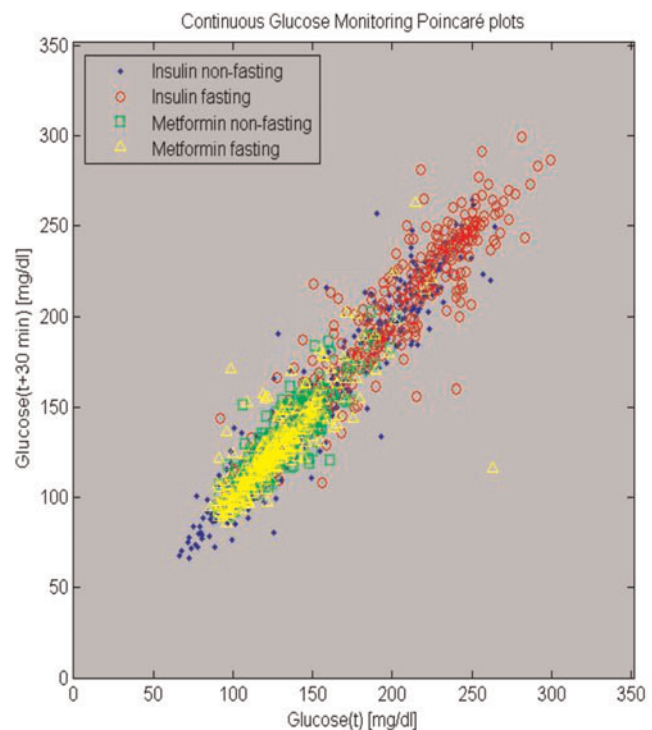
Conclusion: We have used PCP for the first time in order to assess changes in glucose stability in the context of Ramadan fasting. PCP may provide a graphical method of quantifying risk in different medication groups in this context.

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A GOLD NANOPARTICLES-ENHANCED ELECTROCHEMICAL SENSOR IN MICROFUIDICS FOR CONTINUOUS GLUCOSE MONITORING

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Continuous glucose monitoring of transdermally extracted interstitial fluid in subcutaneous tissue allows timely detection and correction of abnormal blood glucose excursions. Recently, MEMS technology has been used to produce miniaturized devices for transdermal interstitial fluid extraction and glucose sensing. For the volume of interstitial fluid transdermally extracted is small, it is necessary to dilute the interstitial fluid for convenient collection. After dilution, the glucose concentration of the interstitial fluid decreases significantly. To measure the concentration accurately, a glucose sensor with high resolution is needed. At the same time, the volume of the diluted interstitial fluid transdermally extracted is very small, it is crucial to integrate the transdermal interstitial fluid extraction with the glucose sensor in a single device. Here we address these limitations by integrating interstitial fluid transdermal extraction microfluidics and gold nanopaticles-enhanced electrochemical glucose sensor in a single lab-on-a-chip system. The microfluidic system for interstitial fluid transdermal extraction is fabricated from five PDMS layers using micromolding techniques. A three-electrode enzymatic glucose sensor consists of an Au working electrode, an Ag/AgCl reference electrode, an Au counter electrode, whose working electrode is decorated with gold nanoparticles by electrodeposit to enhance the electron transfer rate. And then glucose oxidase is immobilized on the surface of the working electrode to catalyze glucose specifically. The glucose sensor, which is fabricated on the glass, is bonded with the interstitial fluid extraction system. The single-chip device can potentially enable automated, accurate, and continuous monitoring of subcutaneous interstitial fluid glucose concentrations for clinical application.

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A CLINICAL TRIAL OF THE ACCURACY AND TREATMENT EXPERIENCE OF THE DEXCOM G4 SENSOR AND ENLITE SENSOR TESTED SIMULTANEOUSLY IN AMBULATORY PATIENTS WITH TYPE 1 DIABETES

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Background: Continuous glucose monitoring (CGM) is a tool widely used in the treatment of patients with type 1 diabetes. The purpose of the current study was to evaluate whether accuracy and patient treatment satisfaction differ between the Enlite™ (Medtronic MiniMed, Inc., Northridge, CA) and Dexcom® (San Diego, CA) G4 PLATNIUM CGM sensors.

Subjects and Methods: Thirty-eight ambulatory patients with type 1 diabetes used the Dexcom G4 and Enlite sensors simultaneously for 4–6 days. Patients measured capillary glucose levels with a HemoCue® (Ängelholm, Sweden) system 6–10 times a day. In addition, two inpatient studies were performed between Days 1–3 and 4–6. This study was performed independently from manufacturers of CGM systems. All end points were predefined and registered on ClinicalTrials.gov with other trial information.

Results: MARD in blood glucose for the Dexcom G4 was significantly lower (13.9%) than for the Enlite sensor (17.8%) ($P < 0.0001$). The corresponding MARDs for Days 1–3 were 15.0% versus 19.4% ($P = 0.0027$) and 13.6% versus 15.9% ($P = 0.026$) for Days 4–6. For glucose levels in the hypoglycemic range, the MARD for the Dexcom G4 was 20.0% compared with 34.7% for the Enlite ($P = 0.0041$). On a visual analog scale, patients rated the Dexcom G4 more favorably than the Enlite in 12 out of the 13 user experience questions.

Conclusions: The Dexcom G4 sensor was associated with greater overall accuracy than the Enlite sensor. Patients reported a significantly more positive experience using the Dexcom G4 than the Enlite.

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VALUE OF IMPROVED ACCURACY FOR SELF-MONITORING OF BLOOD GLUCOSE DEVICES

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Objective: To simulate and compare the clinical and economic outcomes of self-monitoring of blood glucose (SMBG) devices along ranges of accuracy and strip price.

Methods: We programmed a long-term type 1 diabetes natural history and treatment cost-effectiveness model. In phase one, using In Silico modeling validated by the Food and Drug Administration, we associated changes in accuracy error rates of SMBG devices to changes in HbA1c and severe hypoglycemia rates requiring an inpatient stay. In phase two, using Markov cohort simulation modeling, we estimated lifetime clinical and Canadian payer perspective economic outcomes. The primary comparison was a SMBG device with strip price $0.73 Canadian dollars (CAD) with accuracy error rate of 10% versus a SMBG device with strip price $0.60 CAD with accuracy error rate of 15%. Additional scenarios compared 10% accuracy error rate versus 20%. Outputs for the average patient, discounted at 3%

Table 1. Lifetime Results (2014 Canadian Dollars)

	Costs	QALYs	Severe Hypoglycemic Events[d]	Incremental Cost Effectiveness Ratio (cost per QALY)
Scenario 1: % Error associated with HbA1c but NOT directly associated with severe hypoglycemic events requiring inpatient stay[a,b]				
SMBG Device with 10% Error, .73 per strip	$115,600	11.5	29.7	-
SMBG Device with 15% Error, .60 per strip	$113,800	11.3	29.6	$13,400
Scenario 2: % Error associated with HbA1c AND directly associated with severe hypoglycemic events requiring inpatient stay[a,b]				
SMBG Device with 10% Error, .73 per strip	$106,200	11.5	24.9	-
SMBG Device with 15% Error, .60 per strip	$113,800	11.3	29.6	Dominated[c]

a HbA1c was increased from a baseline of 7.6% (assuming no error)

b Changes in HbA1c and hypoglycemic events derived from in silico modeling results from Breton et al. 2010 JDST

c SMBG device with 10% error is less costly and more effective than SMBG device with 15% error

d The same severe hypoglycemic risk was applied to both arms, however events are not the same in scenario 1 because of the added survival of a cohort with improved HbA1c

per annum, were severe hypoglycemic events requiring an inpatient stay, quality-adjusted life years (QALYs), costs, and incremental cost-effectiveness ratios (ICERs).

Results: Assuming the benefits translate into HbA1c improvements only, the ICER with accuracy error rate of 10% versus 15% including was $13,400 CAD per QALY. Assuming the benefits translate into HbA1c improvements and reduced severe hypoglycemic events requiring an inpatient stay, an SMBG device with accuracy error rate of 10% dominates an SMBG device with accuracy error rate of 15% (Table 1).

Conclusions: Improved accuracy of SMBG, even at higher strip prices, ranges from cost savings to good value for the additional health gained.

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THE FLUCTUATION IN BLOOD SUGAR AND BLOOD PRESSURE OF INSULIN-DEPENDENT DIABETIC PATIENTS WITH CHRONIC KIDNEY DISEASE

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Among type 2 diabetics patients with CKD(chronic kidney disease), we observed different fluctuational patterns of blood sugar between CKD patients and non-CKD patients. On the other hand, non-dipper type blood pressure change is the risk of organ damagements and mortality. We performed cross-sectional study to elucidate the characteristic of the fluctuation of blood glucose and blood pressure at insulin-treated diabetic patients with chronic kidney disease. From March 2011 to April 2013, at the Ichikawa Hospital of Tokyo Dental College, we recruited 20 outpatients. All participants are insulin-treated type 2 diabetes with CKD. We collected serum samples, urine samples for several hormone measurements, and performed CGMS(Continuous glucose measurement system), ABPM (ambulatory blood pressure monitoring), brain computed tomography, carotid artery thickness, ankle brachial index, PWV, CVR-R, and analyzed these data statistically. Among all 20 participants, hypoglycemia was detected in blood glucose 70 mg/dl by CGMS of 9 participants (45.0%). The event of hypoglycemia was recognized lower eGFR (29.8±6.2 ml/min:41.3±8.5 ml/min, P<0.05), lower HbA1c (6.44±0.57%:7.53±0.49%), higher PWV (1858 ±

97.3 cm/s:1665±109.2 cm/s), higher serum glucagon (194.2 ± 34.8 pg/ml:117.0±37.1 pg/ml), higher free cortisol of urine (53.8 ± 12.8 μg/day:34.8±7.1 μg/day), and higher metanephrin of urine (0.162±0.031 mg/day:0.076±0.029 mg/day). Non-dipper type blood pressure change in ABPM were detected 8 among 9 praticipants with hypoglycemia (88.9%), 4 among 11 participants (36.4%) without hypoglycemia. Multiplex logistic-regression analysis revealed that the event of hypoglycemia is the independent factor of non-dipper type blood pressure change. Among insulin-treated type 2 diabetic patients with CKD, the events of hypoglycemia were frequently detected, and can associate with the organ derangements through the medium of non-dipper type blood pressure change.

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VARIABILITY OF GLYCAEMIA IN CHILDREN WITH TYPE 1 DIABETES MELLITUS, WHO HAVE AN OPTIMAL LEVEL OF GLYCOSYLATED HEMOGLOBIN

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Aim: to analyses the variability of glycaemia in children with type 1 diabetes mellitus (T1DM), who have an optimal compensation on the level of glycosylated hemoglobin (HbA1C).

Materials and methods: the analysis was made among 9 patients with T1DM (average age 10.44±4.4 years; average level of HbA1C 6.8±0.69%) on continuous glucose monitoring system (CGMs, on average 999±62.19 measurement). We have set values from 3.9 to 10.0 mmol/l as our target values of glycaemia. Variability of glycaemia was estimated by the standard deviation (SD) from the mean glycaemia for the entire period of the CGMS. Variability was considered optimal if 3SD was less than the mean glycaemia. Satisfactory if 2SD was less than the mean glycaemia. High if 2SD was more than the mean glycaemia.

Results: two out of nine children with T1DM with an average level of glycaemia 7.9±0.6 mmol/l (7.4; 8.5 mmol/l) mean SD was 4.25±0.25 (4; 4.5), indicating a high variability of

glycaemia. However 36% of measurements outside of target values of glycaemia (hyperglycemia 25%; hypoglycemia 11%).

Among the four patients average glycaemia was 6.2 ± 0.69 mmol/l (5.1; 5.2; 6.4; 8.1) average SD was 2.55 ± 0.37 (1.9; 2.0; 2.8; 3.5), reflecting the satisfactory rate of glycaemia. However 30.7% of glycaemia were outside the target values (hyperglycemia -10%; hypoglycemia -20.7%).

Only three patients, the average level of glycaemia was 7.23 ± 0.58 mmol (6.6; 7.3; 8.4), the mean SD was 1.66 ± 0.2 (1.3; 1.7; 2.0) that testified to an optimum of variability of glycaemia. Only 7.7% of measurements exceed the target limits of glycaemia (hyperglycemia - 6, 1%; hypoglycemia - 1.6%).

Conclusion: research has shown that the glycosylated hemoglobin target values in some patients with T1DM, can be obtained as a result of the high variability of glycaemia, which today is recognized as a risk factor for vascular complications.

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PROJECTION OF HEALTH ECONOMIC BENEFITS OF SENSOR-AUGMENTED PUMP (SAP) VERSUS PUMP THERAPY ALONE (CSII) IN AN UNCONTROLLED T1DM IN FRANCE

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Aims: Main objective of this study was to estimate health-economic impact of Sensor-Augmented Pump (SAP) compared to pump therapy alone (CSII) in an uncontrolled Type 1 Diabetes population (T1DM) in France.

Methods: Core Diabetes Model was used to project incidence of diabetes-related complications over a lifetime horizon, based on a recently performed meta-analysis comparing SAP versus

Table 1: Cohort & Intervention Characteristics Used	
Mean baseline age	36 years
Proportion of male	53%
Diabetes duration	17 years
Mean baseline HbA1c	9%
HbA1c reduction SAP	-0.88%
HbA1c reduction CSII	-0.47%
ΔHbA1c reduction SAP-CSII	-0.41%

CSII. The meta-analysis was done on a cohort of T1DM using exclusively Medtronic devices with at least 70% use of SAP. The cohort and intervention characteristics used are presented in table 1. The quality of life was adjusted for a reduced fear of hypoglycaemic event in SAP arm. Sensitivity analyses were carried out on several key parameters.

Results: Improvement in discounted Quality Adjusted Life Year (QALY) was 1.27 year in favour of SAP. Undiscounted life expectancy was increased by 1 year for SAP versus CSII. Incremental Cost-Effectiveness Ratio (ICER) was 27,796€ per QALY gained. Additional SAP related costs were partially offset by the savings due to the reduction in diabetes related complications and the lower frequency of SMBG tests. Remaining extra annual costs for SAP were 1,258€ per patient. When indirect costs were considered, the ICER was reduced to 23,300€ per QALY.

Conclusion: Using a well-accepted simulation model in an uncontrolled T1DM, projection of improvement in HbA1c of SAP versus CSII translated into cost-effective ratio, generally considered as very good value for money in France. Extensive sensitivity analysis on key drivers confirmed the robustness of results under a wide range of assumptions.

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RETROSPECTIVE VS REAL-TIME CONTINUOUS GLUCOSE MONITORING IN TYPE 1 DIABETES: WHICH IS BETTER?

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Background and Aim: The aim of the study is to evaluate the glycemic outcomes of two different Real-Time (RT) and Retrospective Continuous Glucose Monitoring (CGM) systems in patients with type 1.

Materials and Methods: A total number of 94 patients with type 1 diabetes on insulin pump (45%) or multiple daily injections (55%) with HbA1c > 7.5% were randomized in two groups:

RT CGM group, 48 patients using real-time CGM (Medtronic Veo for pump Users and Guardian RT with Minilink and Enlite sensor, Medtronic, Northridge, CA), where patients could see the glucose value and respond adequately and

Retrospective CGM group, 46 patients using retrospective CGM (Ipro2 with Enlite sensor, Medtronic, Northridge, CA), where patients could not see the glucose value (blinded CGM).

Patients from both groups used the CGM device for 7 days. After each session, data was downloaded using specific software (Carelink Pro and Carelink Ipro, Medtronic, Northridge, CA) and specific instructions in basal and bolus insulin, education on food, physical activity and hypoglycemia/hyperglycemia were given to the patients. HbA1c was obtained before and three months after the study.

Results: Both groups significantly improved glucose control (HbA1c) from $7.9 \pm 0.9\%$ to $7.5 \pm 0.6\%$ in RT group and from $7.9 \pm 1.1\%$ to $7.5 \pm 0.8\%$ in retrospective group, but there was no significant difference between both groups at the end of the study. Patients prefer retrospective CGM.

Conclusions: Both RT and retrospective CGM can improve glucose control in type 1 diabetics Further investigation on larger groups should be performed to confirm our findings.

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3RD GENERATION BIOSENSOR TECHNOLOGY FOR CONTINUOUS GLUCOSE MONITORING SYSTEMS

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DirectSens GmbH developed a novel sensor technology for continuous glucose monitoring systems based on unique properties of the enzyme cellulose dehydrogenase (CDH). Intense studies lead us to design a 3rd generation sensor technology where the amperometric glucose response is fully governed by direct electrons transfer between the electrode surface and immobilised CDH (Patent PCT/EP 2010/052488). The main advantage of our sensing system is its high performance without the presence of mediators or *nano*-structures in the sensor matrix. The sensor showed a high response towards glucose at very low operating potential of $-0.1\,V$ vs. the silver/silver chloride reference electrode. As a result, signals from common interferences including ascorbic acid and acetaminophen were minimised to a range of 0–10% without employing selective polymer coating (Felice *et al.*, 2013). The sensing technology proved to work effectively at different electrode materials, including gold and different types of carbon and thus shows great potential for *in vitro* and *in vivo* applications.

Currently, our focus is to tune the sensors properties by chemical modification of the sensor matrix in order to achieve a broad linear range, high sensitivity and operating stability to meet the requirements of CGM systems. Progress of the *DirectSens* technology will be presented and discussed in respect to its impact for commercial systems.

Felice, A.K.G., Sygmund, C., Harreither, W., Kittl, R., Gorton, L., and Ludwig, R. (2013). Substrate specificity and interferences of a direct-electron-transfer-based glucose biosensor. J. Diabetes Sci. Technol. *7*, 669–677.
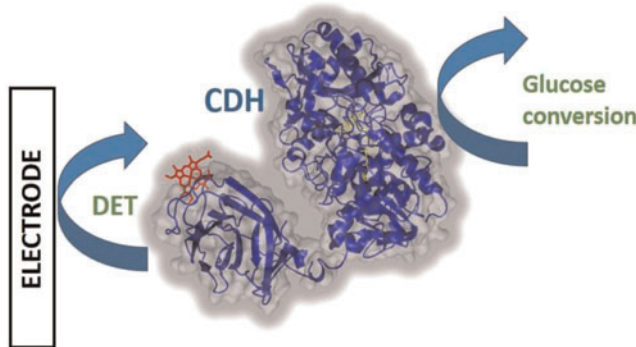
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EVALUATING CLINICAL ACCURACY OF FOUR BLOOD GLUCOSE MONITORING SYSTEMS USING SURVEILLANCE ERROR GRIDS

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Background: Recently, the surveillance error grid (SEG) has been proposed for the assessment of a blood glucose monitoring system's (BGMS) clinical accuracy. It was suggested that at least 96.8% of results should fall in the 'no risk' range for the BGMS to be considered clinically accurate. In ISO 15197:2013, clinical accuracy is assessed in the consensus error grid (CEG), where 99% of results have to fall within clinically acceptable zones A and B. In this retrospective analysis, clinical accuracy of four BGMS was assessed by SEG and compared to earlier results of a system accuracy assessment applying ISO 15197 accuracy limits.

Methods: Data were obtained in a study in which system accuracy was assessed following ISO 15197. Detailed study procedures and system accuracy results of that study were previously presented. Clinical accuracy was assessed by SEG and interpreted in relation to the corresponding earlier results.

Results: Averaged over three test strip lots each, the four BGMS showed 100%, 99.3%, 97.2% and 93.5% of results within ISO 15197:2013 accuracy limits. 100%, 100%, 100% and 99.8% of results were found within CEG zones A and B, respectively. In the SEG analysis, these BGMS showed 99.7%, 98.3%, 97.0% and 96.3% in the 'no risk' range.

Conclusions: The newly suggested SEG cutoffs are more restrictive than the previously established CEG criterion of ISO 15197:2013. For the four BGMS, sufficient clinical accuracy coincided with sufficient analytical accuracy. Further comparative analyses are necessary to provide more insight into the agreement of SEG and ISO 15197 results.

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EVALUATION OF GLYCEMIC CONTROL PROFILE IN TYPE 1 DIABETIC PATIENTS USING CONTINUOUS GLUCOSE MONITORING

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Introduction: Despite the importance of glycated hemoglobin (A1C) levels, it is necessary to evaluate glycemic profile and variability in type 1 diabetic patients in order to provide better control. For this purpose, continuous glucose monitoring system (CGMS) is a useful tool.

Methods: Twenty three patients with diabetes type 1 were recruited to CGMS to investigate hypoglycemia or high A1C. CGMS was applied for a median period of 4.8 days in their daily routine. The following parameters were analyzed: glycemic media, variability, area under curve of blood glucose above 180 mg/dL (AUC > 180) and also below 70 mg/dL (AUC < 70), duration of nocturnal (0–6 hs) and daily hypoglycemia (6–0 hs).

Results: These type 1 diabetic patients have high socioeconomic level with mean age of 32.9 ± 14.2 years, female/male ratio of 1.8 and 16.8 ± 11.3 years duration of diabetes; 60.8% use insulin pump and 39.2% multiple analogs daily injections (MDI). The mean A1c was 7.35% (6.1–8.8%), and mean glycemic levels of 164.5 ± 32.0 mg/dL, with 322.5 ± 56.4 mg/dl (184–435 mg/dl) variability during the period. The mean AUC > 180 was 24.8 (mg/dL/4.8 days) and AUC < 70 0.52 (mg/dL/4.8 days). Regarding hypoglycemia, the mean duration of events in the period was sixty six minutes/day and ninety minutes/night.

System 1

Degree of Risk	Absolute Value	Color	# Hypo.	# Hyper.	# Total	Hypo. %	Hyper. %	Total %
None	0 - 0.5	D. Green	527	47	598	87.83%	7.83%	99.67%
Slight, Lower	>0.5 - 1.0	L. Green	2	0	2	0.33%	0.00%	0.33%
Slight, Higher	>1.0 - 1.5	Yellow	0	0	0	0.00%	0.00%	0.00%
Moderate, Lower	>1.5 - 2.0	L. Orange	0	0	0	0.00%	0.00%	0.00%
Moderate, Higher	>2.0 - 2.5	D. Orange	0	0	0	0.00%	0.00%	0.00%
Great, Lower	>2.5 - 3.0	L. Red	0	0	0	0.00%	0.00%	0.00%
Great, Higher	>3.0 - 3.5	D. Red	0	0	0	0.00%	0.00%	0.00%
Extreme	>3.5	Brown	0	0	0	0.00%	0.00%	0.00%

Color-Coded Surveillance Error-Grid
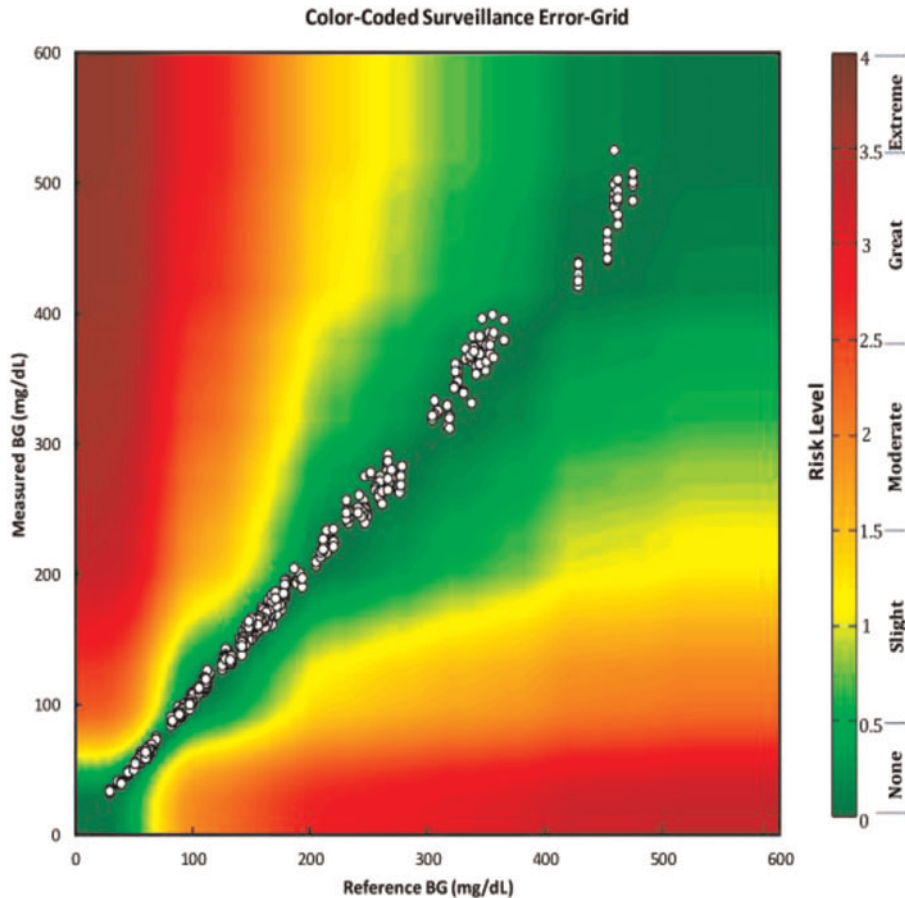
Conclusion: This study demonstrates that even type 1 diabetic patients with high socioeconomic level and good A1c present high variability and can stay hypoglycemic for long periods, during days and nights. CGMS is a useful tool in these patients to diagnose changes in glycemic profile independently of A1c.

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EASE OF USE AND COMFORT OF A NOVEL SENSOR INSERTION DEVICE FOR CONTINUOUS GLUCOSE MONITORING

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Background: In continuous glucose monitoring (CGM) the accurate positioning of the sensor in the subcutaneous tissue is a prerequisite for adequate sensor performance. In this study a novel insertion device was investigated with regard to success and reliability of sensor insertion, ease-of-use of the device and discomfort associated with the insertion procedure.

Methods: 50 people with diabetes inserted themselves two sensors, one at the abdomen and a second at the hip/buttock. To determine the insertion length, a sensor with a special scaling was used. The study was approved by the Institutional Review Board and subjects had signed written informed consent.

Results: The sensors were inserted successfully with an insertion length ≥ 8 mm leading to a success rate of sensor

insertion of 100%. Pain upon sensor insertion was reported to be low (77.5%) or moderate (18.3%). In comparison to any of the compared measures in diabetes treatment, the discomfort associated with insertion was reported to be equal or less than finger pricking (79.6%), insulin injection (77.6%) and applying other CGM systems (83.3%). Regarding the handling of the insertion device, 80% of the subjects assessed it very easy to use, and 98% rated the operating steps easy to understand.

Conclusion: The novel CGM sensor insertion device can provide people with diabetes a reliable and easy to perform procedure for safe and successful sensor insertion with a minimum of discomfort, also when compared to other CGM devices and in comparison to other measures in diabetes treatment like insulin administration or finger pricking.

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A NOVEL GLUCOSE MONITORING SYSTEM VERSUS A CONVENTIONAL SMBG SYSTEM: TIME AND STEP ANALYSIS

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Background: Recently, a novel glucose monitoring system (FreeStyle Libre) has been developed consisting of a sensor which is inserted on the back of the upper arm for up to 14 days and a portable reading device which can wirelessly scan and display sensor glucose values. Each scan displays a real-time glucose result along with an 8-hour history and a trend arrow. The sensor is factory calibrated; thus, finger prick calibrations are not required. In this investigation, the reduction of time and handling effort required with the novel system to obtain a glucose value was analyzed and compared with a conventional system for self-monitoring of blood glucose (SMBG).

Methods: Steps required to scan and display a sensor glucose value (FreeStyle Libre, Abbott Diabetes Care, Ltd., UK) were counted and compared with steps required to perform a capillary blood glucose (BG) measurement (FreeStyle Precision Neo, Abbott Diabetes Care, Ltd., UK). In addition, the required time was analyzed.

Results: The number of steps to scan and display a real-time glucose result is reduced (decrease of 91%) when compared with a capillary BG measurement. In addition, less time is required (FreeStyle Libre: ∼6 seconds; SMBG system: ∼2 minutes).

Conclusion: The novel system does not require finger prick calibrations and enables a fast scan and display of real-time glucose values within a few seconds and with only a few handling steps. A reduction of steps may also reduce potential handling errors sources and enhance the adherence to frequent glucose monitoring.

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COMPENSATION OF OXYGEN PARTIAL PRESSURE VARIATIONS DURING OPTICAL, ENZYMATIC GLUCOSE SENSING IN ADIPOSE TISSUE

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[2]*Institute of Analytical Chemistry and Food Chemistry, Graz University of Technology, Graz, Austria*
[3]*Department of Internal Medicine Division of Endocrinology and Nuclear Medicine, Medical University of Graz, Graz, Austria*

Background: This single-port concept combines an optical, enzymatic glucose measurement and an insulin delivery system, placed at the same location in subcutaneous adipose tissue (AT). Changes in oxygen partial pressure (pO2) among the AT influence the glucose determination and thus require pO2 measurement in AT for mathematical correction of the measured glucose values. The aim of this work was to assess the homogeneity of the pO2 in AT and possible compensation of tissue pO2.

Methods: During in-vivo experiment in domestic pigs, the blood pO2 level was changed between different steady state plateaus. In between these plateaus, three different systems were used to measure the tissue pO2. Fibersensors and microsensors recorded tissue pO2 profiles over a distance of 21 mm. Six stationary needle based sensors, two sensor elements each, were randomly placed over the abdominal area and recorded the tissue pO2 over time. Fiber- and microsensors were read-out through light guiding, the needlesensors were read-out transcutaneously by a phase fluorimeter.

Results: All measured tissue pO2 values were comparable to literature values. The medians of absolute differences between two 2 mm averaged pO2 profile values have a maximum inter system deviation of 1.6 mmHg. The microsensor shows the largest interquartile range of all used systems.

Conclusion: We were able to show that the tissue pO2 is very variable among the cut-off canal (microsensor). An increased sensing area (such as fiber- and needlesensors) would overcome these heterogeneities, so that a mathematical correction of the glucose measurement should be possible.

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GLYCATED HEMOGLOBIN DOES NOT ACCURATELY PREDICT AVERAGE CAPILLARY GLUCOSE IN NON INSULIN-TREATED TYPE 2 DIABETES: THE PRISMA STUDY EXPERIENCE

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In our clinics we commonly observe patients with diabetes whose capillary glucose (SMBG) does not reflect A1c. We

studied the relationship between A1c and average capillary glucose (ACG) among patients with well controlled, non insulin-treated type 2 diabetes who were PRISMA Study participants.

Eligible patients (n=205) had ≥120 capillary glucose measurements over 100 days prior A1c measurement at visit2. Capillary glucose values were measured with Accu-Chek Aviva (Roche Diagnostics) (before breakfast and lunch, 2 and 5 hours after lunch, three times/week) and downloaded to a computer using a wireless device (Accu-Chek Smart-Pix) at visit2. A central laboratory assayed A1c using the DCCT-traceable Variant-II method (Bio-Rad) on whole blood stored at $-80°$ C.

We modelled the relationship between A1c and ACG using linear regression [ACG=28.110 + 14.858*A1c]. Adjusted R-square was 0.431, meaning that 53% of ACG variability was unexplained by A1c: in 14.7%, 23.3% and 27.2% of the patients differences between observed and predicted ACG were larger than $\pm 20, \pm 17.5$ or ± 15 mg/dl, respectively. Separate multiple linear regression analyses, with A1c, ACG or ACG residuals as dependent variable and gender, age, education, BMI, mean arterial pressure, creatinine clearance, HDL and LDL cholesterol, triglycerides as independent variables, showed that these covariates only accounted for <9% of ACG variance.

In patients with non insulin-treated type 2 diabetes A1c does not accurately predict ACG, with many patients showing a less than desirable difference between observed and predicted ACG. Unless combined with SMBG, A1c alone may not be sufficient for tailoring diabetes treatment in these patients.

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3RD GENERATION CGM SENSOR EMPLOYING DIRECT ELECTRON TRANSFER PRINCIPLE WITH IMPROVED OPERATIONAL CONDITIONS

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Objective: We are developing a 3rd generation CGM sensor based on the Direct Electron Transfer (DiET) technology employing a unique FAD glucose dehydrogenase. This study reports the detailed features and the improvements of the performance of this novel CGM sensor. Data is presented to show *in vitro* performance of the sensor operating at various potentials to provide

information on accuracy improvement of the sensor and *in vivo* studies to evaluate the continuous operation of the sensor with modified conditions.

Method: The sensor performance, as well as its stability, was evaluated by operating under various potentials (100 mV - 400 mV, phosphate buffer, pH 7.4) to the working electrode versus Ag/AgCl electrode. The interferences of electrochemically active substances were also evaluated under these potentials. The *in vivo* study was performed at some potential by inserting the sensor into the subcutaneous tissue of the abdomen of a healthy internal volunteer subject. Capillary blood glucose values were also obtained.

Result: Little change was observed in the sensitivity after seven-day *in vitro* continuous measurement at lower potential. The influence of interfering substances, such as acetaminophen and ascorbic acid, became negligible under lower potential. CGM operation of the *in vivo* human study showed good correlation to capillary blood glucose values for seven days.

Conclusion: A novel CGM sensor was developed employing DiET technology. The sensor showed stable CGM response when measurements were performed at lower potential. Improvement of accuracy is expected by the measurement at lower potential due to reduction of interference substances.

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EVALUATION AND IMPROVEMENT OF EPOXY POLYURETHANE MEMBRANE FOR A MICROPROBE ARRAY BASED CONTINUOUS GLUCOSE SENSOR

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Introduction: Closed loop systems depend on the accuracy of the sensing component for the successful management of type 1 diabetes. Various approaches have been used to improve the accuracy of continuous glucose monitoring (CGM) devices, including improvement of the sensor's coating membrane.

We have developed a minimally invasive electrochemical biosensor for painless, continuous monitoring of dermal interstitial fluid glucose. The device consists of monolithically integrated multiple arrays of microprobes distributed as working and reference electrodes. The working electrodes are functionalised
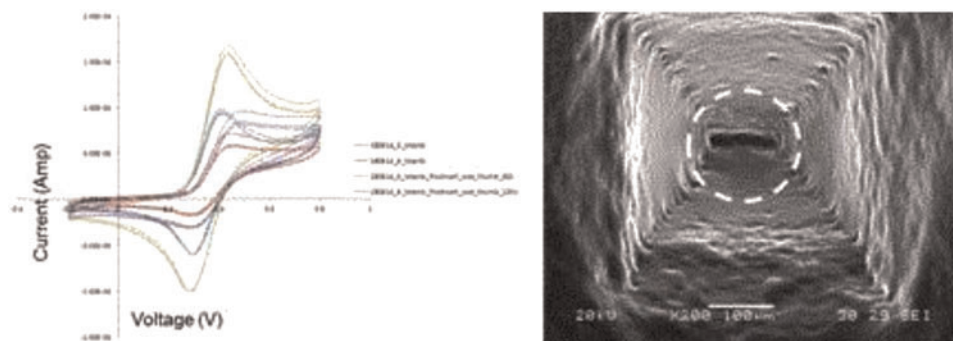

Figure 1 (Left): CV of Ferrocene carboxylic acid for two devices obtained after membrane deposition and post skin insertion. **Figure 1 (Right):** SEM image of the membrane deposited microprobe inserted into skin at thumb pressure for 120 seconds. The pinholes in the membrane structure can be seen at the tip (dotted circle).

with glucose oxidase enzyme and conformally coated with an epoxy polyurethane (PU) membrane.

Aim: Evaluation of the impact of sensor's insertion into human skin on the PU membrane.

Method: Metalized microprobes were conformally covered with PU membrane of variable thickness and composition by controlling the ratio of the constituents and the volume of drop coating in PU membrane solution. The sensors were then inserted for six hours in a healthy volunteer and the effects of insertion after removal was assessed using cyclic voltammetry (CV) and scanning electron microscopy (SEM).

Results: The epoxy PU membranes post insertion and removal exhibit higher permeability as judged by the voltammetry of an external redox probe consistent with the presence of pin holes. This was further confirmed through scanning electron microscopy.

Conclusion: The use of techniques such as CV and SEM helps in understanding the effect of skin insertion on the mechanical stability of the membrane material. Improvement in performance can be achieved through modification in the composition and deposition of the membrane.

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ANALYSIS OF GLYCAEMIA IN PREGNANT WOMEN WITH DIABETES MELLITUS USING CONTINUOUS GLYCEMIC MONITORING (CGM)

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Aim: study of glycaemia in pregnant women with DM using CGM

Materials and methods: 18 pregnant women with diabetes: 14 women had DM type1 and 4 type2. The patients were 27.7 ± 4.9 ys, median of diagnosis diabetes was 10 ys. They had 17.2 ± 6.1 wks of gestation. Level of HbA1c was $7.5 \pm 1.6\%$. CGM was performed during 5.4 ± 1.5 days.

Results: The highest level of glucose was revealed before breakfast 6.6 ± 2.1 mmol/l. It had statistical difference from glycaemia before lunch (5.5 ± 1.9 mmol/l) or before dinner (5.4 ± 1.1 mmol/l), $p < 0.001$. The same difference was noticed after meal: 8.0 ± 1.9 mmol/l 1 hr after breakfast & 6.2 ± 1.1 mmol/l after lunch and 6.7 ± 1.4 mmol/l after dinner, $p = 0.001$; 7.0 ± 1.9 mmol/l 2 hs after breakfast & 5.3 ± 1.3 mmol/l after lunch and 6.2 ± 1.1 mmol/l after dinner, $p = 0.026$. Additionally, glucose level before breakfast was higher than in the early morning time (5.8 ± 1.0 mmol/l at 07a.m.), $p = 0.014$. Probably the additional injection of insulin is required in the early morning.

Pregnant women with DM type1 were compared with pregnant women with type2. Glycaemia dispersion was bigger in pregnant women with type1 during all days: 5.6 ± 2.6 mmol/l & 2.3 ± 1.2 mmol/l, $p = 0.023$. The glucose dispersion was different during the day time (5.4 ± 0.9 mmol/l & 2.4 ± 1.2 mmol/l, $p = 0.015$) but not during the night.

The patients with goal level of HbA1c had lower glucose level after meal but statistically difference was only 1 hr after dinner (5.8 ± 0.9 mmol/l & 7.1 ± 1.0 mmol/l, $p = 0.041$). The time of pregnancy does not influence on glucose level.

In conclusion, the highest glucose level have been revealed around breakfast time, afterwards a diabetologist have to correct the insulin treatment for the morning time, perhaps with the additional injection at 06–07a.m.

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UTILIZATION OF CONTINUOUS GLUCOSE MONITORING AMONG CHILDREN WITH TYPE 1 DIABETES IN A CLINICAL PRACTICE SETTING

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Background: Previous studies have demonstrated a correlation between increased usage of real time continuous glucose monitoring (RT-CGM) in type 1 diabetes mellitus (T1DM) patients, and better glycemic control. However, many children have sensor-related difficulties which lead to an infrequent or discontinuation in use of RT-CGM.

Methods: Fifty children were included in the analysis. A questionnaire was designed to assess the usage of RT-CGM. Hemoglobin A1c (HbA1c) value was obtained from the medical charts.

Results: Average age of participants was 10.5 ± 4.6 years, T1DM duration 4.5 ± 3.1 years, HbA1c $9.3 \pm 3.9\%$. The main reasons for using CGM were hypoglycemic events (50%), glucose variability (42%) and the desire for less finger stick monitoring (36%). Sixty-four percent of the parents believed that using RT-CGM helped manage their child's diabetes better. However, only 32% of the children used it continuously, 16% used it intermittently and 52% did not use it at all. Among the later, 60% stopped using it after less than a week. A continuous usage was associated with younger age ($p < 0.05$). The main reasons for discontinuation of use included pain, discomfort and inaccuracy in glucose measurements. Mean change in HbA1c was -0.5% ($p < 0.05$).

Conclusion: In our clinic most of the children did not use their RT-CGM continuously even though the treatment was provided for free. We believe a larger effort should be invested in parental/patient education and in the selection of patients suitable for this treatment. It is our hope that technology improvements will enhance patient compliance.

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EVALUATION OF A METHODOLOGY FOR ESTIMATING HBA1C VALUE BY A NEW GLUCOSE METER

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Background/Aims: Accuracy and robustness of HbA1c estimation ($\sim$A1C) with an algorithm built into a blood glucose meter (MyStar Extra®) have been demonstrated by *in-silico* testing, but prospective data are missing. We evaluated performance of $\sim$A1C in a clinical setting and patient-assessed ease of use.

Materials/Methods: Subjects (N = 133; mean $\pm$ SE age 60.0 ± 1.3 years, 69 male, 104 patients with type 1 (n = 24) or type 2 (n = 80) diabetes, 29 healthy subjects) used the meter at home for 4 months in this single-center study. Lab HbA1c/corresponding $\sim$A1C were documented every two weeks. Subjects completed a questionnaire at study end.

Results: Mean HbA1c was 7.0±0.1% (min, 5.2%; max, 11.9%). 1008 pairs of ∼A1C/lab HbA1c were available. Of the ∼A1C results in diabetic patients, 97.5% fell within ±20% of lab HbA1c, 95.0% within ±18%, and 90.7% within ±15%. Mean slope of ∼A1C vs. lab HbA1c plot was 0.53 (95% confidence interval 0.51–0.55), mean intercept 0.03 (0.03–0.04). Patients agreed/strongly agreed that they 1) could easily follow the ∼A1C section in the user guide and reference flash cards (72%), 2) would use the system to track ∼A1C (70%), 3) found ∼A1C tool helpful (79%), and 4) were motivated to better manage their diabetes because of the tool (83%).

Conclusion: The accuracy of the device's ∼A1C feature in this clinical setting was similar to performance in *in-silico* studies. The majority of patients found this tool helpful and agreed that it motivated to better manage their diabetes.

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THE ONETOUCH SELECT® PLUS BLOOD GLUCOSE MONITORING SYSTEM: TEST STRIP PERFORMANCE DEMONSTRATES INSENSITIVITY TO HAEMATOCRIT AND MEETS ISO 15197:2013

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The combination of new materials, algorithms and technology have resulted in the OneTouch Select® Plus blood glucose monitoring system (BGMS). Clinical studies have demonstrated that the measurement accuracy of certain BGMS can be adversely affected by variations in the haemocrit level of the blood sample and this can lead to clinically meaningful discrepancies in the resultant blood glucose result.

The OneTouch Select® Plus test strip has 3 glucose electrodes and 2 impedance electrodes coupled to a revised algorithm resulting in the system insensitivity to one of the largest sources of biosensor interference, haematocrit. This system dynamically selects the most appropriate assay time for the blood sample applied. This provides a personalized measurement and as such, irrespective of the patients' haematocrit a more accurate blood glucose measurement can be obtained.

Results: Verification bench testing has been conducted across the haematocrit range (29–56%) typically observed in a clinical setting. Analysis demonstrated that the system remained accurate at glucose concentrations of 2.2–31.1 mmol/L (40–560 mg/dL) irrespective of haematocrit across the entire haematocrit range tested.

Conclusion: The hematocrit performance of the OneTouch Select® Plus System has been demonstrated in the laboratory to

Haematocrit Level	Proportion within ±0.56 mmol/L (±10 mg/dL) or ±10%
29%	99.3% (1430/1440)
35%	99.4% (1431/1440)
42%	99.5% (1433/1440)
50%	99.4% (1432/1440)
56%	98.3% (1416/1440)
ALL	**99.2% (7142/7200)**

be insensitive to variations in haematocrit across the range of 29 to 56%. The OneTouch Select® Plus Test Strip provides individualized blood glucose readings and adjusts for natural variations in red blood cell level or hematocrit. Laboratory studies have demonstrated the OneTouch Select® Plus BGMS also meets the requirements for haematocrit performance as specified in ISO 15197:2013.

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THE ONETOUCH SELECT® PLUS BLOOD GLUCOSE MONITORING SYSTEM: CLINICAL ACCURACY PERFORMANCE - MEETS ISO 15197:2013

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Aim: The combination of new materials, algorithms and technology have resulted in the OneTouch Select® Plus blood glucose monitoring system (BGMS). This study evaluated the performance of this new BGMS with respect to achieving the higher accuracy standards defined by ISO 15197-2013.

Methods:
System Accuracy (SA):

- Testing was performed with three individual test strip lots at clinics using fingertip (capillary) blood samples from 100 subjects with diabetes.
- For each subject, six blood glucose (BG) tests were performed by trained staff (HCP).
- Duplicate comparison testing was performed using the YSI 2300 STAT Plus™ before and after OneTouch Select® Plus BGMS testing.

User Performance: Clinical Accuracy:

- 165 unique subjects (lay users) who had not taken part in the SA study were briefed on user performance procedures after obtaining written informed consent. Each subject performed a blood glucose self-test (including self-lancing) with the OneTouch Select® Plus meter and a OneTouch Select® Plus test strip from one of three randomly-assigned strip lots.
- The HCP performed a blood glucose test on the same blood sample with a second OneTouch® Select® Plus meter and OneTouch Select® Plus test strip from the same lot.
- The HCP collected blood from the same finger puncture for haematocrit and reference plasma glucose testing (duplicate tests on the YSI 2300).

Results:

System Accuracy Results		
Proportion within ±0.83 mmol/L (±15 mg/dL) or ±20% (ISO 15197 – 2003)	Proportion within ±0.83 mmol/L (±15 mg/dL) or ±15% (ISO 15197 – 2013)	Proportion within ±0.56 mmol/L (±10 mg/dL) or ±10%
100% (600/600)	99.5% (597/600)	97.5% (585/600)

User Performance Results	
ISO 15197:2013 Specification (±0.83 mmol/L (±15 mg/dL) or ±15% of reference)	
Lay Users	HCP
98.2 % (162/165)	100% (165/165)
100% of results falling within the A zone of the Consensus Error Grid for type 1 diabetes.	

Conclusion: The OneTouch® Select® Plus BGMS meets the higher accuracy criteria for both system accuracy and user performance accuracy, as defined by the new ISO 15197-2013 criteria.

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ACCURACY OF CONTINUOUS GLUCOSE MONITORING DURING RESTING AND EXERCISE CONDITIONS IN INDIVIDUALS WITH TYPE 1 DIABETES

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Background: The accuracy of real-time continuous glucose monitoring (CGM) has been questioned during exercise. This study evaluated the accuracy of CGM during exercise compared to an antecedent inpatient resting phase.

Subjects and Methods: Seven male recreational athletes with T1DM (age 27 ± 4 y, diabetes duration > 5 y, mean HbA1c $6.9 \pm 0.7\%$) underwent a 90 min pre-exercise resting phase (REST) and a subsequent 90 min moderate intensity cycling session (EX) at 50% VO_{2max} while monitored by the Dexcom G4 Platinum. Venous plasma glucose (VPG) reference sampling was carried out every 10 min throughout the experiment using the YSI 2300 analyzer. CGM accuracy was assessed by mean absolute relative difference (MARD) between paired sensor and reference VPG values and by applying international organization for standardization (ISO 15197:2013) criteria. Clinical accuracy was evaluated using Clark error grid (CEG; point accuracy) and continuous glucose-error grid (CG-EG; rate and point accuracy).

Results: MARD during EX was 14.79% compared to 14.95% during REST (p = 0.19). 62.8% of the CGM-values during EX met the ISO-criteria compared to 69.6% during REST. All CGM values during EX were in zones A and B of CEG (66.4% and 33.6%, respectively), compared with 97.5% (77.2% and 20.3%, respectively) during REST. Combined point and rate accuracy (CG-EG) were 94.6% during EX and 86.4% during REST. During EX 3.6% of the CGM-values were considered benign errors (12.1% in REST) with 1.8% erroneous readings (1.5% during REST).

Conclusion: Accuracy of the Dexcom G4 Platinum CGM was comparable during exercise and resting conditions.

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EXPERIENCE WITH RETROSPECTIVE ANALYSIS OF CGM IN MANAGING THE TREATMENT OF PATIENTS WITH T1DM

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Introduction: In Czech Republic health insurance covers only 4 sensors/year for an adult, thus CGM is used as diagnostic and patient education method. Retrospective analysis of CGM is convenient to accommodate the treatment of DM with correction of hyperglycaemia and hypoglycaemia. However, it is not clear how this intervention affects the glucose control after 6–12 months. The aim of our study is to correlate, on the basis of retrospective CGM analysis, metabolic control of patients with T1DM before modification of treatment and 6–12 months afterwards.

Methods: 14 patients with T1DM (mean age 47.5 ± 12.5 yr, DM duration 8.1 ± 5.6 yr, HbA1C 65 ± 14.1 mmol/mol, 2/14 treated CSII) were using CGMS (RT Guardian, Medtronic) for 7 days. They went through entry education on principles of sensor functioning and about possibility to observe effect of nutrition, physical activity and insulin intake on the glucose level. During CGM patients kept diary. Based on analysis of data obtained we recommended modification of treatment. After 6–12 months patients received checkup CGM. We evaluated metabolic compensation, glycemic variability and frequency and time in HY before modyfying treatment and 6–12 months afterwards.

Results: We proved decrease in: mean percentage of time at hypoglycaemia (< 3.9 mmol/l)/24 hours by 4.64% (-1.11 h) (p = 0.044), HbA1C (p = 0.299), GV measured by SD (p = 0.205), number of nocturnal hypoglycaemia (p = 0.144).

Conclusion: In 6–12 months after change of treatment based on, results showed reduced time in hypoglycaemia. Education derived from the analysis of CGM data improves quality of T1DM patient's life and is invaluable for treatment of diabetes.

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CALIBRATION OF GLUCOSE SENSORS: USE OF A TIME-VARYING CALIBRATION FUNCTION AND BAYESIAN PRIORS

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Objective: Continuous glucose monitoring (CGM) sensors use glucose-oxidase to measure a current signal related to interstitial glucose concentration. This signal is converted to a glucose concentration by a calibration procedure based on a static function whose parameters are identified using a few blood glucose (BG) measurements. However, CGM sensors still suffer from accuracy problems when compared with laboratory instruments. In this contribution, a new on-line calibration algorithm enhancing CGM accuracy is presented.

Methods: The starting point is the deconvolution-based approach proposed by Guerra et al. (IEEE TBME 2012) applied to the CGM current signal. The major novelties are the time-varying calibration function developed to compensate sensor variability-in-time (first order polynomial with time-varying offset) and the procedure for parameter estimation (stated in a Bayesian setting exploiting priors on unknown parameters). The method was tested on 108 CGM signals collected with the Dexcom G4 Platinum for 7 days. BG references on days 1, 4, and 7 were used to assess performance via Mean Absolute Relative Difference (MARD), Percentage of Accurate Glucose Estimates (PAGE) and percentage of data falling in the Clarke Error Grid A-zone (CEGA-A).

Results: Compared with original calibration and using the same BG references used by the manufacturer calibration, the new method drives to a statistically significant improvement for all the considered metrics: MARD reduced from 12.7% to 11.6%, PAGE incremented from 82.0% to 88.9% and CEGA-A increased from 82.2% to 89.1%.

Conclusion: The proposed calibration method improves CGM accuracy, a crucial aspect in both off-line and on-line applications.

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THE NON-INVASIVE METHOD TO MEASURE GLUCOSE WITH INSTANT CALCULATION OF GLUCOSE CONCENTRATION USING PHOTOACOUSTIC MID INFRARED SPECTROSCOPY (PA-MIR-S)

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In non-invasive procedures partial least square (PLS) cross-validation is used to extract relevant information from the large amount of data. PLS is a method to assess the suitability of the technology but cannot be used for instantaneous calculation of the glucose concentration.

We measure epidermal glucose, identical with blood glucose, through the use of PA-MIR-S. The signal of glucose is sensitive enough for the determination by background subtraction, however, changing background indicating epidermal composition represents a major obstacle. We have resolved this issue through mathematical description of the background and background subtraction (BgS). We collected the data of 4 oral glucose tolerance tests, 2 before and 2 after 45 min jogging at two different days. The data were analyzed by PLS and BgS.

The PLS analysis revealed a correlation coefficient r (Pearson) of maximal 0.91 and BgS of 0.88 in single tests. Only in BgS the data of one day could be combined giving a correlation coefficient between PA signal and glucose concentration of 0.84. This equals a RMSECV of 16 mg/dl. In BgS and PLS Jogging did not influence the results.

With BgS we were able to calculate the blood glucose instantly at least during one day. The changes in the body induced by 45 min physical activity did not influence the results. With this new calculation method we establish a non-invasive measuring device with the possibility of instant information about the blood glucose concentration not being influenced by physical activity.

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A NEW 3-STEP CLAMP METHOD FOR THE EVALUATION OF BLOOD GLUCOSE METERS

E. Zijlstra[1], L. Heinemann[1], A. Fischer[1], C. Kapitza[1]

[1]*Medical Technology, Profil, Neuss, Germany*

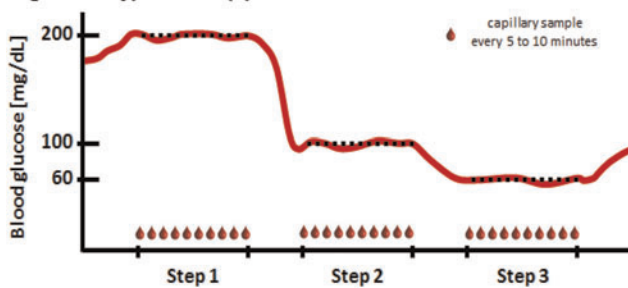Figure 1 – Typical clamp profile with 3 stable BG levels
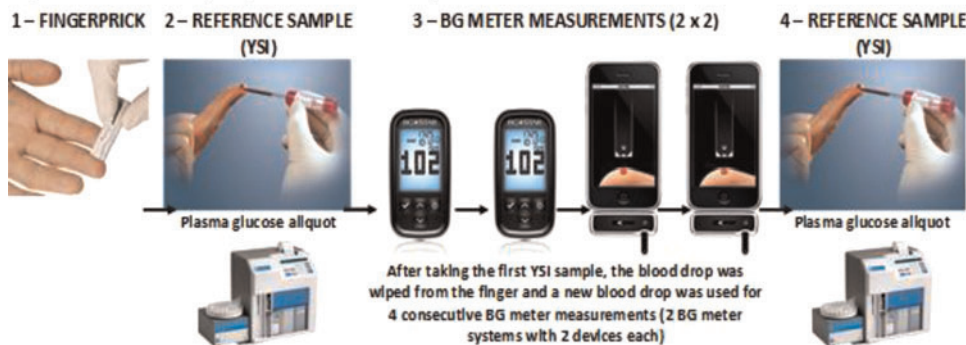

Table 1: BG meter accuracy, precision and bias

	ACCU-Chek Aviva Nano (Roche)	BGStar (Sanofi)	Freestyle Insulinx (Abbott)	iBGStar (Sanofi)	MyStar Extra (Sanofi)	OneTouch Verio IQ (LifeScan)
Measurement accuracy – MARD (%)						
60 (mg/dL)	6.3	5.7	9.5	6.3	4.6	13.2
100	4.6	3.9	6.7	4.1	3.8	10.6
200	3.8	4.1	6.7	4.0	3.8	6.1
Overall	**4.8**	**4.6**	**7.6**	**4.8**	**4.1**	**9.9**
Measurement precision – CV (%)						
60	6.9	7.1	7.4	7.7	5.9	5.3
100	5.5	4.7	4.8	5.1	4.9	4.8
200	4.8	5.1	5.2	4.8	5.9	4.1
Overall	**5.7**	**5.7**	**5.8**	**5.9**	**5.4**	**4.7**
Measurement bias (%)						
60	4.3	-1.9	-8.9	0.5	-0.8	12.0
100	0.9	-1.6	-6.5	0.4	-0.9	9.8
200	-1.4	0.9	-6.1	2.3	0.7	5.4
Overall	**1.3**	**-0.9**	**-7.1**	**1.0**	**-0.3**	**9.0**

Objective: To compare the performance (in terms of accuracy, precision and bias) of six CE-certified and commercially available BG meters using an innovative clinical experimental design with a 3-step glucose clamp and frequent capillary sampling.

Method: Twenty subjects with type 1 diabetes participated in this open label, single center trial. BG was clamped at 60–100 to 200 mg/dL by variable rate infusions of glucose and insulin (Figure 1). Medical staff performed regular finger pricks (up to 10 per BG level) to obtain capillary blood samples for paired BG meter and YSI reference measurements (Figure 2).

Result: One subject was excluded from the analysis due to problems with repeated capillary blood sampling. The data of 19 subjects were analyzed, providing up to 171 paired meter-reference data points per meter. Key results (Table 1) show that at each BG level and overall, the ACCU-Chek®, BGStar®, iBG-Star® and MyStar Extra® meters showed the lowest bias and the highest measurement accuracy. Measurement precision was similar for all six meters.

Figure 2 – Blood sampling and measurement procedures

Conclusion: A new 3-step clamp method with frequent capillary sampling was introduced, which provides valuable data for simultaneous investigations of BG meter accuracy, precision and bias. In this trial, the random error of the tested BG meters is comparable, but a lower systematic error for ACCU-Chek®, BGStar®, iBGStar® and MyStar Extra® gives these meters a highly accurate performance at low, normal and high BG levels.

This investigator-initiated study was supported by Sanofi.

This abstract was submitted previously to DTM 2014.

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BLOOD GLUCOSE METER PERFORMANCE: A COMPARISON BETWEEN TWO TEST PROCEDURES

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Objective: To compare the measurement accuracy and bias of the BGStar® blood glucose (BG) meter evaluated by a reduced scale standard test protocol and a new 3-step clamp method.

Method: Three BGStar® systems were evaluated in two clinical trials. The first used a reduced scale protocol of the ISO15197:2013 accuracy evaluation: including 35 subjects with type 1 or type 2 diabetes, two measurement series per subject and no defined distribution of BG concentrations (instead of 100 subjects with one measurement serie per subject and with a defined BG distribution). BG concentrations ranged from 56 to 397 mg/dL. The second trial, conducted with the same test materials at a different test center, evaluated meter accuracy and bias using a new 3-step (60–100–200 mg/dL) clamp method with frequent capillary sampling (10 samples per clamp level). 19 subjects with type 1 diabetes participated in this trial. Reference samples were analyzed using the YSI2300 STAT Plus glucose analyzer at both sites.

Result: Accuracy was similar between the three systems and comparable between the two procedures (Table 1). Notably, both procedures showed good agreement on the magnitude and sign of the meters' measurement bias, showing that small differences

between monitoring systems can be identified by these two test procedures.

Conclusion: Similar performance results for the BGStar® systems were obtained with the 3-step clamp method and with a reduced scale standard test protocol.

This investigator-initiated study was supported by Sanofi.

This abstract was submitted previously to DTM2014.

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CONTINOUS GLUCOSE MONITORING COMPLIANCE AND BEHAVIOUR PATTERNS AND ASSOCIATIONS WITH PATIENT OUTCOMES DURING 6-MONTH LOW GLUCOSE SUSPEND TRIAL

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Continuous glucose monitoring systems (CGMS) are a critical component in modern diabetes therapy. There is a paucity of long-term CGMS compliance data. Using data from 38 patients (mean age 17.0 years; 25 Male, 13 Female) from a 6-month low glucose suspend trial, we examined CGMS compliance over time, patterns of compliance and technical factors that influence compliance. Compliance was defined as having a working sensor fitted, not voluntarily turned off for > 4 hrs during the day or > 2 hrs overnight, and replacing sensors in a practical and timely fashion.

Mean (SD) CGMS compliance per participant was 75.1% (18.3%) over 6 months. Mean compliance decreased over the 6 months (P2 days), 18 (47%) of these had at least one CGMS holiday of > 7 days. Mean compliance was higher (87.3%) in those aged over 18, compared to those aged 12–18 years (69.4%; P = 0.03) and those aged 0–12 years (72.1%; P < 0.01). The mean number of sensor alerts per week per participant was 55.5 [range 19.4–178.3]. Sex, initial HbA1c, change in HbA1c, sensor alerts, sensor performance (MARD) or episodes of hypoglycemia were not associated with CGMS compliance.

We have shown that with the removal of cost barriers, overall CGMS compliance is variable, and dependent on many factors, and patterns can be identified. This should be considered in CGMS clinical application and patient education.

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EFFICACY AND FEASIBILITY OF FULLY AUTOMATED CLOSED LOOP INSULIN PUMP THERAPY AFTER ISLET AUTO-TRANSPLANTATION

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Background: Patients with chronic pancreatitis may undergo total pancreatectomy with islet auto-transplantation (TPIAT) to relieve pain while minimizing the risk of diabetes. Euglycemia is essential after transplantation as overstimulation of transplanted

Table 1: BGStar system performance comparison

	BGStar System 1	BGStar System 2	BGStar System 3
Accuracy – MARD (%)			
Test 1 (reduced ISO)	4.3	4.6	5.3
Test 2 (clamp)	4.6	5.4	4.8
Accuracy – results within 15/15 limits* (ISO 15197:2013)			
Test 1	139 / 140 (99.3 %)	69 / 70 (98.6 %)	66 / 70 (94.3 %)
Test 2	331 / 334 (99.1 %)	111 / 112 (99.1 %)	110 / 112 (98.2 %)
Accuracy – results within 10/10 limits*			
Test 1	127/140 (90.7 %)	63/70 (90.0 %)	64/70 (91.4 %)
Test 2	314/334 (94.0 %)	102/112 (91.1 %)	102/112 (91.1 %)
Accuracy – Clarke Error Grid Zone A (%)			
Test 1	100	100	98.6
Test 2	99.4	100	100
Measurement bias (%)			
Test 1	-2.4	-1.9	3.7
Test 2	-0.9	-2.6	2.9

Table 1. Interim serum BG and CGM BG analysis

PtID	Serum BG Avg (mg/dL)	Serum BG StDev (mg/dL)	CGM BG Avg (mg/dL)	CGM BG StDev (mg/dL)	CGM BG AUC < 70 mg/dL (min*mg/dL)	CGM BG % time <70 mg/dL (%)	CGM BG AAC > 140 mg/dL (min*mg/dL)	CGM BG % time >140 mg/dL (%)	AM C peptide Avg (ng/mL)	Islet Eq per kg (IEQ/kg)	Insulin TDD (U/day)
Experimental Closed Loop Pump Group											
TPIAT01	112	15	114	17	32	0.5	1729	5.0	0.75	3042	8.15
TPIAT03	115	12	116	21	286	1.1	7040	9.9	1.9	11940	9.7
TPIAT05	107	15	108	24	142	0.3	8055	8.3	2.2	9970	6.3
Control MDI Group											
TPIAT02	122	38	90	39	33875	33.6	9080	10.0	0.37	3696	25.3
TPIAT04	118	11	118	10	0	0.0	45	0.5	1.36	8307	14

Figure 1. Closed-Loop Patient 1 (TPIAT01) Serum BG
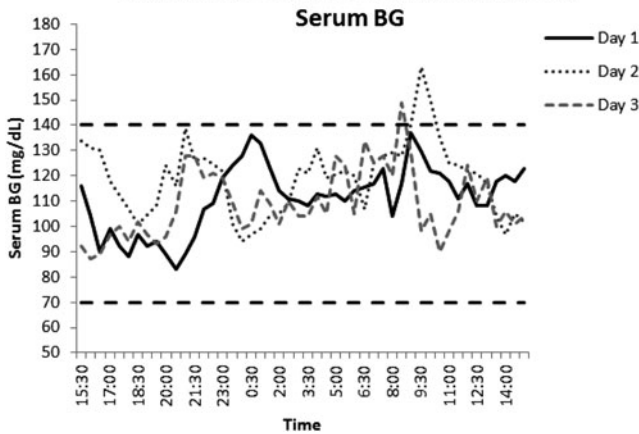
Figure 3. Closed-Loop Patient 3 (TPIAT05) Serum BG
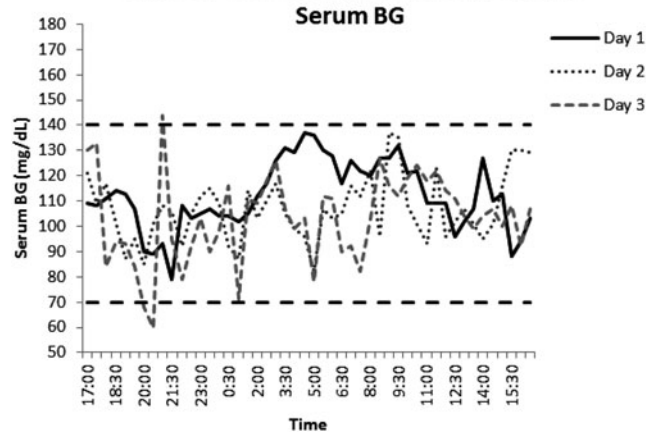
Figure 2. Closed-Loop Patient 2 (TPIAT03) Serum BG

islets is associated with apoptosis. Closed loop insulin pumps have never previously been investigated in islet transplant recipients but these devices may improve glycemic control within a narrow therapeutic target.

Objectives: To determine the feasibility and efficacy of closed loop insulin pump therapy to maintain glucose profiles close to normoglycemia following TPIAT.

Methods: Interim analysis for the first 5 patients (all female; mean age 37.6 ± 11.8 years-old) of the planned 20 patient IRB approved pilot study. At the time of transition from IV to sub-

cutaneous insulin, subjects were block randomized to subcutaneous insulin via a closed-loop pump (n=3) or multiple daily injections (n=2) for 72 hours.

Results: All patients on the closed loop insulin pump had mean serum glucose values in the target range with a low degree of variability (112 ± 15 mg/dL; 115 ± 12 mg/dL; 107 ± 15 mg/dL). Hypoglycemia was uncommon by CGM with only 0.5%, 1.1%, and 0.3% of the study periods spent < 70 mg/dL. All patients had mildly elevated BG in the morning, though only 5.0%, 9.9%, and 8.3% of the study periods were spent > 140 mg/dL.

Conclusions: Initial data suggest that closed-loop pump therapy after islet transplantation can successfully maintain blood glucose in the narrow target range of 70–140 mg/dL with minimal risk for hypoglycemia or significant hyperglycemia.

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HUMAN FACTORS AND HYBRID CLOSED LOOP: FINDINGS FROM A STUDY AT DIABETES CAMP

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Background: Significant progress on the development of hybrid closed loop (HCL) has occurred. During a week-long diabetes camp, 21 teens and young adults were randomized to HCL with an early, pilot version of the Medtronic 670G system (intervention) or Medtronic 530G threshold suspend (control).

The Medtronic 670G is the first fully integrated HCL system consisting of an Enlite3 glucose sensor and a proportional-integral-derivative algorithm incorporated into an insulin pump. In addition to measuring safety and efficacy of the systems, participants completed a human factors assessment.

Method: Participants completed the Diabetes Technology Questionnaire (DTQ), evaluating whether aspects of diabetes technology are problems before and after study completion. The intervention group participated in focus groups at study completion.

Results: The DTQ did not reveal any differences (p > 0.05) between intervention and control. DTQ scores can range to 110 with higher scores indicating fewer problems. Both groups trended toward perceiving slightly more problems after participating in the study (p = 0.07).

	Full Group (n=21)	Control (n=10)	Intervention (n=11)
Age (years)	18.6 ± 3.7	17.7 ± 2.2	19.3 ± 4.7
Mean Diabetes Duration (years)	9.1 ± 4.7	6.6 ± 3.8 *	11.3 ± 4.4 *
Mean A1c (%)	8.6 ± 1.5	8.6 ± 1.0	8.5 ± 1.9
Pre-Problem Score on DTQ	85.1 ± 14.3	85.6 ± 10.8	84.5 ± 17.7
Post-Problem Score on DTQ	82.5 ± 12.4	81.6 ± 11.8	83.3 ± 13.5

*p < 0.05

Nine of 10 intervention participants took part in focus groups. All but one reported a favorable response to the 670G. Less risk of nocturnal hypoglycemia and waking up in the target range were positive experiences. Participants were critical of meal boluses and the correction of high blood glucose levels was less aggressive than expected.

Conclusion: The survey and focus group responses indicate a mostly positive response to HCL and there was minimal evidence of increased burden or problems. Results will be used to modify and improve the HCL user experience in commercial devices.

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EFFICACY AND COMPUTATIONAL EFFICIENCY OF THE DOSE SAFETY HYPOGLYCEMIA PREVENTION MODULE (HPM)

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Objective: Assess the performance and computational efficiency of the Dose Safety HPM.

Method: We generated the baseline statistical model using the procedure described in our 2014 ATTD poster. Glucose and insulin dosing data from ten 24-hr *in silico* test runs; using different subjects from those used to generate the baseline model, were processed by the HPM. Online learning continuously personalized the baseline model for each subject.

Because hypoglycemia events are least likely when glucose values are increasing, predictions and model updates were computed only when glucose was level or falling.

To increase the number of low-glucose events, we set the low threshold to 90 mg/dL. We believe that to be sound because glucose predictions are based solely on machine learning pattern matching of the glucose and Insulin On Board signals; not a mathematical representation of the human glucoregulatory system. For the test, we defined a low glucose event as 2 consecutive glucose values below 90 mg/dL.

Result: Of the 16 low glucose events in the test datasets, 15 were predicted. The mean prediction time before the events was 47 minutes (SD = 30.7). Of the 6 false positive predictions, the mean actual glucose at the time was 98 mg/dL (SD = 11.5). Note that false positives below 100 mg/dL are considered safe.

Restricting the prediction and learning computations to when glucose was level or falling (slope <= 0) resulted in a 39% reduction in computation time.

Conclusion: The Dose Safety HPM is safe and computationally efficient to use in an artificial pancreas device.

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EXAMINING THE EFFECT OF CAFFEINE ON INSULIN-GLUCOSE DYNAMICS IN MALE SPRAGUE DAWLEY RATS

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Previous studies have shown that ingesting caffeine adversely affects insulin-glucose dynamics in humans[1]. Four main pathways have identified the mechanism through which this occurs: 1) increasing non-esterified fatty acid (NEFA) content in plasma[2]; 2) inhibiting phosphodiesterase (PDE) activity[3]; 3) inhibiting cyclic adenosine monophosphate (cAMP) activity[4]; and 4) increasing adrenaline production[2].

It has been shown that an exogenous bolus of adrenaline causes increased plasma glucose levels mainly due to gluconeogenesis, a compensatory increase in insulin secretion, and a counterintuitive reduction in glucose uptake by body cells[5].

The Sprague Dawley rat has been used as a reliable model of human PK/PD responses and other physiological phenomena[6]. Using twenty (20) male Sprague Dawley rats, ten (10) were made physiologically accustomed to caffeine. Test caffeine doses were subcutaneously administered, and the plasma levels of glucose, endogenous adrenaline, and insulin were quantitatively determined via glucose point of care device and ELISA assays respectively. The caffeine dosage was administered as 1, 2, and 4 'cups' respectively.

The plasma levels of adrenaline were significantly higher in the group physiologically acclimatized to caffeine. A first order plus dead time model can be generated for each dose of caffeine leading to establishing control parameters for an *in silico* model.

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OUTPATIENT DAY AND NIGHT HYBRID CLOSED-LOOP CONTROL WITH A PROPORTIONAL-INTEGRAL-DERIVATIVE BASED ALGORITHM IN ADULTS WITH TYPE 1 DIABETES

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DAY 0700-2300	Control	HCL	P-value
Mean	149 ± 12	157 ± 17	0.115
% 70–180	74.0 ± 8.3	70.7 ± 13.2	0.328
% 70–150	55.6 ± 9.5	50.9 ± 14.3	0.287
% < 70	2.3 ± 1.6	1.2 ± 1.2	0.098
Carbohydrates	550 ± 358	811 ± 253	0.021*
NIGHT 2300-0700			
Mean	157 ± 26	158 ± 19	0.848
% 70–150	45.7 ± 20.5	54.8 ± 15.8	0.191
% < 70	2.0 (0.7,4.5)	0 (0,0)	0.016*

Glucose units - mg/dL

The Medtronic Android-based proportional-integral-derivative with insulin feedback (PID-IFB) system is designed for hybrid closed-loop (HCL) in type 1 diabetes. It consists of a Revel 2.0 insulin pump, Enlite2 sensor, Bluetooth-RF translator and an Android phone-based algorithm. The objectives were to evaluate the safety and efficacy of HCL over 5 days in an outpatient setting. Subjects worked within 20 min of staff during the day, slept in a hotel overnight, and continued routine work, meals and exercise. Sensor-augmented pump data from the preceding week served as a control period.

We studied 8 subjects with a mean ± SD age 27.8 ± 5.8 y, duration of diabetes 17.7 ± 5.7 y, insulin dose 0.6 ± 0.2 u/kg/day and A1C 6.7 ± 0.6%. Subjects remained in HCL for a mean of 100 h, or 89 ± 10% of the study period. Glucose control during both periods are presented in the table. There were more carbohydrates consumed during HCL. The time spent in range during the day and night, 70–180 mg/dL, was similar between the two conditions. There was however, improved nocturnal hypoglycemia with almost elimination of hypoglycemia with HCL, p = 0.016.

Hybrid closed-loop with PID-IFB was safe and demonstrated less nocturnal hypoglycemia compared to sensor-augmented therapy. Mean glucose values were similar under both conditions despite almost twice the consumption of carbohydrates.

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DAY AND NIGHT CLOSED-LOOP CONTROL WITH THE DIAS SYSTEM IN PATIENTS WITH TYPE 1 DIABETES AT CAMP

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The DIAS system utilizes a control to range based algorithm for glucose control in type 1 diabetes. The system includes a Dexcom G4 sensor, a Roche AccuCheck pump, and an Android-based DIAS controller. Accelerometer input from a Zephyr Bioharness was also incorporated into the controller.

The objective of this study was to test the safety and efficacy of DIAS in subjects with type 1 diabetes, aged 10–35 y, at diabetes camp. There were 16 subjects randomized to either closed-loop with DIAS (intervention) or sensor-augmented pump (control) over 5 days in a diabetes camp setting. Both groups utilized premeal boluses.

OVERALL	Control	DIAS	P value
Mean glucose	147.7 ± 6.9	139.4 ± 3.1	0.250
%70–180	70.4 ± 5.3	80.4 ± 2.2	0.075
%80–150	50.6 ± 4.8	62.4 ± 2.7	0.034*
% < 70	5.8 ± 1.2	2.4 ± 0.5	0.020
NIGHT 2300-0700			
Mean glucose	145.6 ± 7.4	125.8 ± 3.3	0.029*
%70–180	71.2 ± 6.8	91.3 ± 2.0	0.015*
%80–150	53.1 ± 5.9	77.7 ± 2.8	0.002*
% < 70	5.3 ± 1.5	1.9 ± 0.7	0.079

The mean ± SD age of all subjects was 22.1 ± 5 y, duration of diabetes was 14.1 ± 5.5 y, A1C was 7.6 ± 1.2% and insulin dose 0.8 ± 0.3 u/kg/day. Glucose control for the two groups is shown in the table. The overall percent time in range, 80–150 mg/dL, was greater with DIAS, p = 0.034. The differences were most prominent overnight with a 20 mg/dL reduction in mean glucose values, increased percent time in range, and a reduction in both hyperglycemia and hypoglycemia.

Closed-loop control with the DIAS system was effective in this cohort of subjects with well-controlled diabetes. The improvement in glucose control was most prominent at night.

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PERFORMANCE OF A NEW CONTINUOUS GLUCOSE MONITORING SYSTEM (CGM) IN YOUTH

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We performed a study in youth age 2+ to determine performance of a new Dexcom G4 Platinum CGM system with advanced software algorithm, improved for artificial pancreas systems.

Continuous (Parkes) Error Grid
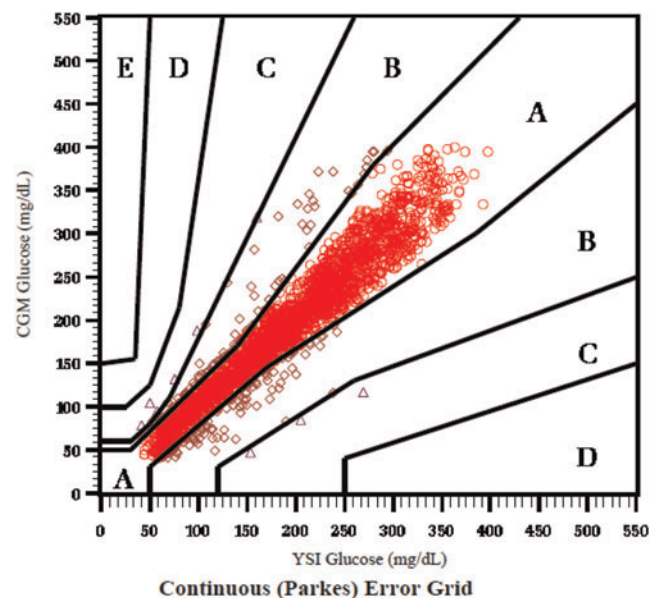
79 youth wore 1 CGM either on abdomen or upper buttocks for 7 days. A single in-clinic session occurred on sensor days 1, 4, or 7. In youth ≥ 6, the session lasted up to 12 hours with YSI sampling q15 and SMBG q30 minutes; in youth 2–5, SMBG sampling occurred q30 for 4 hours. In youth 13–17, carbohydrate intake and insulin dosing were safely manipulated to obtain wide glucose ranges under medical supervision.

Compared to YSI reference glucose, the Mean Absolute Difference (MARD) was 10% (N = 2262) and improved from 13% on day 1 to 8% on day 4, and 10% on Day 7. 91% of CGM readings were within 20% of YSI (or 20 mg/dL for YSI ≤ 80 mg/dL). In hypoglycemia ranges (CGM ≤ 80 mg/dL), the Mean Absolute Differences was 13.4 mg/dL (N = 228). The clinical accurate readings in A zone of the Parkes error grid were 93% and in the CEG A zone was 90%. Compared to SMBG, the MARD was 12.5% (N = 4264); no significant differences were found by age. The CGM readings were slightly closer to YSI than SMBG references; the MARD of SMBG to YSI was 5% (N = 1065, 95% CI: 4.5%-5.1%).

This study demonstrated accurate CGM performance in youth, comparable to that in adults. Accuracy improvements were observed across all days of wear, most notably in the hypoglycemia range.

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INTERVAL-BASED MODEL PREDICTIVE CONTROL FOR AN ARTIFICIAL PANCREAS

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Objective: A significant challenge of an artificial pancreas is to provide robustness against the uncertainty and variability inherent in diabetes management. In this work, a novel model predictive control algorithm that uses interval analysis to deal with such a challenge is proposed.

Method: The proposed interval-based model predictive controller (iMPC) uses an explicit-form model to predict blood glucose levels. This model has the advantage of being easily identifiable using plasma insulin and glucose measurements. Using an original technique, model parameters are identified as interval values to account for modelling errors and glucose sensor errors. Interval analysis is then used to obtain robust glucose estimates over the prediction horizon.

Ten adult virtual subjects from the UVa-Padova T1DM simulator were assessed over a 24-hour meal scenario (i.e. 7am(60 g), 1pm(70 g) and 7pm(80 g)). Realistic uncertainty on carbohydrate intake estimation was considered (± 20%). A variable glucose target range (i.e. fasting: [70,140]mg/dl; prandial: [70,180]mg/dl) was employed. iMPC was compared against its scalar counterpart (eMPC).

Results: iMPC performed better than eMPC on all the evaluated glycaemic control metrics: percentage time in target range [70,180]mg/dl (98.4 vs. 92.4 p < 0.05), percentage time below target (0.1 vs. 4.2 p < 0.05) and percentage time above target (1.4 vs. 3.4). Figure 1 shows the corresponding Control Variability Grid Analysis (CVGA) graph for both controllers.

Conclusion: A novel robust model predictive controller based on interval analysis has the potential to improve glycaemic control in T1DM diabetes management.

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VALIDATION OF A CLOSED LOOP SYSTEM IN PAEDIATRIC PATIENTS, 6 TO 12 YEARS, WITH TYPE 1 DIABETES

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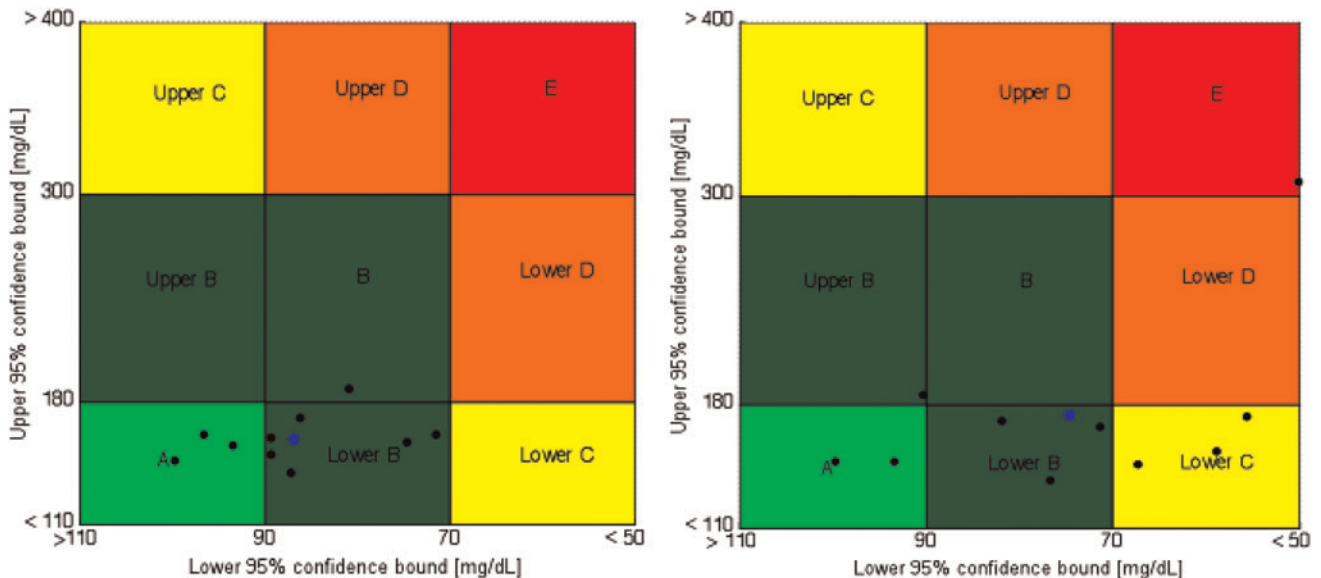[1]*Clinique Pédiatrique, Centre Hospitalier, Luxembourg, Luxembourg*

Figure 1. CVGA graph for iMPC (left) and eMPC (right).

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Objective: Evaluation of safety and efficacy of closed loop insulin delivery in children with type 1 diabetes, 6 to 12 years.

Patients and methods: 15 children, HbA1c < 11%, using insulin pump, participated in this open-label single center randomized cross over study. Outcome of the automated closed loop glucose control system (**closed loop arm**, CL) was compared to real time continuous glucose measurement (CGM) augmented insulin pump treatment (**open loop arm**, OL). Devices: Florence D2, Navigator II. All children were evaluated during 4 nights, two overnight in-patient stays and 2 nights at home.

Primary outcome was time spent in target glucose range from 3.9 to 8.0 mmol/l based on a secondary CGM (Dexcom). Secondary outcome was time spent in hypoglycaemis < 3.3 and < 2.5 mmol/l.

Results: 12 patients were analysed. There was a clear tendency to improve time in target in closed loop arm. This difference was not statistically significant neither between the groups for the 2 nights (CL 57%, OL 46%) nor when evaluating hospital stay (CL 61%, OL 58%) compared to home setting (CL 53%, OL 34%). Hypoglycaemia prevalence in closed loop was also lower (< 3.3 mmol/l: CL3%, OL 7%, < 2.5 mmol/l: CL 1%, OL 3%), not statistically significant.

Conclusion: Overnight closed loop pump treatment in children between 6 and 12 years has not caused metabolic adverse event and demonstrated tendency to more time in glucose target and less hypoglycemia. Further studies with larger patient population and longer duration are needed to confirm outcome of this preliminary study.

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THE ARTIFICIAL PANCREAS: USE OF CONTROLLED IN-PATIENT STUDIES TO ASSESS PERFORMANCE DURING PUTATIVE HIGH-RISK CONDITIONS ANTICIPATED TO OCCUR WITH PROLONGED AT-HOME USE

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Background: Artificial Pancreas (AP) studies often have power to show benefit during frequent day-to-day events such as meals or sleep, but lack power to characterize control during infrequent events that could lead to serious hypo or hyperglycemia. If the event is infrequent, at-home studies will need to be conducted over long periods, and in large numbers of subjects, before sufficient data to characterize the events can be expected to be available. In-patient studies effecting the same event in every subject can be powered with a small numbers of subjects and conducted without putting the subjects at significant risk. We used this approach to characterize a Physiologic Insulin Delivery (PID) system during periods of high sensor error together and other putative risk factors expected with prolonged home AP use. Eight adult subjects with Type 1 diabetes were studied for 17 hours on 3 occasions. Sensor glucose (SG) was set 20% lower than, equal to, or 33% higher than the blood glucose (BG).

Results: Median nighttime BG (116 mg/dL IQR [93–136]) was near target (120 mg/dL). Breakfast BG was never anticipated to fall below 60 mg/dL when the correct, or 20% lower than correct, SG was used; however, when 33% higher than correct was used, supplemental carbohydrates were required to prevent hypoglycemia (BG < 60 mg/dL) in 4 subjects. In each instance SG falsely reported glucose as in-target (80–170).

Conclusion: nighttime, but not daytime, PID control can be achieved with sensors reporting BG between 20% lower and 33% higher than the true BG.

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ESTIMATION OF THE CARBOHYDRATE TO INSULIN RATIO USING EMPIRICAL MODELS

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Recently, various empirical models have been proposed to describe glycemia dynamics in type one diabetes mellitus subjects. Carbohydrate intake and insulin infusion are considered as the inputs and glycemia measured by a Continuous Glucose Monitor (CGM) as the output. Models by M. Cescon et al. and H. Kirchsteiger et al. (Model No. 2) are continuous time systems with only few parameters. They are not physiology-based, but exploit a special structure. The structure is clinician-friendly, control-oriented and, most importantly, allows the parameters to have a clear physiological interpretation, e.g. the carbohydrate to insulin ratio (CIR).

However, the mentioned models include an integrator term which makes it difficult to simulate more than one meal event.

We have proposed an empirical model (Model No.3) without an integrator, which maintains the above-mentioned benefits.

The breakfast data have been used to assess the model. The mean data values for couple of days have been used for identification and the model has been validated separately on data for each day.

The performance evaluation has shown that the Model No.2 and No.3 are comparable. Identification: Model No.2 VAF = 97.05[%]; No.3 VAF = 97.62[%]. Validation: No.2 VAF = 96.72[%]; No.3 VAF = 97.14[%], where VAF is the variance accounted for.

The results have shown that the model parameters can be interpreted as CIR and the model can be used to simulate more meal events.

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PERFORMANCE DURING UNSUPERVISED CLOSED LOOP IN CHILDREN AND ADULTS WITH TYPE 1 DIABETES: WHAT MAKES THE DIFFERENCE?

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Objectives: Overnight closed-loop (OCL) insulin delivery is safe and effective in the home setting but outcomes vary between individuals. Identifying explanatory factors may help target those benefitting most whilst guiding further developments.

Methods: We combined two randomized OCL free-living home studies in 16 adolescents and 24 adults with T1D. Participants underwent, in random order, two periods of sensor augmented insulin pump therapy (SAP) or SAP combined with OCL insulin delivery, each lasting three-(adolescents) or four-weeks (adults). We stratified the study population by quartiles according to mean overnight glucose and overnight time in target during OCL. Comparisons of baseline characteristics (age, body mass index BMI, total daily insulin dose TDD, HbA1c) and utility (time of OCL start, duration of OCL application per night) between top and bottom quartiles were made.

Results: Using data from 866 OCL nights, only baseline HbA1c differed between top and bottom quartile of mean overnight glucose (58.4 ± 10.2 vs. 69.6 ± 8.2 mmol/mol, mean $\pm$ SD, p = 0.015). Participants in best quartile of time in target were significantly younger (17.28 [15.77,23.23] vs. 36.78 [27.21, 48.7], median[IQR]; p = 0.029), had lower BMI (21.71 ± 1.81 vs. 25.18 ± 2.54 kg/m^2; p = 0.002), and higher TDD (0.72 ± 0.11 vs. 0.52 ± 0.21 U/kg/day; p = 0.014). There was trend towards longer OCL use and earlier OCL start in best quartiles.

Conclusions: Better outcomes during OCL under free-living conditions were seen in those with lowest HbA1c and in adolescents. Improved outcomes may be observed if OCL is started earlier and applied for longer. Reasons for reduced effectiveness in older participants warrant further investigations.

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REAL-TIME UNDERWATER GLYCAEMIA MONITORING AND RECORDING DURING SCUBA DIVING UP-DATE

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Introduction: Diabetic mellitus type 1 is considered a contraindication to scuba diving [1-2-3-4-5-6-7].

The scope of this work is implement continuous underwater blood glucose (BG) monitoring using a dedicated real time monitor during diving whilst checking that the values recorded underwater are not influenced by the hyperbaric exposure.

Material and Method: Two diabetic divers (one male and one female), were monitored every 5 minutes during 40 dives, by a dedicated Continuous Glucose Monitor & Subcutaneous Glucose Sensor (Dexcom G4). The CGM Monitor was hosted in a waterproof case.

Data were recorded every 5 minutes during the dive and for 1 hour before and after the dive.

BG data about were also recorded, during two other assessments in normobaric conditions and in a hyperbaric chamber. During these tests BG was measured simultaneously using

Dexcom G4, CGM systems, and a capillary BG (OneTouch® Verio®IQ).

Results: 40 dives were recorded; no statistical difference between BG recordings every 5 minutes pre, during and post dives could be found (P < 0.05).

However, occasional borderline hypoglycaemia value was observed (< 70 mg/dL).

Data about the two different instruments showed a difference in recorded data in normobaric condition p = 0.002 and in hyperbaric condition p = 0.001; however, this difference was similar and constant in the two different environmental conditions p = 0.25.

Discussion: Our data confirm that BG values recorded in hyperbaric condition, and underwater can be trusted as the difference in BG reading between the Dexcom device, and the Capillary Blood data are not influenced by the environmental pressure.

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RESULTS FROM AN INTERVIEW-BASED SURVEY OF GLA-300 SOLOSTAR COMPARED WITH THREE COMMERCIALIZED DISPOSABLE INSULIN PENS

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Aims: To evaluate perceptions of people with diabetes (users) and HCPs (trainers) on usability of Gla-300 SoloSTAR disposable insulin pen, compared with Lantus SoloSTAR®, FlexPen® and KwikPen™.

Methods: A 75-minute quantitative face-to-face interview was conducted with trainers (64 nurses, 63 endocrinologists, 59 PCPs, and 4 pharmacists) with experience using ≥ 1 of the devices tested, and users (228 T2DM, of whom 128 were pen naïve; and 26 T1DM, of whom 3 were pen naïve). Following moderator demonstration, participants assessed pen usability, and ranked the devices in 10 different categories.

Results: Participants from six countries (France, Germany, Spain, UK, USA, Japan) were interviewed. More users ranked Gla-300 SoloSTAR first for 'ease of use' (44%), 'ease of injection' (49%) and 'least effort to press down plunger' (55%) vs Lantus SoloSTAR® (21%, 20% and 17%, respectively), KwikPen™ (18%, 18%, 18%) and FlexPen® (17%, 14%, 10%). More trainers also ranked Gla-300 SoloSTAR first for these categories (49%, 59%, 68%) vs Lantus SoloSTAR® (26%, 18%, 13%), KwikPen™ (8%, 13%, 10%), and FlexPen® (17%, 10%, 8%). Fewer users ranked Gla-300 SoloSTAR first for 'visualizing how much insulin is left' vs all tested pens and 'hearing the dial turning' vs KwikPen™ and FlexPen®. The majority experienced no problems preparing Gla-300 SoloSTAR and delivering the dose.

Conclusion: Gla-300 SoloSTAR was ranked first by more participants as being the easiest to use and inject, and requiring least effort to depress the plunger, than the three other disposable pens tested.

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FUNCTIONAL CHARACTERISATION OF FOUR DIFFERENT HALF-UNIT REUSABLE INSULIN PENS

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Objectives: The JuniorSTAR® (Sanofi, manufactured by Haselmeier) reusable, half-unit insulin pen was developed to address the needs of the paediatric type 1 diabetes population. Functional tests were conducted in a laboratory setting to assess dimensions, weight and injection force of JuniorSTAR® and three other half-unit pens: NovoPen® Junior (NovoNordisk), NovoPen Echo® (NovoNordisk) and HumaPen® Luxura™ HD (Eli Lilly).

Methods: 20 of each pen, filled with rapid-acting insulins were tested. Weight, length, size of dose button, dose window, dose digits, and dial extension were measured. Injection force was measured using a material testing machine at various typically used injection speeds and flow rates.

Results: JuniorSTAR® had the lowest weight and shortest length (without cap) for dose settings ≤15 U. HumaPen® Luxura™ HD was the heaviest pen, with the longest dose-setting extension. The dose window width was similar for JuniorSTAR® and HumaPen® Luxura™ HD; both NovoPens® were narrower. JuniorSTAR® had the largest dose window digits and dose button height (**Table 1**). JuniorSTAR® showed the lowest injection forces at the investigated parameters (**Table 2**).

Conclusions: Among the pens tested, JuniorSTAR® had the lightest weight, the shortest length (without cap, for dose settings ≤15 U), the highest dose button, the largest dose window digits, and the lowest injection force. These characteristics could ease the handling of the pen for young people with diabetes and diabetes patients who have limited hand strength. Further studies investigating user preferences for optimal dimensions, ease of reading, and injection forces are recommended.

Study funded by Sanofi

Tests performed by LWS, Brannenburg

Table 1: Pen weight and dimensions

	Dose setting (U)	JuniorSTAR®*	NovoPen® Junior†	NovoPen Echo®†	HumaPen® Luxura™ HD‡
Mean (SD) weight (including cartridge), g					
With cap	-	41.7 (0.16)	61.3 (0.33)	59.3 (0.17)	64.2 (0.34)
Without cap	-	27.4 (0.04)	44.1 (0.20)	44.1 (0.15)	44.3 (0.34)
Mean (SD) length, mm					
With cap	0	160.8 (0.05)	163.4 (0.08)	160.6 (0.00)	166.2 (0.18)
Without cap	0	133.6 (0.10)	140.5 (0.14)	145.5 (0.09)	141.7 (0.09)
	5	138.5 (0.14)	144.8 (0.15)	147.0 (0.13)	147.0 (0.11)
	10	143.5 (0.11)	149.2 (0.13)	148.5 (0.13)	152.3 (0.10)
	15	148.4 (0.10)	153.7 (0.16)	150.1 (0.09)	157.6 (0.07)
	30	163.4 (0.09)	166.8 (0.13)	154.6 (0.16)	173.5 (0.05)
Mean (SD) dose button dimension, mm					
Diameter	-	17.2 (0.00)	16.5 (0.06)	17.3 (0.00)	17.6 (0.05)
Height	-	14.5 (0.00)	7.8 (0.00)	11.2 (0.00)	10.8 (0.06)
Mean (SD) dose window dimensions, mm					
Width	-	8.0 (0.00)	6.7 (0.00)	6.0 (0.00)	8.4 (0.00)
Length	-	8.0 (0.00)	8.0 (0.00)	7.5 (0.00)	9.0 (0.04)
Mean (SD) dose window digit dimensions, mm					
Height	-	3.6 (0.08)	2.4 (0.05)	2.8 (0.06)	3.5 (0.11)
Length	-	2.1 (0.10)	1.5 (0.04)	2.0 (0.05)	1.8 (0.16)

*Sanofi, Paris, France, manufactured by Haselmeier, Stuttgart, Germany; †NovoNordisk, Bagsvaerd, Denmark; ‡Eli Lilly, Indianapolis, IN, USA

Table 2: Injection force measurements

	Injection force (N) at 30U dose setting, mean (SD)			
Pen	JuniorSTAR®	NovoPen® Junior	NovoPen Echo®	HumaPen® Luxura™ HD
Insulin	Apidra®	NovoRapid®	NovoRapid®	Humalog®
Button dialling speed, mm/s				
4.00	4.38 (0.27)	7.95 (0.44)	9.66 (0.28)	5.91 (0.43)
8.00	7.82 (0.61)	12.53 (0.78)	19.12 (0.67)	8.82 (0.70)
Flow rate, U/s				
3.67	4.38 (0.27)	7.27 (0.43)	7.01 (0.15)	5.84 (0.47)
6.00	5.94 (0.35)	9.22 (0.59)	7.25 (0.17)	7.54 (0.65)
7.34	7.82 (0.61)	10.34 (0.67)	7.89 (0.16)	8.52 (0.70)
10.00	9.17 (0.47)	12.89 (0.91)	9.45 (0.23)	10.52 (0.93)

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LONG-TERM USE OF INSUPAD IS ASSOCIATED WITH HIGH TREATMENT ADHERENCE, MAINTENANCE OF EXCELLENT GLYCEMIC CONTROL AND FURTHER REDUCTION OF PRANDIAL INSULIN REQUIREMENTS

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The InsuPaddevice enhances insulin absorption by standardized injection site modulation and was shown to reduce the frequency of hypoglycemia (by ~46%) and prandial insulin requirements (−30%) in a controlled trial with three month Duration. This follow-up investigation aimed to explore the effect of using InsuPad over a period of more than 12 months.

After the study, patients were supplied with the device and disposables to continue device use. Patients in the previous control group were also trained on device use. This long-term use follow-up investigation was performed in 52 patients (22 female, 30 male, age (mean ± SD): 65 ± 8 yrs., HbA1c: 7.1 ± 0.7% at main study start), who were re-contacted after a minimum of 13 months to complete a standardized questionnaire.

Mean usage time was 17.8 ± 2.5 months (13–21 months). Only two patients (3.8%) had stopped device use because of persistent skin reaction to the adhesive. In the remaining patients, body weight had remained stable (3 months: 100 ± 23 kg vs. 18 months: 100 ± 18 kg, n.s.), HbA1c was stable (baseline: 7.2 ± 0.7%; after 3 months: 6.4 ± 0.7% vs. 18 months: 6.3 ± 0.6%), and total daily insulin dose was even further reduced as compared to BARMER-study start (change vs. baseline: 3 months: −16.5% vs. 18 months: −25.3%, p < 0.001).

The excellent glycemic control achieved in the BARMER-study was maintained when all patients used the device over a period of 18 months or longer with further reduction of prandial insulin dose requirements and with a high treatment adherence.

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OBESE PATIENTS ON INTENSIVE INSULIN ANALOG THERAPY REACHING TREATMENT TARGETS (HBA1C < 6.5% AND WEIGHT LOSS > 1KG

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InsuPad applies a standardized skin modulation resulting in lower prandial insulin doses. The purpose of this analysis was to compare the impact of reaching two Treatment Targets (HbA1c < 6.5% and weight loss) on prandial insulin doses and hypoglycemic episodes (< 63 mg/dL).

All Patients who completed the BARMER study and lost more than 1 kg of body weight in the three-month observation period were included. Mean values were calculated for HbA1c, body weight changes, changes in prandial and basal insulin dose, and the number of hypoglycemic and hyperglycemic readings.

Meeting the inclusion criteria were 22 patients in the InsuPad group (IPG, 9 female, 1 Type 1, age: 64 ± 8 yrs., weight: 106.7 ± 18.7 kg) and 17 patients in the control group (CG, 7 female, 3 Type 1, 60 ± 10 yrs., 109.0 ± 18.4 kg). HbA1c treatment target (< 6.5%) was successfully met after three months in both groups (IPG: $6.2 \pm 0.5\%$ vs. CG: $6.3 \pm 0.5\%$, n.s.). Weight loss was IPG: -2.6 ± 1.5 kg and CG: -3.7 ± 4.4 kg (n.s.). IPG patients needed 28% less prandial insulin (CG: +12%, p < 0.001) and 1% more basal insulin (CG: -2%, n.s.). Number of hypoglycemic readings were IPG: 2.8 ± 4.4/patient and CG: 8.9 ± 16.0/patient (p < 0.05).

Treating obese patients to a combined HbA1c (< 6.5%) and weight loss target (> 1 kg) was possible with and without use of the InsuPad device. Patients using InsuPad needed substantially less prandial insulin and had only a third of the frequency of hypoglycemia readings as compared to the control group.

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PLGA PARTICLES AS A VECTOR FOR ORAL INSULIN DELIVERY: IN VITRO AND IN VIVO VALIDATION OF FUNCTIONALITY

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Oral administration of insulin results in low pharmacological effect, due to harsh conditions of the gastrointestinal tract. Encapsulation is one of approaches to protect insulin, Poly lactic-co-glycolic acid (PLGA) particles (NP) are known to be effective drug carrier but have a bioavailability lower than 20% and a long acting profile. The aim of this work was to increase encapsulated insulin bioavailability modifying surface properties of NP to improve interaction with mucus layer.

Particles were prepared in the presence or not of polyvinyl alcohol (PVA), with PEGylated-PLGA or with a coating by chitosan chloride. *In vitro* internalization was tested on epithelial coculture (Caco-2/RevHT29MTX) and caco-2 alone by flow cytometry. Finally, NPs were administrated *in vivo* intraperitoneally (2UI) and intraduodenally (10UI) in diabetic rats.

Without PVA and PEGylated-PLGA NPs had a smaller size (154 ± 24 nm), whereas chitosan coating increased NPs size (236 ± 29 nm) in comparison to control (200 ± 9 nm). Cell NPs uptake was improved by PEGylated-PLGA and without PVA at the opposite of chitosan coated NPs, which adhered on mucus and cell membrane when compared to classical NPs (PLGA + PVA). Administration of NPs (2UI) by intraperitoneal route induced a decrease of glycemia as faster as no encapsulated insulin (4 hours). 10UI if insulin has no effect by intraduodenal route at the opposite to NP decreasing glycaemia. Without PVA, NP were the most efficient.

It appeared that NPs without PVA were the most efficient *in vitro* as *in vivo*, and represent a promising formulation for oral insulin delivery.

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NEW INSULIN GLARGINE 300 U/ML: EFFICACY AND SAFETY OF FLEXIBLE VS FIXED DOSING INTERVALS IN PEOPLE WITH TYPE 2 DIABETES MELLITUS

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Background and aims: The more constant and prolonged PK and PD profiles of new insulin glargine 300 U/mL (Gla-300) vs glargine 100 U/mL (Gla-100), with glycemic control extending beyond 24 h and up to 36 h, provide a rationale for the occasional flexible timing of daily injections depending on individual lifestyle. The 3-month sub-studies of EDITION 1 and 2 compared the efficacy and safety of Gla-300 using a fixed 24-h dosing interval with a flexible dosing regimen allowing between-injection intervals of 24 ± 3 h.

Materials and methods: The background multicenter, 6-month, open-label studies compared Gla-300 vs Gla-100 injected once daily in the evening in people with type 2 diabetes mellitus using basal + meal-time insulin (EDITION 1) or basal insulin + OADs (EDITION 2). Participants (N = 198) using Gla-300 were randomized at month 6 to the fixed or flexible regimen. Efficacy and safety were evaluated in a pooled data analysis.

Results: The frequency of maintaining a 24 ± 1 h interval between injections was 88.0% with the fixed regimen and 58.7% with the flexible regimen. HbA_{1c} change was comparable in fixed vs flexible regimens (Table). Percentages of participants experiencing ≥ 1 hypoglycemic event at any time (24 h), or at night (00:00–05:59 h), were comparable. Severe hypoglycemia was experienced by 1 participant (EDITION 1). There were no differences in adverse events.

Table: Outcomes of flexible and fixed dosing intervals – pooled data analysis of the EDITION 1 and EDITION 2 sub-studies

		Flexible	Fixed
HbA1c, %*	Baseline[†]	7.30 (0.93)	7.30 (0.96)
	Change[‡] [months 6–9]	0.05 (0.06)	0.00 (0.07)
	Difference[§]	0.05 (−0.13 to 0.23)	
Hypoglycemic events, n (%)[¶]	All, at any time [24 h]	48 (48.0)	53 (55.2)
	All, nocturnal [00:00–05:59 h]	22 (22.0)	22 (22.9)
	Severe, at any time [24 h]	0 (0.0)	1 (1.0)
Percentage of injections within dosing intervals, %[¶]	24±<1 h	58.7	88.0
	24±1 to 3 h	25.5	9.8
	24±>3 h	15.8	2.2

*Modified intention-to-treat population (flexible, N=99; fixed, N=95); [†]mean (standard deviation); [‡]least squares (LS) mean (standard error); [§]LS mean difference (95% confidence interval); [¶]safety population (flexible, N=100; fixed, N=96).

Conclusion: Occasional flexibility in timing of daily Gla-300 injections by ± 3 h resulted in similar efficacy and safety compared with advising injections at a fixed time each day.

Study sponsored by Sanofi (NCT01499082/NCT01499095)

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LESS NOCTURNAL HYPOGLYCEMIA AND WEIGHT GAIN WITH NEW INSULIN GLARGINE 300 U/ML VS 100 U/ML: 1-YEAR RESULTS IN T2DM USING BASAL INSULIN + OADS (EDITION 2)

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Background and aims: EDITION 2 investigated glycemic control and hypoglycemia using new insulin glargine 300 U/mL (Gla-300) versus glargine 100 U/mL (Gla-100) in people with T2DM on basal insulin plus OAD(s).

Materials and methods: In EDITION 2, 811 adults with T2DM and inadequate HbA1c control were randomized to receive Gla-300 or Gla-100 for 6 months. In this 6-month open-label extension, participants continued to receive once-daily Gla-300 or Gla-100 plus OADs; 315 (78%) participants in the Gla-300 group and 314 (77%) participants in the Gla-100 group completed 12 months' treatment.

Results: Improved control of HbA1c was maintained at 12 months with each regimen. Over 12 months, fewer participants experienced ≥1 nocturnal confirmed (≤70 mg/dL [≤3.9 mmol/L]) or severe hypoglycemic event with Gla-300 than Gla-100

Table 1 – Glycemic control over 12 months in the EDITION 2 study

mITT population		HbA1c (%) Gla-300 (N=403)	Gla-100 (N=405)
Baseline	Mean (SD)	8.26 (0.86)	8.21 (0.77)
Change from baseline to month 12 (MMRM)	LS mean (95% CI)	−0.55 (−0.67 to −0.44)	−0.50 (−0.61 to −0.39)
	LS mean difference (95% CI)	−0.06 (−0.22 to 0.10)	

CI, confidence interval; LS, least squares; mITT, modified intention-to-treat; MMRM, mixed model for repeated measurements.

Table 2 – Hypoglycemia over 12 months in the EDITION 2 study

Safety population	Nocturnal hypoglycemia (00:00–05:59 h)			Hypoglycemia at any time of day (24 h)		
	Gla-300 (N=403)	Gla-100 (N=406)	RR* (95% CI)	Gla-300 (N=403)	Gla-100 (N=406)	RR* (95% CI)
Any hypoglycemia						
% people ≥1 event	39.7	46.1	0.86 (0.73 to 1.01)	79.9	83.0	0.96 (0.90 to 1.03)
Events/participant-year	1.80	2.94	0.61 (0.41 to 0.92)	11.87	13.70	0.87 (0.70 to 1.07)
Confirmed (≤70 mg/dL [≤3.9 mmol/L]) or severe hypoglycemia						
% people ≥1 event	37.5	44.6	0.84 (0.71 to 0.99)	78.4	82.0	0.96 (0.89 to 1.02)
Events/participant-year	1.74	2.77	0.63 (0.42 to 0.96)	11.60	13.18	0.88 (0.71 to 1.09)

CI, confidence interval; *RR, relative risk for % people ≥1 event; RR, rate ratio for events/participant-year.

(RR: 0.84 [95%CI: 0.71, 0.99]). Annualized event rates of nocturnal confirmed (≤70 mg/dL [≤3.9 mmol/L]) or severe hypoglycemia were 37% lower with Gla-300 than Gla-100 (1.74 vs 2.77, RR: 0.63 [0.42, 0.96]). Severe hypoglycemia at any time (24 h) was infrequent, experienced by 7 and 6 participants in the Gla-300 and Gla-100 groups, respectively. Body weight increase was observed in both groups, and was significantly less with Gla-300 than Gla-100 (LS mean [95%CI]: 0.42 [0.04, 0.80] versus 1.14 [0.76, 1.52] kg, p=0.0091). A similar pattern of adverse events was seen between groups.

Conclusion: Over 12 months' treatment, people with T2DM using Gla-300 and OADs had comparable glycemic control, experienced fewer nocturnal hypoglycemic events and less weight gain compared with those using Gla-100.

Study sponsored by Sanofi (NCT01499095)

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GLYCEMIC CONTROL AND HYPOGLYCEMIA WITH NEW INSULIN GLARGINE 300 U/ML IN PEOPLE WITH TYPE 1 DIABETES (EDITION 4)

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Table – Hypoglycemic events per participant-year in the two insulin groups

	Gla-300 (N=274)	Gla-100 (N=275)	RR (95% CI)
Total participant-years	124.1	126.8	
Nocturnal (00:00–05:59 h) confirmed (≤70 mg/dL [≤3.9 mmol/L]) or severe			
Baseline to month 6	8.0	8.9	0.90 (0.71 to 1.14)
Baseline to week 8	7.8	11.2	0.69 (0.53 to 0.91)
Week 9 to month 6	8.1	7.9	1.04 (0.80 to 1.36)
Any-time (24 h) confirmed ([≤70 mg/dL [≤3.9 mmol/L]) or severe			
Baseline to month 6	78.4	72.5	1.09 (0.94 to 1.25)
Baseline to week 8	87.4	89.5	0.98 (0.85 to 1.13)
Week 9 to month 6	73.9	64.2	1.16 (0.98 to 1.37)

CI, confidence interval; RR, rate ratio.

Background and aims: EDITION 4 studied the efficacy and safety of new insulin glargine 300 U/mL (Gla-300) compared with glargine 100 U/mL (Gla-100) in people with T1DM.

Materials and methods: In this 6-month, multinational, multicenter, open-label study, participants (N=549, BMI 27.6 kg/m^2, diabetes duration 21.0 years, HbA$_{1c}$ 8.1% [65 mmol/mol]) were randomized 1:1:1:1 to once-daily Gla-300 or Gla-100, morning or evening, while continuing mealtime insulin.

Results: Gla-300 was non-inferior to Gla-100 for HbA$_{1c}$ change from baseline (primary endpoint) (LS mean change [SE] −0.40 [0.05] % (−4.4 [0.6] mmol/mol) and −0.44 [0.05] % (−4.8 [0.6] mmol/mol); LS mean difference 0.04 [95% CI: −0.10 to 0.19] % (0.4 [−1.1 to 2.1] mmol/mol)). Event rates of confirmed (≤70 mg/dL [≤3.9 mmol/L]) or severe hypoglycemia at any time (24 h) were similar for the two groups; nocturnal hypoglycemia was lower for Gla-300 versus Gla-100 during the first 8 weeks (Table). Severe hypoglycemia was observed in 6.6% (Gla-300) and 9.5% (Gla-100) of participants. Neither glycemic control nor hypoglycemia differed between insulins or times for morning and evening injection groups. Total insulin dose increased to a somewhat greater extent for Gla-300 versus Gla-100 (change from baseline +0.19 versus +0.10 U/kg). Weight gain was significantly lower with Gla-300 versus Gla-100 (LS mean difference −0.56 [−1.09 to −0.03] kg, p=0.037). There was no difference in AEs between groups.

Conclusion: New insulin glargine 300 U/mL provided comparable glycemic control versus glargine 100 U/mL, while nocturnal hypoglycemia was reduced during the first 8 weeks.

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PREDICTORS OF GLYCEMIC RESPONSE FOLLOWING NEWLY INITIATED BASAL INSULIN AMONG INSULIN NAÏVE ADULTS WITH TYPE 2 DIABETES

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Aims: To determine the baseline characteristics predict the likelihood of attainment of HbA1c goal and change in HbA1c after initiation of basal insulin glargine in insulin naïve people with type 2 diabetes not adequately controlled on oral glucose lowering drugs.
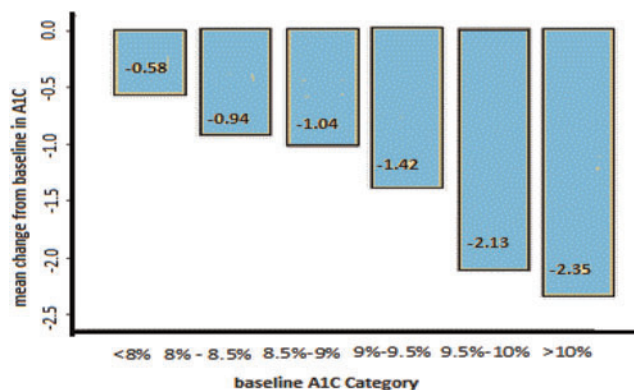
Relationship between baseline characteristics and HbA1c by week 24

	HbA1C =7.0% (visit3) N=157 (36%)	HbA1C >7.0% (visit3) N=276 (64%)	P-value
Gender (Female)	99 (63%)	167 (61%)	0.61
Age (yr)	53.79±11.55	55.24±10.89	0.21
BMI (kg/m²)	28.09±4.43	27.91±5.13	0.71
Diabetes duration (yr)	9.54±6.85	8.74±5.97	0.43
SBP (mmHg)	127.88±16.69	132.60±18.97	0.01
DBP (mmHg)	79.30±9.23	81.00±8.63	0.04
TG (mg/dl)	186.85±86.19	188.17±96.32	0.94
HDL (mg/dl)	44.38±12.47	42.66±11.46	0.28
LDL (mg/dl)	103.93±32.29	107.79±35.74	0.27
Chol (mg/dl)	186.99±39.94	190.54±45.85	0.42
FBG (mg/dl)	194.32±54.84	213.54±65.51	0.001
HbA1C (%)	8.52±0.99	9.07±0.85	0.00
Nephropathy (+)	14 (9%)	30 (11%)	0.56
Neuropathy (+)	33 (22%)	83 (31%)	0.051
Retinopathy (+)	16 (11%)	32 (13%)	0.66
Sulphonylurea use at baseline (yes vs. no)	119 (76%)	216 (78%)	0.56
Glargine daily dose (unit/day)	14.75±7.74	16.40±8.18	0.007

BMI: Body Mass Index; SBP: Systolic Blood Pressure; DSP: Diastolic Blood Pressure; TG: Triglyceride; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; Chol: Total Cholesterol; FBG: Fasting Blood Glucose; HbA1c: Glycosylated hemoglobin

Association between baseline characteristic and HbA1c attainment.

	Odds ratio	CI for odds ratio	p-value
SBP	0.99	(0.97 1.00)	0.07
DBP	0.99	(0.96 1.02)	0.60
FBG	0.99	(0.99 1.00)	0.53
HbA1C	0.54	(0.41 0.69)	0.00
Glargine dose	0.97	(0.94 1.02)	0.06
Neuropathy	0.82	(0.49 1.36)	0.44

SBP: Systolic Blood Pressure
DSP: Diastolic Blood Pressure
FBG: Fasting Blood Glucose
HbA1c: Glycosylated hemoglobin

Methods: Data from the Iran-AFECT study was used for this analysis. Univariate and multivariate analyses were performed on insulin naïve people. We included all people with type 2 diabetes not adequately controlled by oral glucose lowering drugs who completed 24 weeks of the study. Glycemic response was defined as HbA1c ≤ 7.0% and/or change in HbA1c at 24 weeks following insulin initiation.

Results: The mean HbA1c was $8.9\% \pm 0.9\%$ at baseline which decreased to $7.6\% \pm 1.2\%$ (P=0.00). By week 24, thirty six percent of the participants reached to the HbA1c 7.0%. In uni-variate analysis, the strongest association was for the baseline HbA1c (r^2=0.32, P=0.00). In multivariate analysis, predictors of change in HbA1c were baseline HbA1c (r^2=0.29, P=0.00), and glargine dose (r^2=0.01, P=0.02). The baseline HbA1c was accounting for 88% of explainable variance in HbA1c. The best cut-off predicting glycemic response for baseline HbA1c was 8.5%. There was also significant HbA1c change (up to 2.36%) in more poorly controlled patients.

Conclusions: Among factors predicting response to initiating basal insulin therapy with insulin glargine, baseline HbA1c is the strongest predictor, and explains most of variance in HbA1c change.

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EVALUATING ANALOG VS HUMAN INSULIN EFFICACY IN REAL LIFE. OBSERVATIONAL STUDY IN TYPE 2 ALBANIAN DIABETIC PATIENTS, PREVIOUSLY INSULIN TREATED

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Background and Aims: In Albania, specialists still have to demonstrate at the institutions the treatment's efficacy and cost-effectiveness for new insulin analogs. The aims of our study is to evaluate the efficacy of analogs vs human insulins and differences between various analog insulin, in type 2 diabetes patients, previously treated with human insulin.

Methods: This study is realized in real life patients. We retrospectively included 384 patients, previously treated $\geq$24 months with human insulins, switched to an analog insulin for $\geq$12 months. Treatment efficacy was evaluated by HbA1c levels, weight difference and changes in total daily dose (TDD) analog vs human.

Results: 185 (48.17%) males. Mean age 62.19 (SD 10.12) yrs, mean diabetes duration 10.8 (SD5.35) yrs. Mean duration on analog insulin therapy was 19.1 months. GLargine 194 (50.5%), DEtemir 110 (28.6%), All Other Analogs (AOA) 80 (20.8%). Averall Mean HbA1c was 8.86(SD1.06) vs 7.51(SD1.51) on analogs p<0.01. TDD was 54.9 UI (SD20.1) vs 62.56UI (SD27.95) on analogs p<0.05, but smaller basal doses 29.28 vs 28.1UI. 21% of the patients on human insulin had an HbA1c<7%, vs 63.1% on analogs. Patients on analogs had a slight weight increase +3.18 kg during the study period (p 0.55), but DE/GL 1.48 vs 4.14 kg (p<0.01).

Conclusions: A better metabolic control was noted with analog vs human insulins, with smaller daily doses of basal insulin and

minimal weight increase. Even in our study, Detemir group had a smaller weight gain, making it preferable for obese type 2 diabetics.

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BIOMATERIAL USED AS A WAY TO PREVENTION THE DIABETIC FOOT CONSEQUENCES

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The high plantar pressures of the foot during gait in patients with neuropathy have a mechanical etiology due to foot deformities and kinematic changes. These conditions increase the risk of ulceration in these patients and, in consequence, to neuropathy, micro and macro-vasculopathies, people with DM present alterations on foot skin humidity.

Aims: i) Evaluating the insole with shock absorbers confection, made of a variable density material derived from natural latex, for filtering plantar pressure signals and ii) Through of the pressure distribution and analysis of the cell that has been designed to aid tissue regeneration to verify how the skin hydration is showed with the latex insole use.

Results: The essence of this study is intended, under the etiological-mechanical approach, to the intersection of an external element (latex-derived insole) with diabetic passive stride and to show how the foot skin hydration can be modified through the use of biomaterial latex (brasiliensis).

Conclusion: There is an impact on the variation of some key variables to diabetic foot such as change in mass and contact with soil. The research presented in this study will be an intellectual preparation for the emergence of a new concept, proposed with the idea of Organic Control. The proximity of the organ, the complexity of elements involved and their influences and interconnection, since there is little sense in analyzing the system whether disconnected to a mixture of many nutrients, deformity or normality. With this, an understanding of the primary system – Diabetic Foot – is a focus to be worked on and characterized it in this concept.

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EXTRACTION OF FATS FROM DIABETOGENIC DIET RESULT WEAKENING SYMPTOMS OF DIABETES CAUSED BY XANTHURENIC ACID

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Xanthurenic Acid (XA), a diabetogenic metabolite of abnormal Tryptophan metabolism is formed in elderly humans as a result of a deficiency in vitamin B6 and diet enriched by fats. XA-diabetes accompanied by xanthurenuria (XAU) was 7–10 times more high compared with intact animals, and led to destruction and death of B-cells.

Aim of work: To investigate influence of fat extraction from diet on endogenous synthesis of XA and histostructure of islets.

Methods: 2 groups of rats. **Group 1**.12 rats 98–106 days on stimulated synthesis of XA diet (DXA). **Group 2**.11 rats 102–112 days on DXA free of butter. Blood glucose control (BG)-weekly, XAU-monthly. Histology: immunohistochemical (IH), pseudoisocyanine (PS) methods staining of insulin in B-cells with measuring of absorbance and aldehyde fuchsin method.

Results: Group 1. BG: 4.63 ± 0.31 mM before and 10.84 ± 0.44 mM 92–104 days later; XAU: 0.034 ± 0.03 mcg/ml before and 0.376 ± 0.32 mcg/ml 96–98 days later. Histology: destruction and necrosis of B-cells in $64 \pm 7.6\%$ islets; necrobiosis in $18 \pm 4.5\%$ islets; c) fibrinoid changes; thickening of basal membrane of capillaries; vacuolisation of cytoplasm in $56 \pm 5.2\%$ islets; hydropic changes of nuclei. Marked decreasing of insulin content (IC) in B-cells: IH-1.34 ± 0.05 (intacts-1.89 ± 0.07), PS-1.39 ± 0.06 (intacts-2.02 ± 0.11). **Group 2.** BG: 4.38 ± 0.33 mM before and 7.76 ± 0.42 mM 98–103 days later; XAU: 0.031 ± 0.05 mcg/ml before and 0.096 ± 0.015 mcg/ml 96–102 days later. Histology: necrobiosis of B-cells in $34 \pm 4.5\%$ islets; pycnosis of nuclei in $21 \pm 5.2\%$ islets; vacuolisation of cytoplasm in $24 \pm 3.4\%$ islets; stasis and hyperemia in veins; no marked decrease in IC: IH-1.63 ± 0.05 (intacts-1.92 ± 0.08), PS-1.71 ± 0.04 (intacts-2.05 ± 0.07).

Conclusions: 1) extraction of fats from diet resulted in increase of XAU 2.8–3 times compared with 7–10 times in Group 1; 2) diabetes accompanied by no marked histological changes and no marked decrease in insulin content in B-cells are comparable with animals using diet enriched by fats.

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MORE PATIENTS REACH HBA1C TARGET WITH FREQUENT USE OF A BOLUS ADVISOR IN PEDIATRIC T1D PATIENTS WITH INSULIN PUMP THERAPY

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Aims: Use of a bolus advisor (BA) improves glycemic control in type 1 diabetes (T1D) in children; however, the relationship between frequency of BA use and glycemic improvement has not been studied.

Methods: The Bolus Advisor Benefit Evaluation (BABE) study was a single-center, retrospective cohort study that assessed the impact of frequent use of the Accu-Chek Aviva Combo system BA on glycemic control among pediatric T1D patients on CSII treated at a pediatric diabetology clinic in Germany. Measurements of HbA1c, hypoglycemia (<70 mg/dL) and glycemic variability were assessed at baseline, 6 and 12 months (subgroup). A total of 104 patients with mean (SD) baseline: HbA1c 8.0(1.6)%, age 12.7(4.9) years, diabetes duration 46.7(43.7) months were analysed; baseline differences accounted for by ANCOVA analyses.

Table 1.

Measure	LF Users (n=33) 6 mth (n=26) adolesc.	HF Users (n=71) 6 mth (n=28) adolesc.	P-value
% of patients HbA1c <7.5 (change) at 6 mth	27.3 (-9.1)	66.2 (+16.9)	0.0056
% patients HbA1c <7.5 (change) at 12 mth	33.3 (-3.1)	66.4 (+17.1)	0.0427
% of patients HbA1c <7.5 (change) at 12 mth adolesc.	30.8 (-7.1)	67.9 (+19.4)	0.0731
% of patients decrease HbA1c >0.5 at 6 mth*	24.2	38.0	0.0101
% of patients decrease HbA1c >0.5 at 12 mth*	20.0	22.8	0.1253
% of patients decrease HbA1c >0.5 at 12 mth adolesc.*	30.8	67.9	0.0409

* From baseline

Results: After 6 months of BA use, 71 patients reported high frequency (HF) of device use ($\geq 50\%$) versus 33 patients low frequency (LF) use ($<50\%$). Mean (SE) HbA1c among HF users was lower than LF users: 7.5(0.1)% vs. 8.0(0.2)% ($p=0.0252$). More HF patients had reached the HbA1c-target of <7.5 (IS-PAD) and a decrease of $>0.5\%$ at 6 and 12 months **(Table 1)**, with less glycemic variability as assessed by standard deviation (80.1 vs. 100.6, $p=0.0001$) than LF users. There was no between-group difference in percentage of hypoglycemia values at 6 months: 5.5(4.5)% vs. 5.9(5.8)%, $p=0.6526$.

Conclusions: Frequent use of an automated bolus advisor was associated with significant improvements in glycemic control and reaching HbA1c target with no increase in hypoglycemia in pediatric patients treated with CSII therapy.

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DIAGNOSIS AND COMPLICATION RISK ASSESSMENT OF DIABETES MELLITUS WITHIN NORMAL VALUE RANGES OF LEUCOCYTES USING PROCALCITONIN

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Introduction: Procalcitonin (PCT) was originally described in 1984 as a 116 aminoacid protein with a molecular weight of 14.5 kDa. The PCT gene, referred to as Calc-1, is located on chromosome 11p15.4 and was sequenced in 1989. The promoter has sites for basal transcription factors but more interestingly, also has sites for Nuclear factor $|[kappa]||[beta]|$ (NF$|[kappa]||[beta]|$) and activator protein -1 (AP-1), factors induced under inflammatory conditions. Diabetes Mellitus (DM) is associated with oxidative stress and elevation of advanced glycation end products (AGEs). AGEs are produced by a non-enzymatic, maillard reaction between reducing sugars and either proteins or lipids. AGEs interacts the receptor for advanced glycation end products (RAGE) and RAGE activation is caused by elevation of transcriptional factors NF$|[kappa]||[beta]|$ and AP-1. These factors induce procalcitonin gene expression. The aim of this study was to determine whether or not procalcitonin is a specific marker in patients with diabetic complications.

Results: Twenty diabetic foot patients were studied along with age and sex matched normal non-diabetic subjects (10 male and 10 female). Blood samples were taken for measurements of PCT. Serum PCT levels were analized with kryptor analizator. PCT levels were elevated in diabetic foot patients when compared with normal non-diabetic subjects. There was a statistically significant difference in serum PCT of diabetic foot patients versus normal subjects (P<0.01).

Conclusions: Our study revealed a raise in serum PCT. When the level of PCT exceeds the threshold level, the patient is predisposed to DM complications and wherein the threshold level is 0.03 ± 0.002 ng/mL.

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FUTURE ARTIFICIAL PANCREAS TECHNOLOGY FOR TYPE 1 DIABETES: WHAT DO USERS WANT?

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Aim: to gain a greater understanding of the views of potential future artificial pancreas (AP) users.

Method: An electronic survey explored views and preferences of adults with type 1 diabetes (T1DM) and parents of children with T1DM. Hosted on the University of Southampton isurvey site following ethics approval from Santa Barbara Cottage Hospital Ethics Board. Advertised via Twitter, Facebook and DiabetesMine plus advocacy groups and charities including INPUT, Diabetes UK and Diabetes Research and Wellness Foundation.

Results: 266 responders (n = 90 male), mean age 34 years (range 3–74 yrs); mean diabetes duration 19 years (range 7 weeks–68 yrs). 240 participants were extremely or highly likely to use a fully-automated 24 hr AP if available. Approximately half of respondents indicated they would be likely to use overnight AP. Most participants (n = 177) would prefer a target range rather than specific bg level (n = 86). Size (n = 83), visibility (n = 54) and lack of effectiveness (n = 42) were top reasons for not wanting an AP. Despite perceived potential downsides there was a strong need for a device that will help minimize the burden of disease, help facilitate improved psychosocial functioning and improve quality of life.

Conclusion: There remains a gulf in expectation between people who would use the technology and those that are developing it. Until this can be narrowed, it is unlikely that an AP will be sufficiently successful to meet the needs of users and to achieve the ultimate goals of optimal glycaemic control, reduced burden of diabetes self-management and improved QoL for people with T1DM.

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ADULTS WITH T1DM: EXPECTATIONS OF CLOSED LOOP TECHNOLOGY PRIOR TO PARTICIPATION IN 3 MONTH 24 HOUR 'FREE LIVING' TRIAL

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Aim: to explore expectations of closed loop (CL) technology from participants recruited to and about to start a CL trial wearing the device 24 hours a day for three months.

Methods: Adults with type 1 diabetes (T1DM) aged >18 years on insulin pump therapy were recruited to receive real-time continuous glucose monitoring (CGM) with overnight closed-loop or real-time CGM alone (open loop) followed by the alternative treatment randomly, at home for 24 hours a day for 3 months unsupervised. Participants were invited to share their views in semi-structured interviews. Topics covered potential impact, hopes, anxieties, expectations and beliefs about living with CL technology.

Results: Eleven adults with T1DM were interviewed. Key hopes included improved glycaemic control, reassurance, taking away the unexpected and improved sleep; concerns included carrying the additional equipment, the sensors and anxiety about scrutiny by research team. There were no major concerns about potential impact on every day living or device safety. Biggest worries were hypos and fear the device will fail. Nine commented on excitement of taking part in ground-breaking research and potential benefit to others.

Conclusions: A better understanding of the psychosocial impact of CL and the extent to which human factors play a role in the uptake and efficient use of these systems will ultimately lead to the most benefit for people with diabetes. By exploring people's expectations we can begin to introduce targeted interventions to optimize the performance of the system for individuals and promote optimal health and psychosocial outcomes.

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BI-HORMONAL CLOSED-LOOP CONTROL OF BLOOD GLUCOSE FOR PEOPLE WITH TYPE 1 DIABETES—THE DIACON PROJECT

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Recent advances in diabetes technology, such as faster-acting insulin analogues, more accurate continuous glucose monitoring, smart insulin pumps and remote monitoring of blood glucose, have improved insulin therapy and quality of life for people with type 1 diabetes (T1D). Also, glucagon analogues with increased stability in liquid formulation have been invented. Consequently, glucagon can be administered by an insulin pump to prevent or limit hypoglycemic episodes or ensure a fast recovery if they occur.

The Artificial Pancreas (AP) greatly benefited from these advances. A semi-automated (i.e. including meal and/or exercise physical activity announcements) or fully automated AP can free people with T1D from the stress of deciding on managing their insulin therapy and provide a safer regulation of their blood glucose. Thus, it has a great potential to reduce the occurrence of complications related to improper control of blood glucose.

Here, we present our approach to the bi-hormonal AP. In addition to insulin, our prototype of AP uses glucagon as a safety hormone. We test new control strategies for a bi-hormonal AP and compare its performance with a mono-hormonal controller. We use a virtual clinic consisting of a representative population

of people with T1D for simulation. We consider scenarios including meals and changes in model parameters reflecting the daily intra-patient variability.

The results suggest that the use of glucagon improves the safety of the AP and provides a tighter control of blood glucose. In addition, it reduces the postprandial hyperglycemia by allowing more aggressive (but safe) bolus administration.

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RECOMBINANT HUMAN HYALURONIDASE USE DURING FULLY AUTOMATED CLOSED-LOOP (CL) THERAPY: PRELIMINARY RESULTS

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Post-prandial hyperglycemia due to delays in insulin absorption and action has been a common problem during CL therapy, limiting the effectiveness of fully-automated CL without meal announcement. In open-loop pump therapy, priming an infusion site with recombinant human hyaluronidase (rHuPH20) accelerates the time action profiles of bolus doses of rapid-acting insulin analogs. In this abstract, we present the effects of rHuPH20 on CL performance in the first 6 subjects (5 male, mean age 20 ± 5 y, mean HbA1c $7.5 \pm 0.7\%$) with type 1 diabetes who have completed two 24 hour periods of CL control, one without and one with priming of the infusion site with 150 u of rHuPH20, in randomized order. No meal announcements or pre-meal insulin bolus doses were given. As shown in the Table, peak post-prandial glucose levels were reduced and the % of values in the target range were increased after breakfast and dinner during rHuPH20 CL study days. None of our subjects experienced any skin reaction to rHuPH20 injection. These preliminary results suggest the feasibility and effectiveness of using rHuPH20 to blunt meal excursions during fully automated CL control.

		Closed-loop Control (mean±SD)	Closed-loop + PH20 (mean±SD)	p
Peak post-prandial BG (mg/dL)	Breakfast	249±70	211±54	*0.02*
	Lunch	203±41	211±30	0.7
	Dinner	184±25	176±26	0.3
Post-prandial % BG within target (BG<180 mg/dL)	Breakfast	35±36	67±32	*0.02*
	Lunch	75±37	47±34	0.1
	Dinner	80±20	90±15	*0.03*

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DETECTION OF CONTINUOUS GLUCOSE SENSOR FAULTS IN SINGLE- AND MULTI-VARIABLE ARTIFICIAL PANCREAS SYSTEMS

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Faults in subcutaneous glucose concentration (SGC) readings cause errors in the computation of insulin infusion rates by artificial pancreas (AP) control systems and lead to hypoglycemia or hyperglycemia. Model-based and process history-based (data driven) fault detection methods have been used successfully in various fields. Several studies indicated that multi-variable fault detection techniques perform better than single variable algorithms. Since most APs are based on information from a single variable (SGC), the first generation of AP fault detection algorithms is also based on a single variable. This approach may have been satisfactory for use outside of the well-controlled environments of clinical studies, if accurate models of the human body for patients with diabetes were available. The accuracy of first-principles models based only on SGC is limited. The accuracy would improve with a multivariable approach, but model development cost may be high and may challenge the computational capabilities of an AP device. We developed two fault detection approaches for both single (SGC) and multivariable (SGC and physical activity measurements) APs. A combination of model-based and data driven methods is developed for single variable systems. Multivariable virtual variables are derived with SGC, insulin and meal information, and used for fault detection. Process history-based statistical algorithms are developed for multivariable APs. The measured variables are directly used for fault detection. The performances of both techniques have been tested with patient data and promising results are obtained. The methods will be presented and their performance in SCG sensor fault detection will be compared.

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IN SILICO COMPARISON OF INTRAVENOUS, INTRAPERITONEAL AND SUBCUTANEOUS APPROACH FOR CLOSED-LOOP GLUCOSE CONTROL

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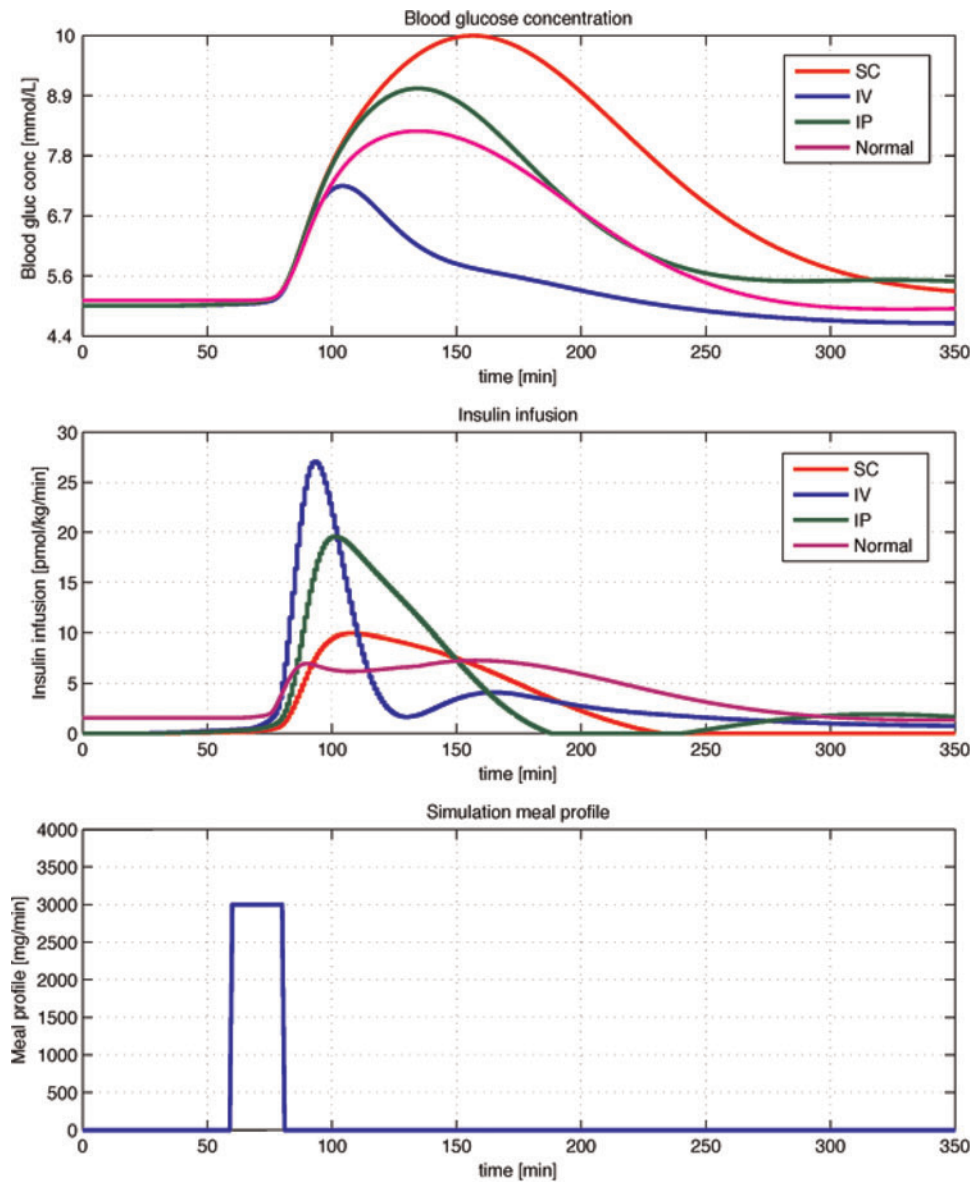
Figure 1: 6-hr simulation scenario with a PID controller

The state-of-the-art approach for closed-loop glucose control in diabetes mellitus type 1 (DM1) is the subcutaneous (SC) approach, i.e. SC glucose sensing and continuous SC insulin infusion. However, this approach has a slow response and poor robustness both with respect to sensing and infusion. A double intraperitoneal (IP) approach may be a better option due to faster dynamics. A double intravenous (IV) route is appealing because it is the fastest option, but it is less practical outside the hospital setting.

A modular mathematical model has been developed to simulate the various approaches (IV, IP and SC) for closed-loop glucose control in DM1. This allows for the comparison of the three routes and for testing the performance of different control algorithms with each of them.

The various approaches were all assessed during simulated meal input using proportional-integrative-derivative (PID) control and with model-predictive control (MPC).

The results shown in Fig. 1 and Fig. 2 indicate that the IP approach gives markedly smaller glucose excursions after meals compared to the SC approach. Actually, in the in silico model the double IP approach gives glucose levels comparable to non-diabetic subjects. This suggests that a double IP approach should be investigated further in the hunt for a robust artificial pancreas aiming at normal or close to normal glucose levels.

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COMPARISON BETWEEN A NOVEL AND CONVENTIONAL ARTIFICIAL PANCREAS FOR PERIOPERATIVE GLYCEMIC CONTROL USING A CLOSED-LOOP SYSTEM

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Background: This clinical study aimed to compare a novel and conventional artificial pancreas (AP) used in surgical
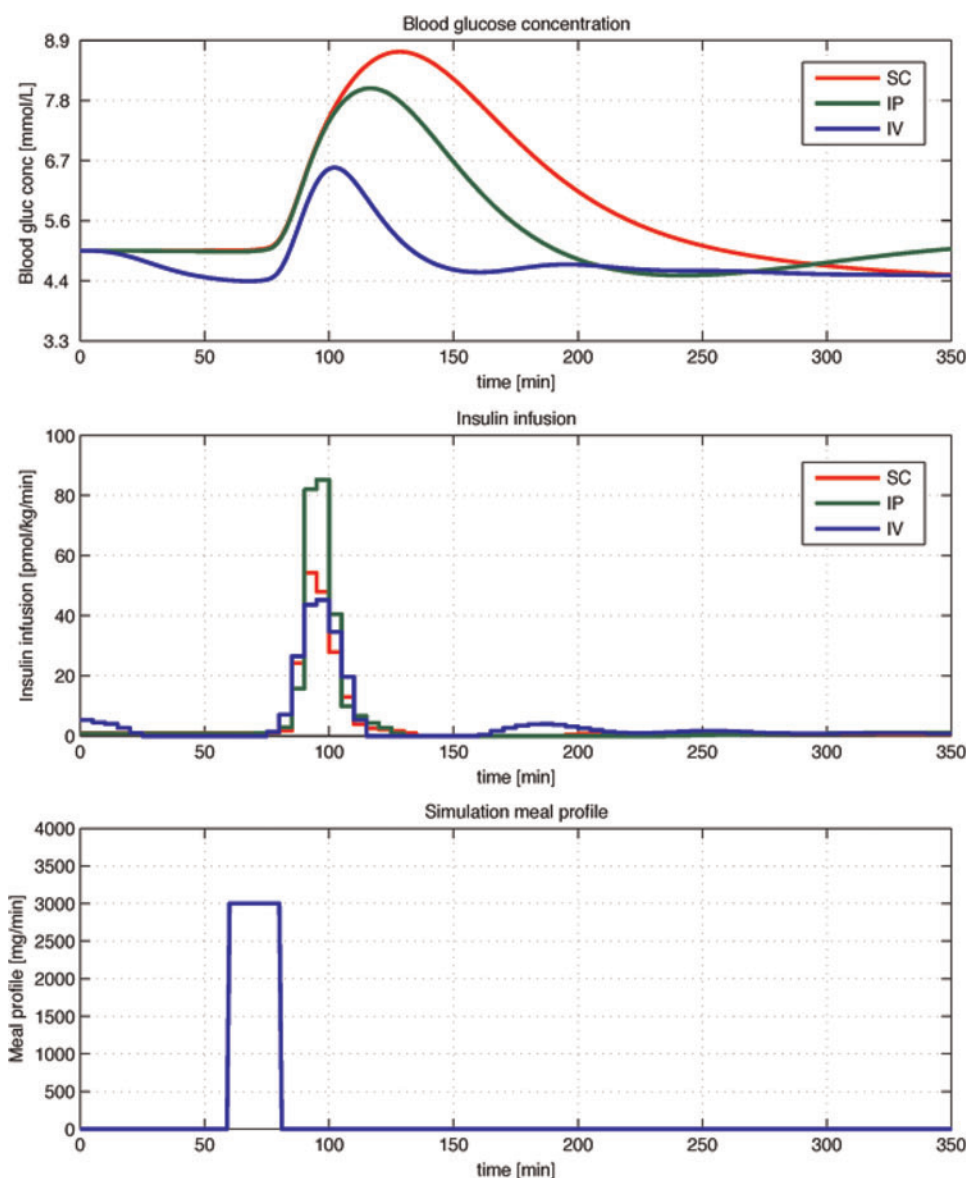
Figure 2: 6-hr simulation scenario with MPC

patients for perioperative glycemic control, with respect to usability, blood glucose measurements, and glycemic control characteristics.

Study Design: From 2010 to 2013, 133 patients underwent perioperative glycemic control using a novel AP. Among them, 124 patients were eligible for inclusion in this study. Intensive insulin therapy (IIT) targeting a blood glucose range of 80–110 mg/dL was implemented in 81 patients (65.3%), and the remaining 43 patients (34.7%) received a less-intensive regime of insulin therapy. Data were collected prospectively and were reviewed or analyzed retrospectively. A comparison study of 323 patients undergoing IIT for glycemic control using a novel (n = 81) or conventional AP (n = 242) was conducted retrospectively.

Results: All patients undergoing IIT had no hypoglycemia. The comparison study revealed no significant differences in-perioperative mean blood glucose level, achievement rates for target blood glucose range, and variability in blood glucose level achieved with IIT between the novel AP and conventional AP groups.

Conclusions: The usability, performance with respect to blood glucose measurement, and glycemic control characteristics of IIT were comparable between novel and conventional AP systems. However, the novel AP was easier to manipulate than the conventional AP due to its smaller size, lower weight, and shorter time for preparation. In the near future, this novel AP system might be accepted worldwide as a safe and useful device for use in perioperative glycemic control.

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INFLUENCE OF GLUCOSE VARIABILITY CAUSED BY AN ARTIFICIAL PANCREAS ON IFLAMMATORY CYTOKINES IN BEAGLES

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Background and Purpose: Recent studies reported that glucose variability as same as average glucose level might influence on mortality in critical ill patients. However, the mechanism remains still unclear. We hypothesized that glucose variability increase inflammatory cytokines and it caused undesirable reaction. Therefore, we established glucose variability beagle model and investigated our hypothesis.

Method: After the approval of the animal ethical review board, six beagles were studied. Total pancreatectomy was done under general anesthesia using sevoflurane and remifentanil. The glucose level was automatically controlled by an artificial pancreas, STG-22 (Nikkiso, Tokyo, Japan). All beagles were stabilized for 60 min. We repeated hyperglycemia (200 mg/dL) and the normal glucose lower limit (70 mg/dL) four times every 60 minutes using an artificial pancreas. The endpoint of the experiment was eight hours after the start of glucose variability. The glucose levels were recorded continuously. C-reactive protein (CRP), insulin, IL-6, IL-10 and TNF-a were measured seven times (before and after pancreatectomy, every 120 min after the stabilization).

Results: Average glucose level in hyperglycemia phase was 198 ± 35 mg/dL. Although CRP after the stabilization was 0.54 ± 0.47 mg/dL, it increased to 2.8 ± 1.3 mg/dL after the start of glucose variability. IL-6 gradually increased and continued increasing until the end of study. TNF-a gradually increased and it became the peak four hours later. IL-10 increased after six hours.

Conclusion: We established glucose variability beagle model. This model showed that glucose variability might increase inflammatory cytokines. It is necessary to examine influence of pancreatectomy on cytokines.

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COMPARATIVE PK/PD STUDY OF LIQUID STABLE G-PUMP GLUCAGON VS. NOVO NORDISK GLUCAGEN, DELIVERED TO T1D PATIENTS VIA AN INSULET OMNIPOD PUMP

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Due to its association with reduced cognition, social embarrassment, coma, seizures and automobile accidents, hypoglycemia in persons with type 1 diabetes is highly feared. The group at OHSU has shown the benefit of small doses of glucagon to prevent two-thirds of cases of hypoglycemia in the setting of closed-loop treatment in patients with type 1 diabetes (T1D). However current glucagon products, approved only for severe hypoglycemia rescue, are based on lyophilized formulations which require reconstitution at time of use and cannot realistically be administered via pump. Xeris is developing a body-temperature stable, soluble liquid glucagon formulation that can be administered with an infusion pump. This Phase 2, randomized, double-blind, cross-over, PK/PD study in patients with T1D (n = 19) tested 0.3, 1.2 and 2.0 μg/kg each of G-Pump™ and GlucaGen® glucagon subcutaneously infused with the Insulet

OmniPod®. G-Pump™ was bioequivalent to doses of Gluca-Gen® across the treatment groups for $AUC_{0\text{-}150\,min}$ (ratio 1.01, 90% CI 0.85–1.21), but exceeded the upper bound for C_{max} (1.11, 0.86–1.42) and T_{max} (1.10, 0.85–1.43). G-Pump™ glucagon effectively increased blood glucose levels in a dose-dependent fashion with C_{max} of 183, 200 and 210 mg/dl, respectively. G-Pump™ was not different from GlucaGen® but was not therapeutically equivalent. No SAEs were reported and no unexpected safety or tolerability issues with the glucagon treatments were observed. Adverse events reported generally included known issues related to administration of glucagon. Overall these data support further testing of G-Pump™ glucagon for management of blood glucose as a component of a closed-loop system.

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CLOSED LOOP ARTIFICIAL PANCREAS USING A NEW ALGORITHM (SADDLE POINT MODEL PREDICTIVE CONTROL, SP-MPC): RESULTS OF A RANDOMIZED OVERNIGHT STUDY

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Introduction: The SP-MPC algorithm has been developed to robustly control blood glucose despite model's uncertainties (e.g. insulin sensitivity).

Objective: To assess the ability of SP-MPC to maintain normal blood glucose levels while reducing the risk of hypoglycaemia.

Research design and methods: In this randomized crossover study, 10 adults with type 1 diabetes were assigned to be treated with overnight open-loop (OL) using sensor-augmented pump (SAP) therapy or closed-loop (CL) delivery. During the CL insulin doses were calculated by the SP-MPC algorithm every 15 minutes from 9pm to 8am. Patients consumed a self-selected meal at 7pm accompanied by their usual prandial bolus. Blood glucose was measured every 30 minutes. The primary endpoint was the percentage of time spent in target (70–145 mg/dl) and below 70 mg/dl from 11pm to 8am.

Results: Time spent in target and total insulin doses did not differ between CL and OL nights. Hypoglycaemia (< 70 mg/dl) was reduced in CL (median = 0/patient/hour; quartiles: 0–0.11) as compared to OL (median = 0.22/patient/hour; quartiles: 0.02–0.22) (p = 0.02). The mean interstitial glucose was significantly lower during CL (128 mg/dl; 95%CI:112–145) than during OL (134 mg/dl; 95%CI:118–151, p < 0.01). The area under the curve for glucose values > 145 mg/dl was lower during CL (p = 0.03) as well as HBGI (p = 0.02).

Conclusion: This study did not show any difference for the time spent in range. Using SP-MPC was associated with a significant lower number of nocturnal hypoglycaemia and lower glucose values as compared to OL using SAP. The algorithm's performances will be confirmed in a longer study including a larger number of patients.

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BIOARTIFICIAL PANCREAS, NEW STRATEGY TO TREAT TYPE 1 DIABETES

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Bioartificial pancreas is an autonomous system that can control glycaemia in type 1 diabetic patient. Thus no immune suppressive regimen is required. However optimization of cell survival is needed to optimize function regulation and glycaemia. The present work aims to maintain survival of a high number of islets in a confined and hypoxic environment using oxygen carrier (perfluorodecalin combined to adenosine).

Rat islets at different density (150; 300; 600IEQ/cm^2) were cultured under hypoxia conditions (2%O_2) in presence or absence of perfluorocarbons (10%) supplemented with adenosine (1 mM) oxygenated (PFCAdO$_2$) for 30 minutes in the culture medium. After 24 h in culture, islet viability (FDA/Pi, ATP levels), function (GSIS index) and expression of hypoxia (HIF-1α) were assessed.

ATP levels of 300IEQ/cm^2 (0.64 ± 0.08) and 600 IEQ/cm^2 (0.65 ± 0.10) decreased in comparison to control (0.93 ± 0.12, n = 9, p < 0.05). HIF-1α mRNA level increased with density (300IEQ/cm^2: 1.76 ± 0.14; 600IEQ/cm^2: 1.8 ± 0.09) as compared to control (0.77 ± 0.02, n = 9, p < 0.05) and was correlated to a loss of cell function (300IEQ/cm^2: 0.98 ± 0.34; 600IEQ/cm^2: 0.44 ± 0.08 vs. control 1.62 ± 0.35). The presence of PFCAdO$_2$ increased ATP level for all the densities (150IEQ/cm^2: 2.98 ± 0.44; 300IEQ/cm^2: 1.90 ± 0.15; 600IEQ/cm^2: 1.75 ± 0.21, n = 6) and decreased HIF-1α mRNA level for 300IEQ/cm^2 (0.40 ± 0.10, n = 6, p < 0.05). Function was restored with PFCAdO$_2$ for the condition 150IEQ/cm^2: (1.74 ± 0.21) and 300IEQ/cm^2 (1.51 ± 0.39, n = 6).

This study showed that the use of PFCAdO2 improved oxygenation of islets in a hypoxic environment and would permit the transplantation of a sufficient number of islet to restore normoglycaemia.

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DEVELOPMENT OF AN AUTOMATIC INSULIN DELIVERY SYSTEM FOR EFFECTIVE LONG-TERM CONTROL OF BLOOD GLUCOSE CONCENTRATION

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A critical advancement necessary for long-term, fully automated, control of blood glucose concentration (BGC) (i.e., artificial pancreas or automatic insulin delivery system) is a control algorithm that can effectively maintain tight control of BGC under extreme variations of critical disturbances such as activity, stress, and food consumption. Theoretically, the most effectively control algorithm to compensate for disturbances is feedforward control (FFC). Effective FFC requires accurate *casual* impact of the disturbances and insulin infusion on the response, BBC. This talk presents a novel and powerful multiple-input FFC modeling methodology and modeling results for 15 type one diabetic (T1D) cases; each case has two weeks of outpatient data collection. The FFC algorithm is given and its potential for success is discussed. In addition, the effectiveness of this algorithm to model real data is demonstrated on a real chemical process, specifically, a pilot distillation column. The results show the effectiveness of the modeling and control algorithm to substantially reduce variance in the controlled variable. Based on this approach, a prototype insulin delivery system will be built based on this FFC algorithm that will include glucose dynamics, insulin dynamics, and will also compensate for BGC level as described in this talk. For this device, modeling data will be fully obtained in outpatient, free-living, data collection. The subject-specific FFC algorithm will be totally determined offline so that it will be operational during the complete time of inpatient studies, and thus, giving maximum duration for control runs.

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OXYGENATED-PLASMA MATRIX AS SUPPORT FOR ISLET CULTURE, IN VITRO VALIDATION

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Introduction: Cell therapy is promising therapy to replace solid organ transplantation. Type 1 diabetic patients can be transplanted with pancreatic islets to restore physiological insulin secretion and avoid hypoglycemia unawareness. However, immune-suppressants are required unless grafted islets are encapsulated in a protective environment such as bioartificial pancreas. Engineering of the inner of the device is mandatory to improve islets survival and function in an artificial environment. The aim of the project was to test oxygenated plasma based matrices, a biological scaffold, as a support for islets in vitro.

Material and methods: Rat islets were cultured after isolation in standard condition or in plasma matrix supplemented or not with 10% perfluorodecalin (PFD). After 24 h islet viability (FDA/PI), function (insulin release), cell-matrix interaction (Integrin, FAK, Akt), apoptosis (Caspase 3, TUNEL) and hypoxia (HIF-1 α, DHE) were assessed.

Results: In matrices, islets expressed higher level of integrin (CTL: 0.73 ± 0.28; Plasma: 3.28 ± 1.19; PFD: 4.14 ± 0.38; p < 0.05 plasma vs. CTL and PFD vs. CTL), FAK and Akt phosphorylation. This activation leads to a decrease in caspase 3 level and confirmed by a TUNEL staining. Hypoxia was enhanced in plasma but was counteracted by the addition of PFD (CTL: 0.05 ± 0.01, Plasma: 0.21 ± 0.07, PFD: 0.09 ± 0.03, p < 0.05 CTL vs. Plasma, p > 0.1 CTL vs.PFD).

Conclusions: Matrices can decrease islet apoptosis while preserving viability and function. Hypoxia created by this matrix is counteracted by the oxygen carrier that is PFD. This kind of matrix should so be used in the bioartificial pancreas, to improve islets survival.

	Mean Plasma Glucose (mg/dL)	% Glucose Values 70–180 mg/dL	# Hypoglycemic Episodes (<60 mg/dL)	# Hyperglycemic Episodes (>250 mg/dL)	Prandial Glucose Excursion (mg/dL)	AUC Glucose after Meals
CL-NoIP	129 ± 13	81	6	9	100 ± 45	245 ± 176
CL + IP	123 ± 13	77	4	2	99 ± 48	239 ± 162

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EFFECT OF AN INSULIN INFUSION SITE WARMING DEVICE ON PERFORMANCE OF A CLOSED-LOOP SYSTEM

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The effectiveness of closed-loop (CL) systems in mitigating post-prandial hyperglycemia is limited by slow absorption of subcutaneously delivered insulin and prolongation of the 'meal bolus' over several hours by the controller algorithm. Warming the skin at the site of insulin infusion with the InsuPatch (IP) accelerates insulin absorption following a standard subcutaneous bolus in an open-loop setting, but whether skin warming improves the performance of closed-loop systems has not been established.

Nine T1D subjects (age 20±7 y, duration 11±9 y, A1c 7.4±0.7%) were studied during two 24 hours of CL control using Medtronic ePID + IFB controller: without (CL-NoIP) and with skin warming (CL + IP) to 40°C. Meals were identical for both conditions and were accompanied by small manual insulin boluses (0.08 units/kg). Mean blood glucose was slightly lower with CL + IP vs CL-NoIP (p = 0.01); but time within target, prandial glucose excursion, and AUC post-prandial glucose were similar (Table). There were fewer instances of hypoglycemia (BG < 60) and hyperglycemia (BG > 250) in CL + IP condition vs CL-NoIP.

Skin warming with the InsuPatch resulted in lower mean glucose levels and fewer instances of hyperglycemia and hypoglycemia, but did not significantly change glycemic responses to meals. To best utilize site warming technology, larger subcutaneous depots of insulin given as manual pre-meal manual doses may be required for optimal prandial glucose control.

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HYPOGLYCEMIC ALERT BASED ON ONLINE GLUCOSE PREDICTION USING MODEL MIGRATION METHOD FOR SUBJECTS WITH TYPE I DIABETES

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Avoiding hypoglycemia episodes are major challenges for diabetes mellitus. A timely alert of hypoglycemia episodes before they occur can allow enough time for the patient to take necessary actions to avoid hypoglycemia.

In our previous work, a rapid model development strategy using the idea of model migration, which is developed by adjusting the model parameters of inputs based on only a few samples from new subjects, was successfully used for online glucose prediction using simulation data. Here, more focus was put on hypoglycemic alert using model migration method and evaluation based on clinical data provided by BD. Twenty-four unidentified clinical subjects are used to test the model migration method (MM) where only 24 samples (two hour) are required to adjust parameters. Also, it is compared with subject-dependent standard modeling method (SD) where about 288 samples were used for model development.

The results in Table 1 indicate that the prediction accuracy of MM is comparable to that of SD. Also, it reveals similar time lag for hypoglycemic alert. The sensitivity and specificity of MM are comparable or even better than SD. Therefore, the proposed MM can be regarded as an effective and economic modeling method instead of repetitive SD for hypoglycemic alert.

TABLE 1. HYPOGLYCEMIC ALERT USING TWO DIFFERENT METHODS FOR 30 MIN AHEAD GLUCOSE PREDICTION

Method	RMSE (mg/dL)	Time Lag for hypo alert (samples)	Sensitivity for hypo alert (%)	Specificity for hypo alert (%)
MM	19.55 ± 7.03	4.10 ± 2.85	66.97	99.33
SD	19.49 ± 6.60	5.00 ± 2.07	64.71	99.68

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AN AUTOMATIC DETECTION METHOD FOR VARIABILITY OF SIGNAL-TO-NOISE RATIO IN CONTINUOUS GLUCOSE MONITORING

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One major difficulty of denoising methods for continuous glucose monitoring (CGM) is that the noise level can vary with time which may cause unreliable filtering performance. Here, to make sure that the filter parameters can be tuned in time, an automatic noise variability detection method is proposed for Kalman filter (KF) by checking previous filtering residuals. A confidence interval $[x-2\sigma, x + 2\sigma]$ is enclosed where σ is the standard deviation of residuals between filtered and measured

TABLE 1 NOISE VARIABILITY DETECTION RESULTS FOR 20 *IN SILICO* SUBJECTS

standard deviation of noises	Detection delay (samples)	False detection ratio (%)	Missing detection ratio (%)
3	58.95 ± 66.30	0	0
4	7.35 ± 37.24	5%	0
5	4.95 ± 1.47	0	0

signals and x denotes the filtered signal from which 2σ measures the amount of variation or dispersion (95%). Also, a larger σ is separately used for those rapid rising CGM signals. By comparing the measured signals against the confidence interval, the reality of the current filter performance is checked and any violation of confidence interval will indicate changes of measurement noises.

Noisy CGM signals with 5 min as sampling interval are generated using UVa/Padova metabolic simulator. The initial KF is estimated based on the first-day noisy data where the noise standard deviation is two. Then it is used to filter CGM signals with different noise levels. The results in Table 1 indicate that noise variability can be clearly and quickly detected and the detection is more sensitive to larger noise variability in comparison with the original noise level.

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DIABETES PATIENT PREFERENCES FOR USING TECHNOLOGY TO COMMUNICATE WITH PHYSICIANS

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Objective: The patient-physician axis of communication is critical for effective monitoring and treatment of diabetes. Our objective was to characterize the current role of technology in patient/physician communication and identify patient preferences for this interaction.

Methods: We surveyed 103 patients in the United States with diabetes; questions focused on patients' technology use and preferences for communicating with their physician.

Results: Patients ranged in age from 30 to 79 years and were 51% female. 49% owned a smartphone and 66% reported using the internet daily or weekly. Most patients (83%) reported that they tracked or monitored their disease and shared their results with their physician. Patients reported that doing online research about their disease might lead them to ask more questions about medication (42%), treatment options (21%), and new technologies to help manage their disease (17%). Over half of patients (54%) reported that they always understand information their physicians have shared with them, but of patients that require clarification, 30% wait until their next visit, while others use family and friends (22%), internet research (21%), or call their physician (19%). Most patients preferred a phone call from their physician (57%) if they needed to be contacted between visits, rather than an email (27%) or text message (16%).

Conclusions: Most patients with diabetes are using some method of tracking and monitoring their disease and agree that increased education would encourage patient-physician communications. Programs seeking to improve patient-physician communication with technology can draw from this baseline knowledge to identify potential areas for intervention.

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LONG ACTING INSULIN GLARGINE TITRATION WEB TOOL (LTHOME) VS ENHANCED USUAL THERAPY OF GLARGINE TITRATION (INNOVATE) TRIAL DESIGN

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Background: Delays in insulin initiation and titration are often due to complexity and hypoglycemia. LTHome is a web tool, providing insulin titration advice directly to the patient, based on prior fasting plasma glucose (FPG) and hypoglycemia. LTHome uses a rules engine-based algorithm that will facilitate dose progression for insulin glargine with less hypoglycemia.

The INNOVATE study will evaluate the safety and effectiveness of the LTHome web-based tool in a randomized, multicenter approach for insulin glargine dose management in T2DM subjects.

Methods: 138 subjects undergoing insulin glargine initiation or titration will be randomized to titration through either the LTHome tool or through an HCP-driven diabetes education program (Enhanced Usual Therapy, EUT), to reach FPG goal over 12 weeks.

Patients signing informed consent, with T2D, between 18–75 years, HbA1c > 7.0%, scheduled to initiate or to increase basal insulin, will be eligible. Computer literate patients with no hypoglycemia unawareness nor severe hypoglycemic episode in the prior 90 days will be included. The INNOVATE protocol was approved by a research ethics board.

The primary objective will compare LTHome vs. EUT (two sample t-test) at 12 weeks, for a composite end-point:

A. ≥4 (of 7) FPG within the target range of 5 mmol/L to 7.2 mmol/L;
B. mean FPG between 5 and 7.2 mmol/L;
C. no severe hypoglycemia episode.

Secondary objectives will assess safety, effectiveness, satisfaction and adherence of LTHome.

Table 1. Titration rules for insulin glargine as per LTHome; median FPG is based on prior 3 consecutive results

	Resulting dose adjustment
Dose increase if FPG >10.0 mmol/L	+4U every 3 FPG values
Dose increase if FPG > target 7.2 mmol/L	+2U every 3 FPG values
FPG target range 5.0 – 7.2 mmol/L	0
Dose decrease for FPG below target (3.9-4.9 mmol/L)	-2U or 5% Greater of unit or %
Dose decrease if any PG < 3.9 mmol/L or any hypoglycemic symptoms	-4U or 10%* Greater of unit or %

FPG= Fasting Plasma Glucose

Conclusion: INNOVATE will evaluate the potential utility of LTHome to facilitate more effective and safe real-world insulin initiation and titration.

Investigator-initiated study sponsored by Sanofi.

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DIABETES FOR LIFE— A HOLLISTIC APPROACH TO MEET THE DIABETES PATIENTS' CHALLENGES REQUIRES FOCUS ON A MULTITUDE OF RESEARCH AREAS

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Diabetes4Life is a Norwegian initiative aiming to provide better care through challenging traditional processes and reinvent diabetes care. Diabetes care will improve significantly by involving people with diabetes, diabetes associations, healthcare providers, and research and commercial partners. The initiative – including 14 partners – will target innovative diabetes technology solutions and services, testing in clinical trials, and document results so new innovations can give anyone with diabetes better possibilities to understand and manage their disease.

During a half-year long process with meetings and workshops we identified the following 13 research tasks, focusing on the effects of:

1. Self-management: increasing patients' confidence and ability to manage their symptoms and illness.
2. Self-monitoring: monitoring e.g. blood glucose, medication, physical activity, nutrition, and blood pressure.
3. Supporting health behaviour: increasing situation-adaptability by tailored systems.
4. Psychosocial support: integrated in the management of diabetes in both children and adults.
5. Human aspects: potential differences in perception and use related to gender, age, social background, etc.
6. Social media and education: online diabetes communities and new ways of education.
7. Serious gaming: increasing knowledge and understanding of health factors.
8. Healthy activities: increasing physical activity and establishing healthy diets.
9. Sensor and short-range communication: sensor fusion and new developments.
10. Software and apps: innovative self-management apps and collaborative platforms.
11. Data-driven recommendation systems: new ICT recommendation tools.
12. Patient-health care communication: simplified patient communication and data presentation.
13. Evaluation: cost and health-related parameters.

The research aims to improve diabetes care by integrating systems in a holistic approach.

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THE NEXT GENERATION MOBILE SELF-MANAGEMENT TOOLS FOR PEOPLE WITH DIABETES – HAVE TO BE DYNAMIC, INTEGRATED, VISUALLY ATTRACTIVE AND TAILORED

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Through several years we have developed and refined self-management tools, lately in form of mobile phone-based applications with options to interact with different sensors and
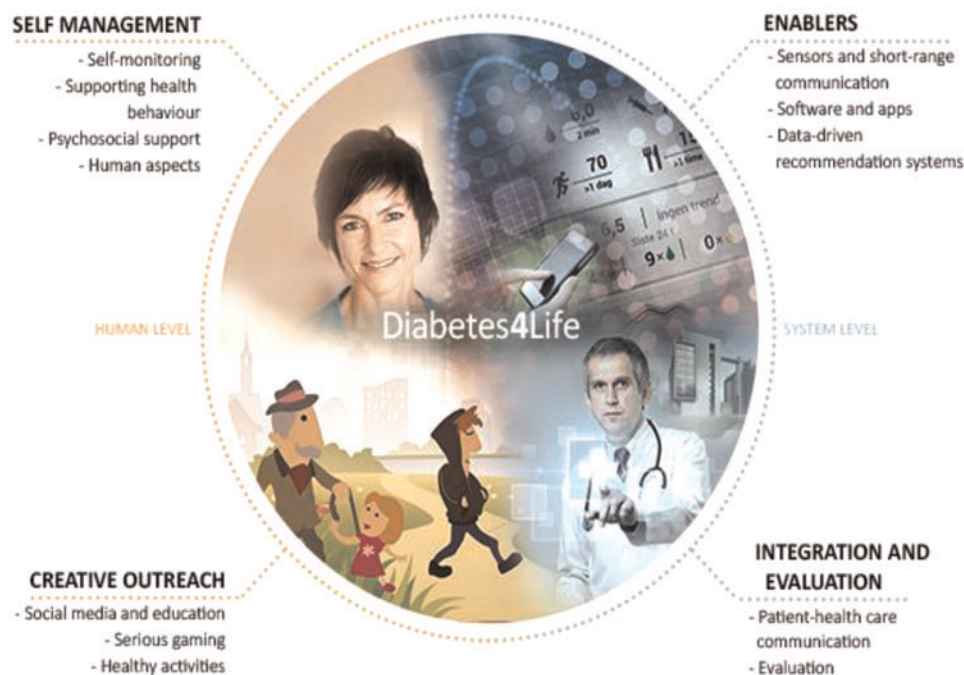
databases. In our recent study involving 30 adults with Type 1 diabetes we investigated preferred features and suggestions for future features in the Diabetes Diary (DD) application. The application includes possibilities to enter data and get visual feedback on their mobile phone. Users could enter insulin, carbohydrates and physical activity, while blood glucose (BG) values were transferred automatically and wirelessly from their BGM. The effect of the data-driven feedback module known as Diastat was investigated, comprising BG periodicity graph, BG trend and Insulin help function.

All participants got the DD and one group received Diastat. There were no significant differences in HbA1c between the groups, but overall patients had a decrease of 0.6 percentage points (p < 0.001) 4–6 months after study start, using the DD. Qualitative data was gathered through questionnaires (n = 30) and focus group meetings (n = 25). What patients expected the most from the system were improved HbA1c, increased motivation and better overview – something they confirmed that they had achieved after the study. This was in line with that 53% said they managed their diabetes pretty good before the study, in contrast to 76% after (p = 0.10). In focus group meetings patients suggested new features such as being able to take notes spanning periods, sharing data with health care personnel, Runkeeper integration, CGM integration, insulin pump integration, tailored food database, and several other innovative visual feedback concepts.

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TOOLS FOR INTERACTIVE LEARNING AND SELF-MANAGEMENT OF DIABETES

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Introduction: Carbohydrates are the major determinant in post prandial glucose level. Carbohydratecounting (CHC) is an established approach used by type 1 diabetic patients. Those patients calculate pre-prandial insulin based on blood glucose values and on the amount of CH to be consumed. Is crucial that CHC is correct.

Aim: To develop strategies for helping diabetic patients to do correct CHC and to calculate pre-prandial insulin.

Results: We create an application that teaches patients to relate different foods and different meal contents with the amounts of CH, using interactive displays organized by food types and meals in an intuitive manner that allows patients to explore and learn. It also helps on other details (reading food labels). This application includes games as they are a powerful tool for learning. The first game presents typical meals. Patients must guess CH count. Another game allows users to drag foods and beverages from food image scrollbars into a tray, increase or decrease quantities just by dragging, and asks the user to guess the CHC for the total and for each of the parts in the tray. The application provides feedback. Patient can also guess the amount of insulin that should be administered. Integrated with the application, patients can store information concerning insulin sensitivity factors and insulin carb ratio.

Conclusions: Patient education is the key to success. Technology can help our patients. These tools are useful both for teaching patients at the beginning of the therapy as for the self-training afterwards. It will be put online for patients to access and use.

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WHAT DO DIABETIC PATIENTS SEARCH FOR ON INTERNET – THE FIVE YEAR DIABETES SPECIALIZED WEBSITE EXPERIENCE BASED ON ANALYSIS WITH GOOGLE ANALYTICS

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Background: Internet is one of the modern ways of spreading information. Number of households equipped with internet in the Czech Republic increased from 41.7% in 2008 to 67.0% in 2013.

Methods: Web site was created in 2008 to provide information for patients with diabetes mellitus particularly if treated with insulin. Site contains 192 pages of disease dedicated information.

From the results: Within five years there were 119,958 visits registered on the website (94,033 new visitors), starting with 17, 201 visits in 2008 which gradually increased to 26,646 visits in 2013. All the visitors spent on the site 4165 hours. Number of visits lasting between 3 and 10 minutes was 10,019, those of which lasted between 10 and 30 minutes were 6, 076 and 1,268 visits took more than 30 minutes. The most frequent keywords which brought patients to the site were hypoglycemia, hyperglycemia, insulin delivery, MODY diabetes, glycemic index of food, gestational diabetes mellitus, diabetes mellitus Type 1 and Type 2. The most visited pages were those related to the glycemic index and energy content of food, insulin sensitivity, and

insulin/sacharide ratio calculation and insulin delivery During the 5 years we answered 1 375 patient's questions.

Conclusion: The internet is used by diabetic patients as a method of information searching and provides a cost effective way how to deliver information. It can be used as a supplementary method of education and it also give the patients opportunity to communicate directly to a doctor.

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CLINICAL USE OF BLUETOOTH-ENABLED SMARTPHONE APP INTEGRATED WITH A LONG TERM IMPLANTABLE CGM SYSTEM

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As smartphones and their accompanying mobile Apps become a ubiquitous part of everyone's lives, their functionality may also be used to ease the day-to-day management of chronic diseases such as Diabetes. Currently, the commercially available Continuous Glucose Monitoring (CGM) systems typically consist of a sensor, a Transmitter and a Receiver. Separately, the currently available smartphone Apps only provide data storage and logging capabilities to the user. Senseonics has developed an App that is integrated along with its CGM system and eliminates the need for a separate hand-held device. In the new Senseonics CGM, a mobile App directly communicates via Bluetooth-LE, to a wearable Transmitter to then display real-time glucose readings.

The Senseonics CGM system includes an implanted, fluorescence-based glucose sensor. The co-located Transmitter wirelessly communicates via NFC with the sensor. The wireless transmitter then sends the calculated glucose data directly to the smartphone mobile App. The App then enables display of the current glucose value, as well as the rate and direction of glucose change, graphical trends, and alerts for impending hypoglycemia or hyperglycemia.

The extended report will focus on user interaction with the iOS App used in a 90-day feasibility study of 14 subjects with Type I diabetes mellitus. In addition to the subjects utilizing various

functions of the App for understanding their real time glucose and glycemic history, there were 79% of the subjects that also utilized the event logging feature to track events related to insulin dosing, exercise, carbohydrate intake and SMBG logging.

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METHODOLOGY OF THE EVALUATION OF THE NEW EMMINENS ECONECTA EDETECT MODULE

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Diabetes management based on blood glucose (BG) patterns is associated with improved patient outcomes, but they are not always easy to detect or interpret. emminens eConecta® is a modular and customizable web-based platform that enables personalized management of Diabetes Mellitus. Its new eDetect module with data-mining algorithms and automatic analytic tools should help HCPs to detect patterns more effectively and efficiently.

Objective: To evaluate eDetect module performance in relation to time needed and patterns detected in diabetes data analysis.

Method: Randomised, international, multicentre evaluation. Thirty endocrinologists, regular users of emminens eConecta® platform will participate (25 in Spain, 5 in Belgium). Each HCP will get used to the new eDetect module with at least 4 patients before they get access to the evaluation web platform where they will analyse data from 4 simulated clinical cases (2 CSII, 2 MDI) presented in random order and will complete two questionnaires.

Time needed and patterns detected manually in the total 120 cases will be recorded upfront and compared with time and patterns obtained analysing the same cases with the eDetect module afterwards.

Results: The evaluation will show potential differences in time and pattern detection performance of the eDetect module to HCPs when analysing patient data. It will also provide information about ease of use, reliability and HCP satisfaction with the new eDetect module.

Conclusion: This evaluation will provide essential information about whether the new emminens eConecta eDetect module can help clinicians to detect more rapidly and effectively clinically relevant patterns in diabetes management.

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COMPARTATIVE USE OF RAPID-ACTING INSULIN CALCULATOR (EXPERT AND INSULINX): ADVANTAGES ON METABOLIC CONTROL

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Sex	Male 51,6%		Female 48,4%	
Weight classification	Normal weight 35,5%	Overweight 38,7%	Obesity 22,6%	
Micro and macrovascular Complications	Retinopathy 41,9%	Nephropathy 12,9%	Neuropathy 3,2%	Macrovascular complications 9,7%
Basal insulin	Glargine 83,9%		Detemir 16,1%	
Short acting insulin	Aspart 61,3%	Lispro 35,5%	Glulisine 3,2%	

Table 1

	BCI		Sig	BCE		Sig
	Basal	3 months		Basal	3 months	
HbA1c	7,98±0,94	7,6±0,77	0,018	8,20±0,77	7,5±1,08	0,02
UI basal/kg	0,39±0,11	0,42±0,12	0,674	0,42±0,11	0,41±0,09	0,917
UI prandial/kg	0,29±0,14	0,29±0,13	0,722	0,29±0,13	0,34±0,26	0,575

Table 2

Introduction: It is essential to empower patient's autonomy management to improve glycemic control. One of the hardest works is properly dosing of rapid-acting insulin according to different situations. Emerging glucometers with bolus calculator (BC) helps management of disease.

Objective: To evaluate metabolic changes of DM1 patients provided with glucometers with BC in short-term. Analyze differences between Insulinx (BCI) easy mode against Expert (BCE) requiring counting rations.

Material and Methods: Retrospective study of 31 DM1 patients treated with basal-bolus therapy, provided with BC. Compare glycemic control after 3 months depending on type of BC.

Results: Mean age 40.6 years ± 10.4 SD, 21.9 years of disease evolution ± 7.2 SD. Table 1 collects characteristics of our sample. Mean HbA1c at first visit was 8.06 ± 0.89%. After three months using bolus calculator HbA1c was 7.6 ± 0.89 (0.46% lower, p = 0.001). We provided 20 BCI and 11 patients BCE. Table 2 shows pre/post results.

Both groups decrease HbA1c (0.38 to 0.7 in BCE and BCI) without changes on insulin dose. The choice of calculator depends just on patient's characteristics.

Conclusions: Improvement of metabolic control at short term is higher in patients using advanced BC with carbohydrate portions counter. These changes appear to respond more accurate dosage and not higher dose of insulin.

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COST UTILITY ANALYSIS OF LONG-TERM TELEMONITORING OF DMT2 PATIENTS AMONG DIFFERENT EU HEALTH SYSTEMS: THE RENEWING HEALTH MULTICENTER TRIAL

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[5]Pflegewerk Managementgesellschaft mbH, Pflegewerk Managementgesellschaft mbH, Berlin, Germany
[6]Veneto's Research Centre for eHealth Innovation, Arsenál.IT, Treviso, Italy
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Objective: To study the impact of a long-term telemonitoring program for patients with type 2 diabetes mellitus (DMT2), in three European regions (Berlin-Germany, Thessaly-Greece and Veneto-Italy), on health-related quality of life (QoL) and costs compared to usual care.

Methods: 823 patients with DMT2, HbA1c > 53 mmol/mol (7.0% NGSP), were randomly assigned in the telemonitoring (I), (N = 555) and the control (C), (N = 268) group. In the (I) HbA1c levels were collected weekly via a telemonitoring device, for a period of one year. Allocated health professionals provided by phone counseling on lifestyle and medication adjustments, whenever required. Patients in (C) received usual care with face-to-face consultations. QoL was assessed using a generic (SF36v2) questionnaire and SF-6D was used to calculate quality adjusted life years (QALYs) in the cost-utility analysis. (registration NCT01498367/NCT01569893)

Results: The meta-analysis revealed that the mean differences in the SF36v2 Physical Component Scale (CS) (0.23) and the Mental CS (0.30) were not statistically significant [95%CI − 1.32,1.77 and − 6.37,6.96, respectively]. Only the sub group of patients with a mean age of 58.28 years in Greece, showed a statistically significant health utility increase in (I) [0.11, p = 0.000] and the incremental cost-effectiveness ratio (ICER) calculated [€5,460.11 per QALY] indicated that even though telemedicine is more expensive it is a cost-effective choice for the Greek national health system.

Conclusion: The study revealed that the impact of telemedicine implementation varies among age groups due to different treatment objectives, and among health systems due to differences in wages and prices for the telemedicine equipment.

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WEB AND MOBILE TECHNOLOGY FOR TYPE 1 DIABETES MANAGEMENT IN ADOLESCENTS AND THEIR PARENTS

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Objective: This study examined access to and interest in using web and mobile technology for managing type 1 diabetes (T1D) in a sample of adolescents and parents.

Methods: During an outpatient clinic visit, adolescents (n = 40, 55% female, 13.4 ± 2 years, 73% Hispanic, HbA1c = 8.8 ± 1.8%) and their parents (n = 39, 55% household income < $49K) completed surveys assessing access to and interest in using web technology and smartphone applications for diabetes management.

Results: Most adolescents reported having Internet access (98%), using email regularly (63%), texting (93%), and having a smartphone (88%); 38% used existing apps for their diabetes care, with most (93%) reporting carbohydrate counting as the apps' primary function. Most parents and adolescents reported being interested in using apps for diabetes, but more parents than

adolescents expressed high interest in apps to track glucose (74% vs. 43%), count carbohydrates (79% vs. 50%), calculate insulin doses (74% vs. 45%), track insulin use (69% vs. 43%), and receive diabetes-related reminders (79% vs. 53%). Eighty-six % of parents versus 48% of adolescents reported definite interest in using a diabetes management program that used the Internet with smartphone apps.

Conclusions: Results indicate adolescents with T1D across a range of household income have high access to various forms of technology, including smartphones. While most parents expressed high interest in diabetes-related apps, there was variability in the degree of adolescent interest. Involving ethnic minority adolescents in the process of developing smartphone apps for diabetes care may increase their interest and adoption of this technology.

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METABOLIC CONTROL AND COMPLIANCE WITH SELF-MONITORING OF BLOOD GLUCOSE IN ADOLESCENTS AND YOUNG ADULTS WITH TYPE 1 DIABETES: RESULTS OF THE I-NEWTREND RANDOMIZED CLINICAL TRIAL

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The ''i-NewTrend'' study is a multicenter, open-label, randomized (1:1) trial involving T1DM subjects aged 14–24 years, treated with basal-bolus insulin regimen, HbA1c ≥ 8.0% and poorly compliant with SMBG (i.e < 30% of the recommended frequency). Participants were randomized to two different glucose meters: iBGStar™ + DMApp (experimental meter plus telemedicine system - EXP) vs. a traditional meter (CNT). Co-primary endpoints were changes in HbA1c and compliance with SMBG (i.e. ≥30% of the recommended frequency) after 6 months of use of glucose meters.

Of 182 (51% males; age 17 ± 3 yr; T1DM duration 8.8 ± 4.7 yr) randomized patients, 92 were allocated in EXP and 90 in CNT; 7.7% dropped-out. HbA1c levels decreased from 9.9% ± 1.3 to 9.5% ± 1.4 in EXP and from 10.2% ± 1.5 to 9.8% ± 1.6 in CNT (mean between groups difference − 0.12%; p = 0.51). Compliance with SMBG was reached by 53.6% of subjects in EXP and by 55.0% in CNT (p = 0.86). The number of weekly SMBG increased from 9 ± 5 to 16 ± 14 in EXP and from 9 ± 6 to 17 ± 11 in CNT. In both groups, compliant patients reduced their HbA1c levels by − 0.6%. Within EXP, subjects who used the telemedicine features (38.0%) had reduced HbA1c by − 0.58 ± 0.18 (p = 0.001), while those who did not, have increased HbA1c by 0.26 ± 0.21 (p = 0.25). The study highlights that in adolescents and young adults with poor metabolic control increasing the compliance with SMBG, irrespective of the meter used, is associated with an improvement in HbA1c levels; advanced technologies and telemedicine might play a role.

Study funded by Sanofi.

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VALIDITY AND RELIABILITY OF VIDEO TELECONSULTATION FOR THE MANAGEMENT OF DIABETES: A RANDOMIZED CONTROLLED TRIAL

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A large proportion of diabetes patients do not receive a basic minimum standard care. Telemedicine holds the promise of improving access to health care. However, the validity of remote consultation for diabetes has not been researched. This randomized control trial was designed to evaluate the agreement on prescription decisions of endocrinologists between two consultation formats: videoconferencing and in-person consultation. Seventy-three patients were randomized to telemedicine (n = 36) and reference group (n = 37). Each participant in the telemedicine group received one in-person (face-to-face) consultation and one video consultation. The reference group received two in-person consultations. The paired consultations for each patient were performed by two different endocrinologists. The level of agreement between endocrinologists was evaluated by comparing their recommendations on anti-diabetes and cardioprotective medications. The level of agreement between two endocrinologists on changing anti-diabetes drugs was 64% in the telemedicine group, and 78% in the reference group. Although the level of agreement was lower when one of the consultations was provided via videoconference, the difference was not significant. The level of agreement on changing cardiovascular drugs was 78% in the telemedicine group and 76% in the reference group, again not significantly different. The results of this study indicate that video teleconsultation is a valid means of communication between endocrinologists and patients. Known limitations of videoconferencing for clinical purposes did not have remarkable impact on the outcome of consultation in terms of adjustment of patient's medications. Video teleconsultation can substitute a considerable proportion of conventional outpatient specialty consultations for people with diabetes.

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DIASEND AS A TOOL FOR THE ASSESSMENT OF THE ADHERENCE TO SELF-MONITORING AS IN PATIENTS WITH TYPE 1 AS TYPE 2 DIABETES

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The **aim** of our study was to compare theadherence to the SMBG between patients with type 1 and type 2 DM and efficacy of our intervention.

Methods: We included into our prospective study 29 patients with DM type 1 and 24 patients with DM type 2 (mean age 63.4 ± 7.7 years, diabetes duration 24.4 ± 11.2 years, HbA1c 73 ± 13.8 mmol/mol) who were treated by MDI or CSII in our diabetic clinic and had at least 2 uploadings from glucometers via Diasend (before and after an education). Patient's adherence to

SMBG was defined by numbers of SMBG measurements/day, total SMBG measurements and structured SMBG (≥ 3 measurements/day)

Results: Patients with type 1 DM were significantly younger ($p < 0.01$), with longer DM duration ($p < 0.05$) compared to type 2 diabetes patients and received more glucose strips ($p < 0.05$) during one year study period. Structured SMBG was performed more frequently by type 1 diabetes patients compared to type 2 diabetes (65.5 vs.25%; $p = 0.0033$) that corresponded to higher numbers of measurements (2 ± 1.2 vs.1.2 ± 1.1 SMBG measurements/day; $p < 0.05$). After education intervention patients with type 1 DM increased the number of SMBG measurements (2 ± 1.2 vs. 2.4 ± 1.6 measurement/day; $p < 0.05$) that led to decreased average glycemia (10 ± 2.2 vs. 9.6 ± 1.8 mmol/l; $p < 0.05$) and increased percentages of target glycemia values ($45.1 \pm 13.8\%$ vs. $48.3 \pm 13.8\%$; $p < 0.05$). However, type 2 diabetes patients did not follow educational recommendations.

Conclusions: Diasend helps to detect areal patient adherence to SMBG and to identify patients indicated to education intervention. Based on our results education of patients treated by MDI or CSII should be performed more frequently and especially in type 2 diabetes patients more aggressively.

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USING BOLUS CALCULATOR IMPROVES METABOLIC CONTROL OF PATIENTS WITH DIABETES IN TREATMENT WITH MULTIPLE DAILY INSULIN INJECTIONS

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Background: Many patients with diabetes in treatment with multiple daily insulin injections do not calculate correct insulin dose. We used the automated bolus calculator as a support tool to improve metabolic control of ours patients.

Objectives: To assess the response at 3, 6, and 12 months on HbA1c in patients with diabetes in treatment with multiple daily insulin after using bolus calculators.

Material and Methods: Retrospective observational study included 91 patients with diabetes with multiple daily insulin injections who use bolus calculators in our endocrinology consults (Juan Ramón Jiménez Hospital in Huelva, Spain) since January 2012 until September 2014. For statistical analysis we used SPSS 22.0. We used Kolmogorov-Smirnov test, Student's t-test and Mann Whitney U test as appropriate.

Results: The sample was composed of 56 women (61.5%) and 35 men (38.5%) with a mean age of 31.14 ± 11.91 years and with diabetes evolution 15.02 ± 9.18 years. No significant difference between baseline HbA1c group (3-month group $p = 0.3611$, 6-month group $p = 0.7931$, 12-months group $p = 0.3751$). The use of bolus calculator at 3 months was 73.6%, at 6 months 72.5% and 58.2% at 12 months.

Conclusions: We observed a significant improvement in glycemic control (HbA1c) after the introduction of using the bolus calculator at 3, 6, and 12 months of use. No significant

difference in HbA1c decreased after 6 months, therefore it is important insist on using the calculator specially at this time.

Comparison HbA1c as usage time calculator

Time of calculator use	USE	NO USE	
3 month's	7.743%	8.505%	$p = 0.022^1$
6 month's	7.475%	8.660%	$p \leq 0.001^1$
			$p = 0.001^2$
12 months's	7.531%	8.525%	$p = 0.001^1$

(1:Student's t-test 2:Mann Whitney U test)

Comparison changes HbA1c as usage time calculator

	USE	NO USE	
- From baseline to 3 months	-0.1926	0.421	$p = 0.004^1$
- From baseline to 6 months	-0.4762	0.645	$p \leq 0.001^1$ $p \leq 0.001^2$
- From 3 months to 6 months	-0.3583	0.3667	$p = 0.002^1$ $p = 0.002^2$
- From baseline to 12 months	-0.3654	0.3	
- From 3 months to 12 months	-0.2051	0.34	$p = 0.006^1$ $p = 0.006^2$
- From 6 months to 12 months	-0.0149	0.2474	$p = 0.027^1$ **p = 0.151^1**

(1:Student's t-test 2:Mann Whitney U test)

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REMOTELY MANAGING PATIENTS USING A NEW MOBILE HEALTH INSULIN PATCH PUMP SYSTEM (CELLNOVO): THE FUTURE HAS ARRIVED

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Background: The Royal Derby Hospital Insulin Pump Service, which provides care to over 250 patients on insulin pump therapy, is the UK's largest provider of the innovative mobile health (mHealth) Cellnovo Insulin Pump System. Cellnovo is a unique patch pump that automatically and continuously uploads data from the handset to the web via a mobile phone network. The system captures patients' glucose, insulin and carbohydrate data and objectively records physical activity via the accelerometer integrated within the Cellnovo pump. The Derby insulin
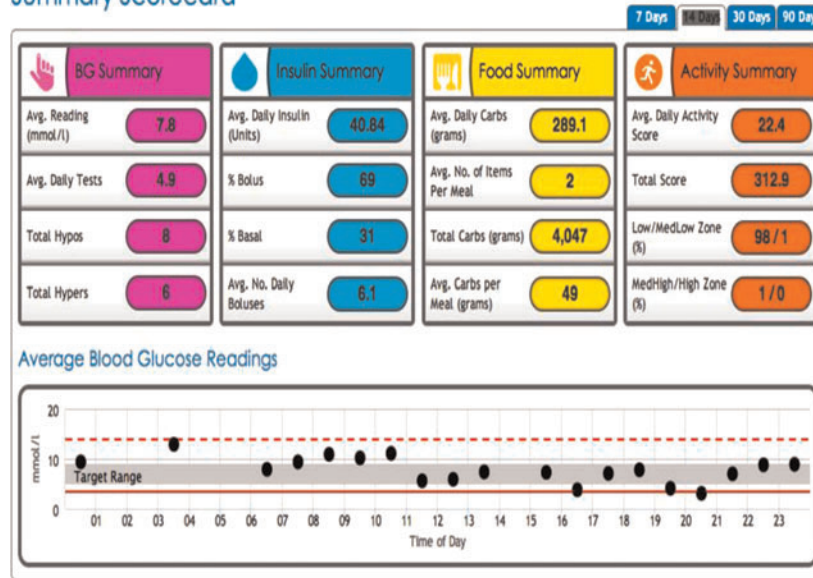
pump team adopted this system in response to patient interest and also due to the need to manage a rapidly expanding service with limited health care professional time.

Methods: We report our experience using the Cellnovo System in 25 patients with over 1500 patient days of data.

Results: The automated upload of information via Cellnovo Online provides unprecedented access to real-time patient data, which includes physical activity alongside insulin, carbohydrate and blood glucose recordings. The ability to view patients' data via Cellnovo Online, without the need to manually upload

data, reduces time spent collating data and allows users and health care professionals to remotely and instantaneously access and analyse a wealth of information. This has facilitated improved diabetes care. In Derby this has reshaped the delivery of care and enabled the service to incorporate increased remote management of patients.

Conclusions: Cellnovo has facilitated the integration of mHealth by providing up-to-date and accurate information for use during remote patient consultations within the Royal Derby Hospital Insulin Pump Service.

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DEVELOPMENT OF A WEB-BASED TYPE 2 DIABETES EDUCATION PROGRAM FOR HEALTH PROFESSIONALS: A PILOT STUDY

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Aim: This study aimed to develop a Web-Based Type II Diabetes (T2D) Education Program for health professionals.

Method: The pilot study employed a quasi-experimental design and examined the pre- and post-test results of a single group, which consisted of 20 nurses. Data was collected online via the Information Form, the Evaluation of Web-Based Education Material Scale (EWBES), the Opinion Form for Web-Based T2D Education Program, and assessment tests. In data analysis, descriptive statistics and the Wilcoxon signed rank test were used.

Application: The program was developed according to the Kemp Teaching Design Model. Presentations were prepared in accordance with the storyboards created by the researcher and software, sound recording, animations, and videos were generated by receiving support from professional teams. All of these were put together on a website and a pilot study was carried out.

Results: The mean age of the study group was 30.31 ± 3.84 and the EWBES mean score was $4.52 \pm .41$ (min = 3.96–max = 5.00). Participants' responses to the Opinion Form are summarized below: *"It provides that the user easily finds clear and understandable information", "I think that all of the teaching methods are necessary. I think it's very well prepared."* There were statistically significant differences between the mean pre- and post-test scores of the assessment tests that evaluate 3 topics included in the education program (p = 0.000, Z = −3.992; p = 0.000, Z = −3.983; p = 0.000, Z = −3.972; respectively).

Conclusion: According to our results, the Web-Based T2D Education Program was found to be "very good" by the study group and was determined to be effective in increasing their level of information on T2D.

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VALIDATION OF USING PHOTOS TO EVALUATE DIETARY INTAKE – THE METHOD USED BY DIALBETICS, A SMARTPHONE-BASED SELF-MANAGEMENT SYSTEM FOR DIABETES PATIENTS

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Objective: The accuracy of estimating nutritional intake and balance from photos of meals has not been well studied. The aim of this study was to examine that accuracy using smartphone photos of their meals taken by type 2 diabetes patients. This is part of an ongoing study of our ICT-based diabetes self-management support system, DialBetics.

Methods: We prepared 61 dishes whose actual amount/value for each nutrient was known: total energy—carbohydrate, fat, protein, dietary fiber—and salt. Their balance—PFC (protein-fat-carbohydrate) ratio—was also known. Smartphone photos of those dishes were taken, and, from those photos, three registered dietitians evaluated each dish, naming the dish and estimating the amount of each nutrient in it, and the dish's balance. Actual values and estimated values were compared using paired t tests; Spearman correlation coefficients were calculated. Bland-Altman analysis was used to assess the agreement between the two values.

Results: There were no statistically significant differences between estimated and actual values of each nutrient and balance. Indeed, there were significant correlations between actual values and estimated values (the correlation coefficient from 0.70 for fat to 0.92 for carbohydrate). Bland-Altman analysis showed that differences between the two values were random and did not exhibit any bias against nutrient intake; 95% limits of agreement were acceptable, but wide (−198 to 210 kcal/dish for energy, −22.7 to 25.8 g/dish for carbohydrate).

Conclusion: Diet evaluation by photo used by DialBetics is reliable at group level, and appears to have potential in dietary assessment.

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USE OF A COLOR RANGE INDICATOR IN A BLOOD GLUCOSE MONITOR IMPROVES GLUCOSE RANGE AWARENESS

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Aims: The ability of patients to achieve glycemic control depends in part upon their ability to interpret and act upon blood glucose (BG) results. This clinical study was conducted to determine if a simple on-meter color range indicator (CRI) could improve the ability of patients to categorize BG values into low, in-range and high glycemic ranges.

Methods: The clinical study was conducted in 59 subjects with type 2 diabetes (T2DM). Subjects classified 50 general, 15 before and 15 after meal BG values as low, in-range or high based on their current knowledge. Subjects then interactively experienced the on-meter CRI, which showed whether alternate BG values were low, in-range or high. After CRI interaction, subjects repeated the original scoring assessment followed by a survey exploring their awareness of glucose ranges.

Results: Following interaction with the CRI, subjects improved their ability to categorize general, before meal and after meal BG results by $23.4\% \pm 3.0\%$ (SEM), $14.2\% \pm 2.4\%$ and $16.1\% \pm 2.9\%$, respectively (all $P < 0.001$), into low, in-range and high glycemic ranges. Improvement was not accompanied by an increase in time spent categorizing results. There was no correlation between subject HbA1c, test frequency or duration of diabetes and ability to correctly classify results. Subjects agreed the CRI feature helped them easily interpret glucose values and improved their awareness of glucose ranges.

Conclusion: A short interactive session with a meter including a color range indicator feature improved the ability of T2DM subjects to interpret and categorize BG values into recommended ranges.

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ROLE OF HOME BLOOD PRESSURE MONITORING IN HALTING THE PROGRESSION OF DIABETIC KIDNEY DISEASE: 6 YEAR FOLLOW UP DATA

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Chronic Kidney Disease (CKD) is the most disabling & expensive complication of diabetes. The rapid progression of CKD is heralded partly by glucose and partly by fluctuations in blood pressure. Maintenance of acceptable blood pressure (BP) is pivotal in preventing the progression of CKD to one requiring renal replacement therapies (RRT).

We extracted data of CKD patients from our electronic medical records with an average estimated glomerular filtration rate (eGFR) below 50 mL/min/1.73m2 (CKD stage 3 and 4) and have completed at least 6 years of telemedicine follow up with our Diabetes Tele Management System (DTMS®) in frequently titrating drug dosages. From this, data of 22 patients who used automatic BP apparatus (Omron HEM-7120) at their home for BP monitoring were de-identified. We compared serum creatinine, A1c, haemoglobin (Hb), systolic & diastolic BP, eGFR at baseline and at 6 years. Comparison of means was made by paired t-test. There was no statistically significant change in A1c (6.9 vs 7.3, p = 0.053). There was a decline in serum creatinine (1.6 vs 2.3, p < 0.0001), systolic BP (136 vs 162, p < 0.0001), diastolic BP (70 vs 78) and an increase in Hb (12.8 vs. 11.2, p < 0.0001) and eGFR (48.5 vs 32.7, p < 0.0001).

Compared to those on hospital visits once in 3 months, those on home BP monitoring (HBM) & weekly telemedicine visits, at the end of 6 years showed evidence of stable CKD. HBM should be strongly advocated as a cost effective tool in preventing the progression from early stages of CKD to end stage renal disease.

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CLINICAL VALIDATION OF THE COMMODITY12 TELEMEDICINE SYSTEM IN DM2 PATIENTS

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Background: The COMMODITY12 is a telemedicine system designed for continuous monitoring of diabetes type 1 and 2, as well as the cardiovascular comorbidities. The system has been created in collaboration of 9 European academic and industrial partners under FP7 [1].

Aim: The aim of this study was clinical validation of the COMMODITY12 system in DM2 patients, under a design of a mini feasibility trial.

Methods: Outpatients from Lodz region (central Poland) with DM2 were randomly ascribed to either control arm, in which they received standard care, or intervention arm, in which they used COMMODITY12 system for daily monitoring of their diabetes-related parameters (glucose level, blood pressure, weight, ECG, heart rate, mobility, a range of lab tests, and adherence to medication). Primary outcome measures was system operability and whole trial feasibility, defined as harmonic technical functioning of all layers, and appropriateness of the PHS for patient use, respectively.

Results: Sixty outpatients (30 in the intervention arm) took part in this study. In general, the COMMODITY12 system functioned well, with only some problems with transmission of the data from ECG sensor to the hub. Patients accepted telemedicine system well, and found it to be helpful in self-management of diabetes. In some patients using COMMODITY12 system, trend toward better metabolic control was also observed, as compared to the control group.

Conclusion: These results point at the usefulness of COMMODITY12 system in diabetes care. Further studies on larger groups are needed to determine the effect of the system on clinical outcomes.

Reference:

1. www.commodity12.eu

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INFLUENCE OF FREQUENT USE OF MOBILE HEALTH TECHNOLOGY ON BLOOD GLUCOSE CONTROL IN PATIENTS WITH TYPE 1 DIABETES

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Background: Keeping a diabetes diary is thought to be beneficial both for diabetes self-management and therapy adjustment by health care professionals. However, a high number of patients indicate that keeping a structured paper based diabetes diary is a burden. mySugr Companion, a FDA registered and a CE-marked class I medical device, was developed to make this task more appealing. Patients can enter data on BG, meal (including images), insulin, exercise, mood.

Methods: The aim of this retrospective analysis was to investigate whether we can determine characteristics of adherent (≥ 4 BG values/day on an active day) and non-adherent (< 4 BG values/day on an active day) mySugr users. Only active users on active days (≥ 3 meals/day logged) of mySugr companion were analysed. The influence of being an adherent vs. a non-adherent user on BG was evaluated. Data were analysed using R.

Results: 728 adherent users on 31,985 days and 475 non-adherent users on 5,132 days were included. Mean age was comparable: 33 ± 18 vs. 35 ± 16 years (adherent vs. non-adherent). Pen use was similar 73% vs. 71% (adherent vs. non-adherent). Mean morning (144 ± 66 vs. 146 ± 67 mg/dl) and noon BG (135 ± 63 vs. 135 ± 62 mg/dl) were comparable (adherent vs. non-adherent). Evening (144 ± 69 vs. 152 ± 76 mg/dl) and bedtime BG (149 ± 69 vs. 159 ± 87 mg/dl) were lower for adherent users.

Conclusion: Non-adherent users had higher evening and bedtime BG, which appears to be a consequence of less measurements. Research is needed to identify reasons for non-adherence to improve it.

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A RELEVANT GLUCOSE-INSULIN DYNAMICS MODEL FOR TYPE-I DIABETES

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Objective: Several models have been developed for decades. **These models have an inherent drawback**: **for each blood glucose (BG) value, a different insulin infusion rate is needed to maintain constant BG level**. The objective is to review the elementary modelling to eliminate this contradiction with real life.

Method: A new model is derived for type-I diabetics. **It has realistic asymptotic properties** as there is **one single constant insulin infusion rate**, known as the basal rate, independent on the glycemia, and which **ensures the equilibrium of any value of the glycemia in fasting periods as it is in real life**. A standard identification algorithm is used to get the patients' individual characteristics.

Results: Standard clinical data (CGM, injection, CHO uptake) were analyzed for a typical type-I diabetic outpatient. A long term fit over two days with constant parameters is displayed in Figure 1. Moreover, **the new model provides the computation of the tools for the functional insulin therapy like basal infusion rate or the insulin sensitivity factor (ISF)**. This is a major outcome as they can be used for the education of type-I diabetics.
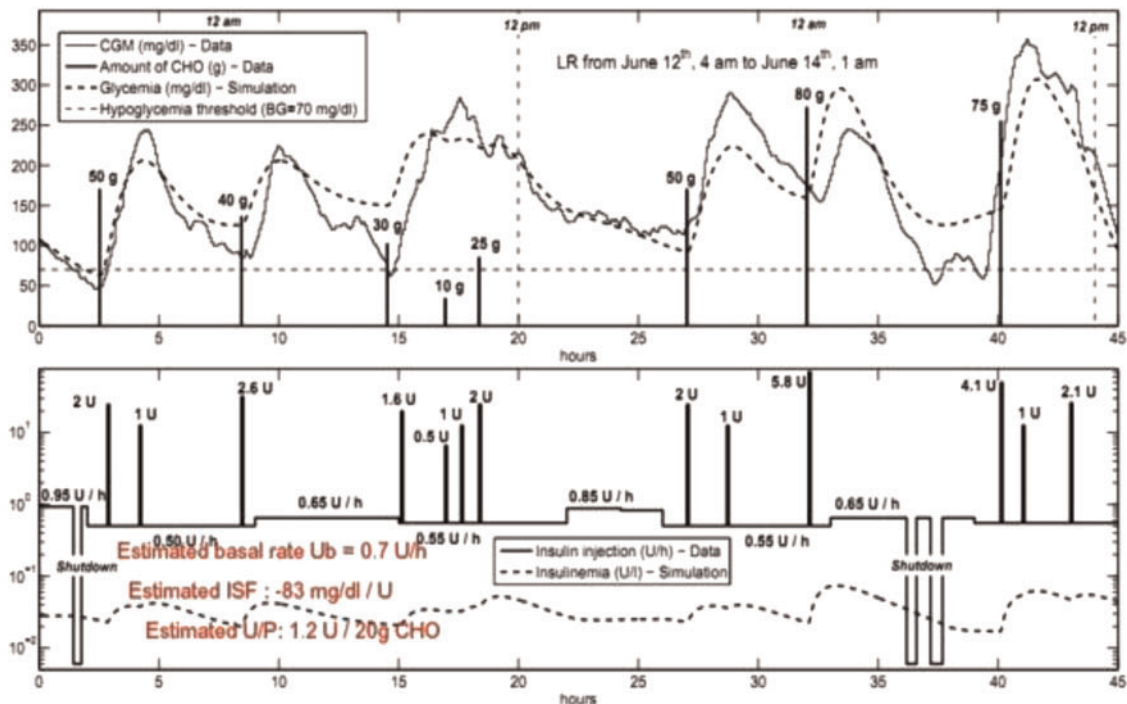

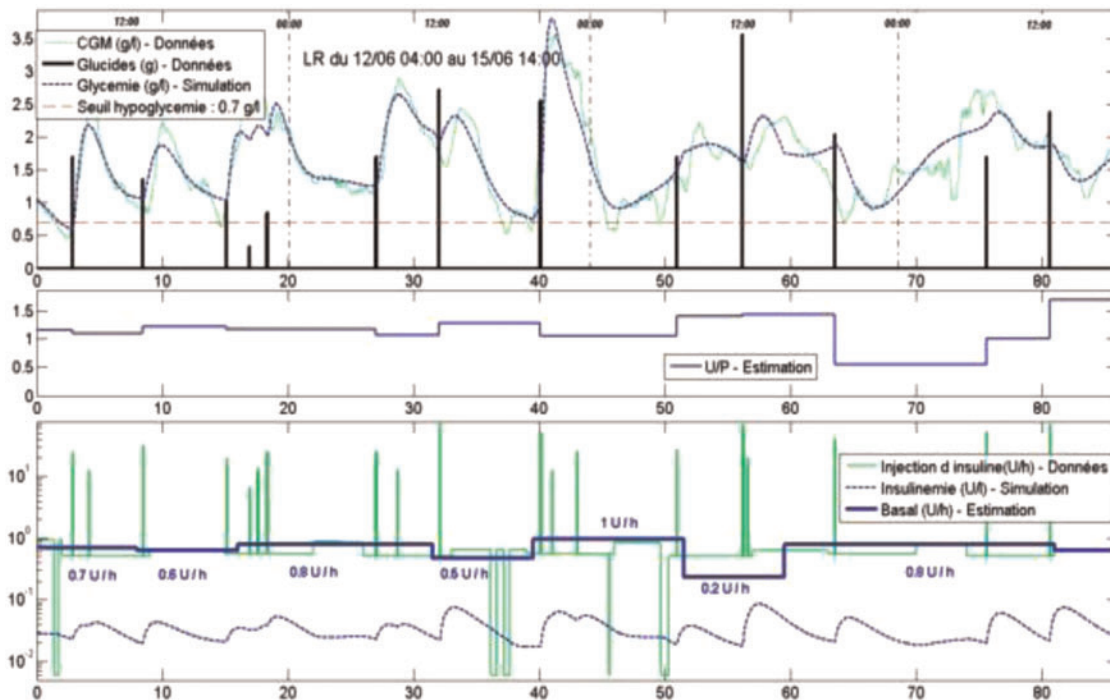Figure 1: Time invariant Model behaviour over 45 hours vs. clinical data

Figure 2. Time varying Model behaviour over 84 hours vs. clinical data

The method is extended to derive a time varying model improving the fit on an even longer period as displayed in Figure 2.

Conclusion: Prediction of the model is improved and a better efficiency of closed-loop algorithms is foreseen for the artificial pancreas.

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MINDFULNESS AND IMPULSIVITY IN DIABETES MELLITUS

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Background: Diabetes is a highly prevalent disease worldwide, characterized by increased blood sugar levels. Growing evidences revealed the strong association of diabetes and psychological disorders like anxiety, depression, schizophrenia, etc. Mindfulness is the awareness which arises out of intentionally attending in an open and discerning way to whatever is arising in the present moment, is positively associated with healthy condition. Impulsivity is a predisposition toward rapid, unplanned reactions to internal or external stimuli without regard to the negative consequences of these reactions to the impulsive individual or to others which is negatively associated with the individual's health.

Aim: This study was intended to see the association of mindfulness, impulsivity with diabetes.

Method and material: Two hundred subjects (100 = diabetic and 100 = non diabetic) from local communities were enrolled in this study. All the subjects were administered Mindfulness, attention and awareness scale (MAAS) and Barrat impulsivity scale.

The results: There was a significant low MAAS score and significantly higher Barrat impulsivity scores in the diabetic group than in a non diabetic group.

Conclusion: Diabetic people have more impulsivity and less mindfulness state than non diabetic people.

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TRENDS IN THE EPIDEMIOLOGY OF TYPE 1 DIABETES MELLITUS IN MOSCOW REGION DURING THE PERIOD 2004-2013

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Background: It is extremely important to know about main epidemiological indicators characterizing situation on type 1 diabetes mellitus (T1DM).

Aim: To assess dynamics of main epidemiological indicators of T1DM for 10-year period (2004–2013).

Materials and methods: There was analysis of the Moscow Region DM Register, which contained information about 11236 patients with T1DM. This Registry contains information on age at diabetes onset, date of death, causes of death of patients with T1DM. Indicators are presented per 100,000 of population. State Register of Patients with Diabetes (SRPD) is an information-analytical system, which allows keep records of prevalence and incidence of diabetes, morbidity and mortality of patients, its immediate causes, and the prevalence of diabetes complications, providing medicines and self-control.

SRPD is actively developing with support of FGBI Endocrinology Research Center together with ''Aston Consulting.'' New on-line version of software ''Register diabetes - 2014" introduced and widely used by all endocrinologists in the Moscow region.

Results: T1DM prevalence increased from 132.09 to 166.6 per 100,000 within 10-year period. T1DM incidence consistent with 7.7 ± 0.8. T1DM mortality decreased from 0.9 to 0.6 per

100,000. Average life expectancy in adult patients with T1DM (onset of TIDM < 25 yrs), increased by 1.3 yrs. T1DM prevalence increased on 20.5% within 10-year period. Average peak of T1DM onset shifted from 10–14 to 7–9 yrs. Main cause of death was chronic renal failure, if onset of TIDM < 25 yrs, and it was macrovascular complications, if onset of TIDM > 25 yrs.

Conclusion: SRPD analysis reveals features in morbidity and mortality in patients with T1DM depends on age of diabetes onset.

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TRENDS IN THE EPIDEMIOLOGY OF TYPE 2 DIABETES MELLITUS IN MOSCOW REGION FOR THE 10 YEAR PERIOD (2004–2013)

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Background: National Registry for Diabetes is an integrated information and analytical system that keeps record of data pertaining to prevalence and incidence of DM, disability and mortality rates, prevalence of complications associated with DM and supply of medicines and self-monitoring devices.

Aim: To assess dynamics of main epidemiological indicators of T2DM for 10-year period (2004–2013).

Methods: Analysis utilized data obtained from the Moscow Region Diabetes Registry (MRDR), collected over past ten years. MRDR contained information about 191260 patients with T2DM. MRDR is part of State Diabetes Registry. Its software had been designed by Aston Consulting. New on-line version of software ''Register diabetes - 2014'' widely used by all endocrinologists in Moscow region.

Results: Number of T2DM patients has increased by 1.5 times over past decade, mostly due to increase in prevalence among men. Peak incidence of T2DM is in patients aged 65–69 years. Mortality rate has declined over the past decade. Life expectancy from disease onset has increased from 10.7 ± 0.12 to 11.33 ± 0.12 years owing it to female population (11.29 ± 0.14 to 12 ± 0.14 years), whereas it has remained practically unchanged in men. Cardiovascular diseases are still prevailing cause of death (60%). Proportion of deaths from gangrene of the lower extremities dropped by 60.3%, deaths from chronic renal failure caused by diabetic nephropathy dropped by 30.9%.

Conclusion: Moscow region showed an increase of 35% in prevalence of T2DM over the past ten years (2004–2013). Incidence of T2DM in adult population aged below 40 years increased by 1.9 times.

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PRECLINICAL EVALUATION OF A COMPUTER VISION-BASED SMARTPHONE SYSTEM FOR CARBOHYDRATE COUNTING

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Estimating a meal's carbohydrate (CHO) content is of crucial importance in diabetes self-management. To this end, a computer vision-based smartphone system, named GoCARB, was developed and pre-clinically evaluated by individuals with type 1 diabetes (T1D).

In total, 21 adult volunteers with T1D (age > 18 years; 7 female, 14 male) participated in the study at Bern University Hospital [the ''Inselspital'']. The study was conducted on 10 days during July and August 2014. For each day, a total of six meals were taken from the hospital's restaurant (normal menu). The meals were of broad diversity. The food items comprising each meal were weighed and by using the USDA Nutrient Database the corresponding amount of CHO was estimated (ground truth). Each participant was asked to count the CHO content of each meal independently. Then, he/she was asked to estimate the CHO content by using the GoCARB. At the end of each session, a questionnaire was completed, in order to assess the user's experience with GoCARB.

The mean (SD) absolute difference between CHO counted by the patient and ground truth was 28.52 (39.24) g of CHO, while the corresponding value for the GoCARB system was 13.16 (10.16) g of CHO. The preclinical study indicates that the system is able to estimate the meal's CHO content with higher accuracy than individuals with T1D. The feedback gathered by the participants showed that the system is easy to use even for non-smartphone users. Its effectiveness in improving glycaemic control will be investigated in a clinical trial.

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INITIAL INSULIN DOSAGE IN NEW ONSET PEDIATRIC DIABETES: HOW TO START?

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Background: Pediatric patients with T1DM require a wide range of insulin dosages. We evaluated a dosing calculator aimed at safe (home) dosing and rapid normalization of glucose values during the first 10 days of insulin treatment.

Methods: The dosing calculator in our disease management system (VCare) is based on collected and published data on parameters influencing the required dose. It provides a dosage advice for regular insulin at breakfast and lunch, a rapid-analogue at dinner and long-acting insulin analog as basal insulin. We included T1DM patients diagnosed between June 1st 2012 and June 1st 2014 and analysed (a) safety: number of hypoglycemic and profound hyperglycemic episodes; (b) mean glucose levels and percentiles; (c) time needed to reach appropriate glucose control.

Number of patients	82 (48M)
age range at diagnosis (yrs)	2.5 to 17.8
Day 1–10	
glucose measurements	3070
• < 2.7 mmol/L	3
• < 3.9 mmol/L	67 (18 on day 1–5)
• > 33.3 mmol/L	3
	50% < 12 mmol/L: D5
Time to reach target	50% < 10 mmol/L: D8

Results: Mean glucose levels (mean (SD), mmol/L) gradually decreased from *18.1* (7.6) on day 1, to *11.8* (5.8) on day 5 and *8.6* (3.7) on day 10. No night time hypoglycemia was observed.

Conclusion: our VCare dosage advice is feasable and safe for home dosing of insulin. Patients are provided with pre-scheduled doses of insulin, resulting in normalization of glucose values within 10 days. The safety of the dosage advice allows the family to adapt to the new situation with diabetes without fear for hypoglycemia.

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AMBIENT LIGHT AS AN INFORMATION MEDIATOR FOR PARENTS TO CHILDREN WITH DIABETES

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For parents to children with diabetes, it is often important to have instant knowledge of their vital diabetes-related parameters. One way of providing such information is through use of ambient light, as a way to provide easily understandable information that can be unconsciously processed throughout the day [1, 2].

In this study we use a remotely controlled color-tunable light bulb to indicate one of 3 levels of the child's last BG measurement, which is made available through our mobile phone-based Diabetes Diary (DD) [3]. In our implementation we use red (0–4 mmol/L), green (4–10 mmol/L) and yellow (>10 mmol/L) light to symbolize BG measurement values in different intervals. We integrated the automatic transfer of BG measurements into our existing application, DD. To transfer the information to the bulb-connected setup we use a custom-formatted SMS, as an ordinary communication instrument, which is available to a wide range of mobile phones. Utilization of SMS also allows running the parents' part of the setup at most places from ordinary mobile networks, and also to follow measurement updates in real-time. The video at http://youtu.be/cxH6qDGe0to illustrates an example scenario of a parent-child interaction, using such a setup.

The setup is composed of commonly available, cheap components and it is designed to run on a long-term basis without maintenance. The mobile app integration also allows to add multiple receiver phone numbers and therefore it has the potential to be used with multiple bulb-enhanced receiver setups and/or include other caretaker/caregiver relationships (e.g. siblings, grandparent-child, etc.).

[1] Gibson, J. J. (2002). A theory of direct visual perception. Vision and Mind: selected readings in the philosophy of perception, 77–90.

[2] Wisneski, C., Ishii, H., Dahley, A., Gorbet, M., Brave, S., Ullmer, B., & Yarin, P. (1998). Ambient displays: Turning architectural space into an interface between people and digital information. In Cooperative buildings: Integrating information, organization, and architecture (pp. 22–32). Springer Berlin Heidelberg.

FIGURE 1. Available options for set-up of a new receiver's phone number in the Diabetes Diary application and basic schema of data flow when authorizing the change of the light bulb's color.

[3] Årsand E, Skrøvseth SO, Joakimsen RM, Hartvigsen G. Design of an Advanced Mobile Diabetes Diary Based on a Prospective 6-month Study Involving People with Type 1 Diabetes. The 6th International Conference on Advanced Technologies and Treatments for Diabetes, February 27. – March 2. 2013, Paris. France.

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SITUATED USER EXPERIENCE WITH TAKE-HOME MEDICAL TECHNOLOGY INFLUENCES ADHERENCE TO SELF-MANAGEMENT PLANS FOR ADULTS WITH TYPE 1 DIABETES

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Discussions of chronic conditions like Type 1 diabetes (T1D) have focused on whether 'compliance' or 'adherence' are appropriate terms to describe self-management regimes. However, as self-management encompasses 95% of care for T1D, it is necessary to understand not just what people should do, but what they actually do. My qualitative exploratory research on the everyday use of T1D devices suggests that that they are not just used as medical devices, but also as consumer products. Using a pragmatic approach to understand situated use through contextual interviews, group observation, and a diary study, has uncovered how the situated user experience (UX) of these

technologies influences self-management. Situated UX impacts how people carry devices day-to-day, whether they incorporate the devices into regular practice, and their daily use of these technologies. This ranges from not adopting an insulin pump because wearing a ''90's pager'' causes embarrassment; to not carrying a glucometer as it does not fit into a purse at a wedding; to using devices as props to get flight upgrades. Engaging with participants from Canada, the US, and the UK highlighted the influence of physical environment, cultural context, individual differences, and social situations on the experience and practices of everyday T1D self-management. This research points to the importance of understanding situated use in the design of mobile medical devices, the varied technology preferences of adults with the same condition, and the significance of consumer needs when designing a self-care device that is to be adopted, carried and used by laypeople.

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CHAIR-SIDE SALIVA DIAGNOSTIC TESTS: AN EVALUATION TOOL FOR XEROSTOMIA AND CARIES RISK ASSESSMENT OF ADOLESCENTS WITH TYPE 1 DIABETES

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The aim of this study was to evaluate the prevalence of dry-mouth symptoms (xerostomia) and compare it with alterations in salivary characteristics of adolescents with type 1 diabetes (DM1), as measured with the use of chair-side saliva tests. This study also investigated the possible association between salivary dysfunction and incidence of caries, in relation to the level of metabolic control.

A cross-sectional study was performed on adolescents (12–18 years old) allocated among 3 groups: 20 patients poorly-controlled (DM1-A, HbA1c > 8%), 20 well-controlled (DM1-B, HbA1c ≤ 8%) and 20 age- and sex-matched healthy controls. The study was approved by the Research Ethics Committee of University of Athens and the parents signed written informed consent. All subjects were examined for dental caries, oral hygiene and salivary factors. Assessments of salivary function included self-reported xerostomia, quantification of resting and stimulated whole saliva flow rates, pH values, buffering capacity and saliva's viscosity. Salivary characteristics were evaluated with the use of GC Saliva Check Buffer (3M ESPE). Data were analysed by Chi-square and Kruskal-Wallis tests.

Subjects with diabetes reported xerostomia more frequently than healthy controls (p < 0.05). Unstimulated salivary flow rate and pH values remained significantly lower in DM1-A compared to DM1-B and controls. Low values of resting salivary flow rate were associated with a higher prevalence of dental caries in adolescents with poorly-controlled DM1 (p < 0.05).

The results suggested that diabetes-induced alterations in salivary characteristics are indicative of higher caries susceptibility of diabetics and chair-side saliva tests are a useful tool for the evaluation of caries risk assessment.

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SHARED GENETIC ETIOLOGY UNDERLYING ALZHEIMER'S DISEASE AND TYPE 2 DIABETES

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Background: Diabetes may increase the risk of Alzheimer's disease (AD). Many epidemiological studies indicate that people with diabetes are at higher risk of eventually developing AD or other dementias. It is estimated that hyperinsulinemia in the elderly accounts for 39% of cases of AD. However, the exact nature of how these two diseases are connected remains unknown. Possible mechanisms include shared genetic or microbial risk factors, which were systematically investigated in this study.

Methods: We used data from public genome-wide association studies (GWAS) to explore the associated single-nucleotide polymorphisms (SNPs) between AD and type 2 diabetes (T2D). Furthermore, we explored the function of the AD-T2D shared GWAS SNPs by integrating pathway and gene ontology data, expressional quantitative trait loci, co-expression networks, and regulatory elements.

Results: We found a significant overlap ($p = 4.9^{-19}$) between association SNPs from large scale GWAS of AD and T2D. 927 SNPs were associated with both AD and T2D with $p \leq 0.01$, and we found that these SNPs influence 190 genes in brain tissue and 416 genes in T2D relevant peripheral tissues (liver and adipose). Lipid metabolism and antigen processing/presentation pathway genes were significantly enriched.

Conclusions Applying systems biology approaches, we leveraged GWAS, eQTLs, gene co-expression networks, etc., and found that AD and T2D share common genetic risk factors, which at least partially explain the epidemiological observation of the disease incidence correlation. Such risk factors mainly affect immunity, lipid metabolism, and protein folding pathways or functional categories.

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THE EFFECTIVENESS OF FAMILY-CENTERED EMPOWERMENT EDUCATION ON METABOLIC CONTROL OF PATIENTS WITH DIABETES MELLITUS TYPE 2

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Background: Education in diabetic patients and their family can facilitate our management and will result in better control. The purpose of this study is the effectiveness of Family-Centered Empowerment Education on metabolic control of patients with diabetes mellitus type 2.

Methods: This study is a clinical trial in which 153 type 2 diabetic patients were randomly divided into 3 groups: control group (A), patient-Centered intervention (B) and family-Centered intervention (C). Before intervention and 3 months after that, a knowledge questionnaire was about diabetes and HbA1C test was developed. Intervention began on patient-Centered empowerment education and family-Centered empowerment in groups B and C respectively. Routine education

was done in group A. To do the data analysis spss v. 16, x2, paired T test and ANOVA has been used.

Findings: No significant differences were noticed among the 3 groups before the intervention, as demographic factors show (p > 0.05). No significant difference was noticed between patients' knowledge and HbA1C degree too (p > 0.05), but a significant difference was between these two factors after intervention (p < 0.001). A significant difference was between their knowledge and HbA1C degree in groups B and C compared with control group (p < 0.05). Although there were no significant difference between group B and C, but Coefficient changes showed more decrease in HbA1C degree in group C in comparison with group B.

Conclusion: This study revealed that education Centered on patient and family empowerment will have a positive effect on metabolic control.

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ACCEPTABILITY OF A PATIENT AND CLINICAL PLATFORM OF AN ADVANCED BOLUS CALCULATOR FOR TYPE 1 DIABETES (ABC4D)

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Objective: To evaluate acceptability of an Advanced Bolus Calculator for Type 1 Diabetes (ABC4D). ABC4D utilizes Case-Based Reasoning (CBR) as a learning methodology to personalize insulin bolus therapy for people on multiple daily injections. For safety, the system is divided into a patient and a clinical expert platform. The patient platform provides real-time insulin bolus advice and runs on a smartphone while the clinical expert platform runs on a desktop computer and is used to monitor and accept adaptations made by the CBR algorithm.

Method: Participants used the ABC4D smartphone application for insulin bolus advice over six weeks at home. They attended the research facility weekly where a clinical expert used the revision platform to accept case adaptations proposed by the algorithm. Each participant completed a questionnaire at the end of the trial period assessing usability of the patient platform.

Results: This trial is currently ongoing and to date three participants have completed the study. On average, the patient platform has been used 6.2 times/day; 2.6 times for bolus advice, 3.4 times to log glucose related events. Out of a total of 331 insulin bolus recommendations, 95% were accepted by the participant. The clinical platform has been used 18 times by a clinical expert, reviewing 272 case adaptations of which 53% were accepted.

Conclusion: Initial results show good acceptance by participants using the ABC4D smartphone application for insulin bolus advice, as well as by the clinician using the clinical expert platform for accepting adaptations proposed by the software.

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A NOVEL PATHOPHYSIOLOGICAL MECHANISM OF DIABETIC INTESTINAL DYSRHYTHMIA

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The destruction of interstitial cells of Cajal (ICC) has been suggested as a pathophysiological mechanism of altered intestinal motility in diabetic patients. It is referred to clinically as intestinal dysrhythmia.

Aims: To investigate the role of basal and diabetically perturbed pacemaker activity of ICC on electromechanical processes in the gut.

Methods: The study applied a computer model to analyze the spatial distribution and the dynamics of myoelectrical patterns, frequencies, velocities, and active forces in the gut.

Results: The model reproduced accurately under normal physiological conditions the development of migrating myoelectrical complexes, the production of spikes and active forces of contraction in the small intestine. Variations in pacemaker settings, a reduction in number of ICC and a decrease in the firing rate, led to a distortion of the regular pattern of myoelectrical activity and the formation of spiral waves. They were recorded in the circular and longitudinal smooth muscle layers of the organ and showed a periodic self-sustained activity. The velocity, frequency and amplitude of them did not differ from normal ones. Essential changes were observed in the dynamics of active contractions. They became irregular, of low intensity and failed to maintain the propulsion of intraluminal content. The content remained trapped indefinitely within the affected segment of the gut.

Conclusion: Although the detailed explanation of the observed numerical event cannot be provided, we suggest that histomorphological arrangements among muscle cells and ICC contributed to the outcome. The observed type of self-sustained myoelectrical activity can be related to pathogenesis of intestinal dysrhythmia.

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CLINICAL SAFETY EVALUATION OF AN ADVANCED BOLUS CALCULATOR FOR TYPE 1 DIABETES (ABC4D)

M. Reddy[1], P. Pesl[2], M. Xenou[1], N. Jugnee[1], C. Toumazou[2], D. Johnston[1], P. Georgiou[2], P. Herrero[2], N. Oliver[1]

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Objective: To evaluate safety of the Advanced Bolus Calculator for Type 1 Diabetes (ABC4D) application for mealtime insulin bolus calculation in a controlled clinical environment followed by assessment in the home. The ABC4D system consists of a smartphone-based platform running a novel decision support algorithm based on Case-Based Reasoning (CBR) utilising continuous glucose monitoring data to evaluate solution outcomes. For safety, a PC software application is used for clinical supervision. It provides personalised insulin recommendations, with increased flexibility and adaptability compared to standard rule-based bolus calculators.

Method: Open-label non-randomised study. Informed written consent was obtained prior to screening. Stage 1: Participants spent 8.5 hours in the clinical research facility with two

Glycaemic outcomes (mean) each week during stage 2 of the ABC4D study (n=3)						
Outcome measure	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
Mean glucose (mmol/l)	9.6	9.1	9.6	8.8	8.6	9.4
LBGI	4.1	3.2	3.9	3.1	2.8	4.5
HBGI	11.6	9.8	12.2	9.0	8.8	11.5
% time <2.8mmol/l	1.5%	0.3%	0.2%	0.7%	0.4%	0.3%
% time <3.9mmol/l	3.5%	5.3%	4.8%	4.6%	2.2%	2.5%
% time 3.9-10.0mmol/l	54.2%	59.8%	64.1%	53.1%	57.8%	66.8%
% time >10.0mmol/l	42.4%	34.9%	31.1%	42.3%	39.9%	30.8%
% time >15mmol/l	8.0%	3.8%	5.4%	7.7%	7.7%	3.7%

standardized meals. The ABC4D smartphone application was used for bolus recommendations. Stage 2: Participants used the ABC4D smartphone application for six weeks in their home environment, attending the clinical research facility weekly for data upload, revision and adaptation of the CBR case-base.

Results: Stage 1: 4 adults with T1DM (75% female, mean(SD) age 38(18)years, diabetes duration 14(12) years, HbA1c 61(10) mmol/mol, body mass index 24(5) kg/m^2) on multiple daily injections of insulin participated. The mean(SD) glucose was 9.4(0.4)mmol/l. No episodes of hypoglycaemia (<3.9 mmol/l) occurred.

Stage 2: This trial is ongoing and three participants have completed this stage. The preliminary clinical results are summarised below.

Conclusion: The ABC4D system for insulin bolus calculation is safe in a controlled clinical environment and preliminary data from the home study are encouraging, suggesting increased time in target and reduced time in hyperglycaemia.

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IDENTIFICATION OF DIURNAL VARIATIONS IN INSULIN-TO-CARBOHYDRATE-RATIOS FROM MEASURED CGM DATA FOR PATIENTS WITH T1DM

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Introduction: We propose a method to identify diurnal changes in insulin action in type 1 diabetes patients based on data recorded by continuous glucose measurement systems as well as on meal carbohydrates and bolus insulin injections.

Methods: The data are fitted using a continuous time transfer function including time dependent terms. The method has been verified using clinical data and the calculated values for the insulin needs per gram of carbohydrate (''K_1/K_2'' from the modeling) were compared with patient-specific values of insulin-to-carbohydrate-ratios used for the calculation of the bolus insulin needs (''ICR'').

Results: It was found that the estimated values and the ICR determined by diabetologists agree reasonably well. Fig. 1 and Fig. 2 show exemplary results for the clinical trial. In Fig. 1 the recorded data and the identified model for one patient and one day of the trial are shown together with the diurnal variations in the model parameters (bottom panel). In Fig. 2 the diurnal patterns of K_1/K_2 for one patient and all days of the trial are combined in one plot and compared to the corresponding ICR.
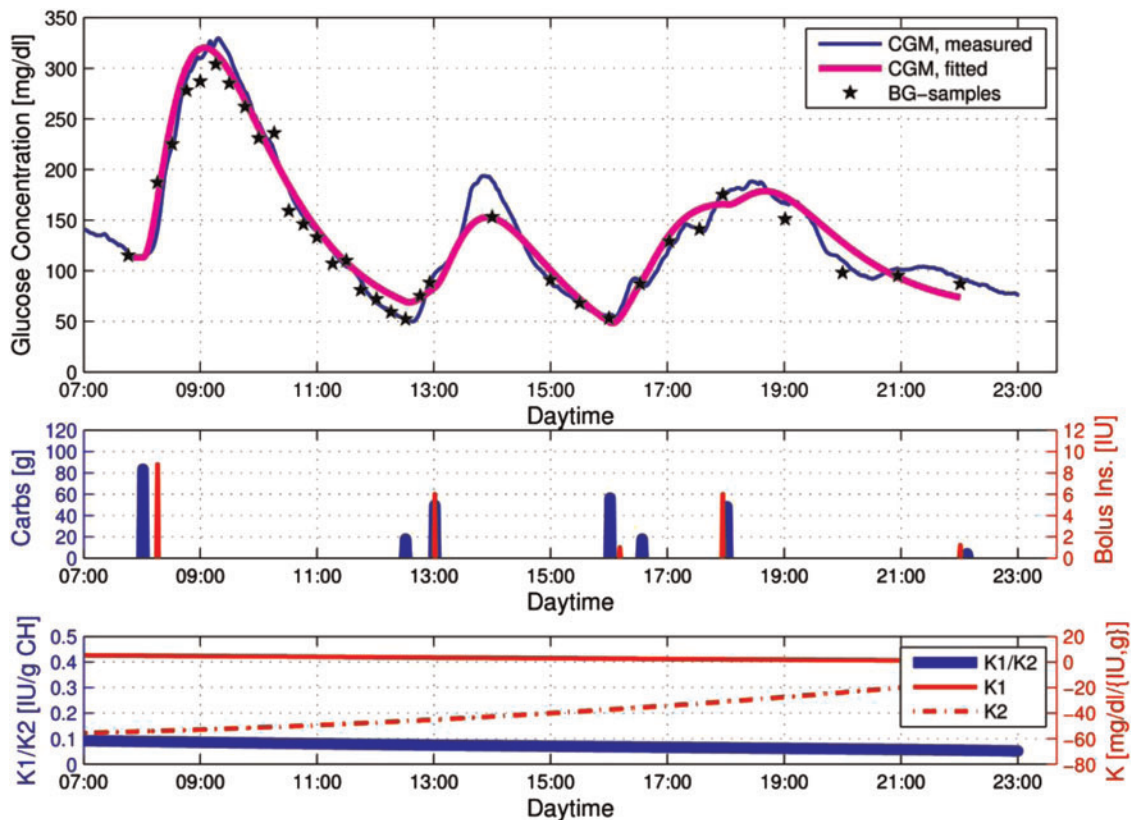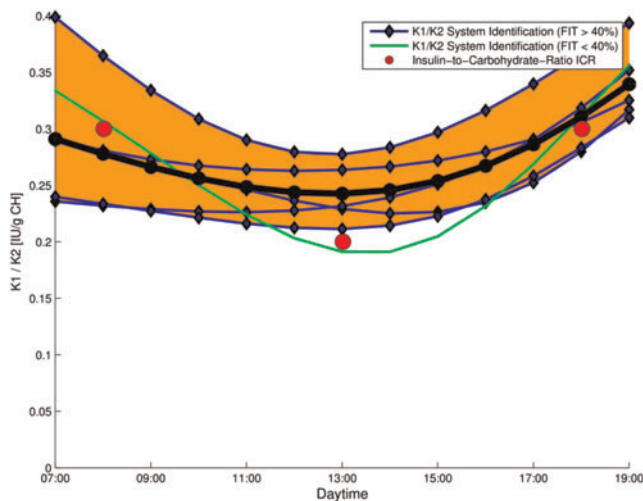

Fig. 1

Fig. 2

Conclusions: The proposed method has the potential to ease the task of determining patient-specific ICR by automatically analyzing recorded data and by giving diabetologists information about mean diurnal profiles and day-to-day variability of ICR. Furthermore, the model structure could be implemented directly in a smart bolus calculator that estimates ICR online and could base advice for bolus insulin injections on the identified model structure and information on intra-patient variability.

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PATIENTS' EXPERIENCE AND ATTITUDES TOWARDS A DIABETES WEB PORTAL

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Background: A patient web portal (PWP) allows patients to access their personal health record and may improve diabetes outcomes but adoption is slow. Insight is needed on patients' experiences with the PWP and how they feel it could be improved.

Methods: A survey among 1500 patients with type 1 and 2 diabetes mellitus with a login to a PWP which is used by 62 primary care practices and one outpatient hospital clinic. We compared patients who requested a login but used it never or once (''early quitters'') with patients who used it at least twice (''persistent users'').

Results: 632 patients (42.1%) returned a questionnaire. There were 413 (65.3%) persistent users (PU) and 219 (34.7%) early quitters (EQ). With insulin use (OR 2.07; 95%CI [1.18–3.62]), more frequently hyperglycaemic episodes (OR 1.30; 95%CI [1.14–1.49]) and better diabetes knowledge (OR 1.02, 95%CI [1.01–1.03]) the odds of being a PU increases. PU perceived the usefulness significantly more favorable, although EQ also appreciated rereading information discussed during consultation, access to laboratory values and treatment goals. Both PU and EQ wished for a reminder function for scheduled visits. PU's second main wish was adding insulin units to the glucose diary, whereas for EQ it was adding information about medication and side-effects.

Conclusion: Patients with insulin use and with hyperglycemia more often become persistent users. They evaluate the portal more favorable. To benefit most patients, we propose creating different portals designed to suit specific needs, e.g., one for patients on insulin treatment and another for patients without.

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EFFECT OF A TELECARE SYSTEM THAT USES SMARTPHONES TO RECEIVE ADVICE MESSAGES AUTOMATICALLY IN PATIENTS WITH TYPE 1 DIABETES ON CONTINUOUS SUBCUTANEOUS INSULIN INFUSION

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Aims: To evaluate the effect on metabolic control and quality of life (QoL) of a telecare program comprising smartphone and web platform, which send automatically advice messages to the participants if blood glucose values were out of range, vs. conventional follow-up in patients with T1DM on CSII.

Methods: Single-center, observational, prospective study performed in the Diabetes Unit of the Hospital Regional de Málaga from March to August 2014, which included 60 adults patients with T1DM on CSII. Telecare group (TG) (n = 30) attended two visits (baseline, 6-months), had a smartphone to receive advice messengers, and had access to a web platform to communicate with their health-care team during the study. Control group (CG) (n = 30) attended two visits (baseline, 6-months). Study variables: SMBG, HbA1c, mean and SD blood glucose, hypoglycemia, hyperglycemia, ketosis/ketoacidosis, and QoL assessed by Diabetes Quality of Life questionnaire.

Results: Patients were 50% men, had mean age of 43 years and mean diabetes duration of 26 years. Patients in TG reduced significantly HbA1c levels during the study (7.3 ± 0.9% baseline vs. 6.8 ± 0.6% 6-months, p = 0.003), however, there were no differences in other variables. Compared with CG, patients in TG did SMBG more frequently at the end of the study (TG 6.4 ± 1.9 vs. CG 5.1 ± 1.3 tests/day, p = 0.017), there were no differences in other variables between groups.

Conclusions: Telecare using smartphones to receive advice messages automatically in patients with T1DM on CSII might reduce HbA1c and increase frequency of SMBG compared with conventional care. Nevertheless, further studies are needed to confirm these findings.

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THE EFFICIENCY OF TELEMEDICINE TO OPTIMIZE METABOLIC CONTROL IN PATIENTS WITH DIABETES IN TURKEY: PRELIMINARY RESULTS FROM THE RANDOMISED CONTROLLED TELEDIAB TRIAL

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Parameter	Difference from Baseline (TeleDiab vs. Control)		
	3-month	6-month	9-month
Weight, kg	$-0.2/+1.4$	$+1.0/+0.8$	$+1.1/+1.6$
BMI, kg/m^2	$-0.2/+0.2$ (p = 0.050)	$+0.5/+0.5$	$+0.4/+0.8$ (p = 0.050)
Waist, cm	$+0.3/+0.1$	$+0.1/+0.6$	0.0/0.9
SBP, mmHg	$-3.4/-1.6$	$-2.8/-2.3$	$-4.6/-6.3$
DBP, mmHg	$-2.0/-1.3$	$-3.2/-0.4$ (p = 0.038)	$-2.2/-2.8$
FPG, mg/dL	$-31/-11$ (p = 0.004)	$-20/-8$	$-27/-14$
HbA1c, %	$-0.7/-0.3$	$-0.8/-0.3$ (p = 0.026)	$-0.7/-0.4$
Optimal control, %*	13 /11	15/8 (p = 0.015)	10/8
Triglycerides, mg/dL	$-14/-9$	$-2/-14$	$-19/-14$
HDL-chol, mg/dL	$+1.0/+1.9$	$-1.7/+0.4$	$-3.4/-1.3$
LDL-chol, mg/dL	$-8/-1$ (p = 0.008)	$-6/-1$ (p = 0.013)	$-9/-2$

*Percent patients with HbA1c ≤ 7.0%.

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Objective: The purpose of this study was to evaluate an in-home transmission system for improving glucose, BP, lipids and weight control in patients with diabetes mellitus.

Research Design and Methods: This prospective, randomized study included 200 adult patients with diabetes. Consecutive patients were equally allocated in two groups. Both groups received routine care visits three-monthly. TeleDiab group additionally sent SMBG data via transmission system and received SMSs.

Results: In TeleDiab group fasting plasma glucose (FPG), HbA1c, LDL-chol, systolic/diastolic blood pressure (SBP, DBP) at 3-month reduced significantly from baseline and maintained at 6-month and 9-month. In control group HbA1c significantly reduced from baseline at 3-month, 6-month and 9-month, in addition SBP and DBP at 9-month. Comparison of the groups by differences from baseline is provided.

Conclusion: Frequent follow-up visits resulted with improved metabolic control in subjects with diabetes. However, greater improvement was observed with the addition of TeleDiab transmission system. Telemedicine is an efficient motivational tool to achieve optimal control not only in glycemic but also BP and lipid parameters.

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HOME BLOOD GLUCOSE MONITORING BY HEALTH CARE PERSONNEL USING MOBILE PHONE APPLICATION

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We have successfully used an application specially created by our team to facilitate the patients. They can access the application through google play store using android and ios platforms. They are provided login details, after entering the details they get to use the application free of cost. They can communicate with the dedicated health care personnel real time. This has been especially useful in patients with sickness, and fluctuating sugars.

The hospital publishes events and health tips are published motivating people to take care of their disorder.

The patients will benefit as follows:

· Saved cost of travel
· Moral support
· Continuous care
· Automated alerts if values cross boundaries
· Reminders for medication or status update
· Instant access to secured cloud based health records/EMRs

Doctor/practice will benefit by:

· Graphical analysis of historic patient data
· Can detect adverse reactions of drugs
· Can build a history of drug effectiveness by specific demographic attributes - adds to knowledge bank
· Exchange of expert opinions
· Can collaborate with pharmacies and path labs
· Increased productivity due to remote availability of data.

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INTENTION OF PATIENTS TO USE ICT-BASED DIABETES SELF-MANAGEMENT SYSTEMS: A CROSS-SECTIONAL INTERVIEW SURVEY

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Background: Our self-management support system—Dial Betics—which is based on information communications technology(ICT), significantly improved HbA1c in diabetes patients. Our aim was to determine which characteristics are associated with patients' intention of using such a system.

Method: We conducted an interview survey with 100 diabetes patients. It collected data on demographics, history of diabetes and how the patients currently manage it (including self-management), and current use of ICT. Patients were classified into two groups—those who have an intention of using such a system and those who don't. Logistic regression analyses were used to identify factors related to the intention of using such a system.

Result: The mean age of patients was 66.1 ± 11.7 years; 63% were male. Only12 patients currently use ICT devices for diabetes self-management. However, besides the 12 who are already using an ICT device for diabetes self-management, 44 of the remaining 88 expressed the intention of doing so. Univariate analysis showed that younger age, frequent hospital visits, having a job, current use of an ICT device, and use of the Internet are all significantly associated with that intention. Multiple logistic regression analysis showed that frequent hospital visits—more than once a month (OR = 3.92, 95%CI, 1.14–13.52)—and current internet use (OR = 5.29, 95% CI, 1.69–16.59) are significantly associated with the intention.

Conclusion: Half of diabetes patients who are not already using an ICT-based self-management system expressed the intention of using it. Patients who make frequent hospital visits would particularly benefit from a self-management support system.

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ICT BASED OBESITY PROGRAM SHOWED EFFECTIVENESS SUPERIOR TO CONVENTIONAL CLINICAL INTERVENTION FOR REDUCING HEMOGLOBIN A1C IN HEALTHY OBESE KOREANS

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Background: Increasing prevalence of diabetes mellitus is closely related to increasing obesity. We developed ICT based obesity program and compared the effectiveness in reducing weight reduction and metabolic markers with conventional clinical intervention.

Method: We developed ICT based obesity program which contained web and android mobile application (HealthOn®, SK Health Connect, Seoul), which consist of goal setting, monitoring of diet and physical activity and feedback. ICT based program or conventional clinical intervention was applied to participants for 12 weeks on their demand. Metabolic markers such as height, weight, fasting glucose and Hemoglobin (Hb) A1c, lipid panel (total cholesterol, triglyceride, high density lipoprotein, low density lipoprotein), and blood pressure were measured at baseline and 12 weeks. Mean differences of these variables adjusted for sex, age, baseline body mass index (BMI) and physical activity were calculated.

Results: Among 97 participants, 76 received ICT based program and 21 received conventional intervention. Baseline BMI were $27.8 + -3.3 \text{ kg/m}^2$ and $28.0 + -2.5 \text{ kg/m}^2$ (P=0.801), fasting glucose were $100.0 + -10.2 \text{ mg/dL}$ and $101.0 + -15.2 \text{ mg/dL}$ (P=0.723), and Hb A1c were $5.5 + -0.2\%$ and $5.5 + -0.3\%$ (P=0.727). There was no significant difference in baseline age, sex, blood pressure, lipid panel between groups. After 12 weeks, adjusted mean differences (aMD) of fasting glucose were $-1.1 + -1.2 \text{ mg/dL}$ and $0.2 + -2.2 \text{ mg/dL}$ (P=0.5923), and aMD of Hb A1c were $-0.3 + -0.02\%$ and $0.0 + -0.04\%$ (P < 0.001).

Conclusion: ICT based obesity program was superior to conventional clinical intervention in reducing Hb A1c in this healthy obese Koreans.

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EMPOWERING AND IMPROVING FOOT CARE IN TYPE 2 DIABETIC PATIENTS REFERRED TO DIABETES CLINIC OF SEMIROM CITY ISFAHAN PROVINCE IRAN:2012-2013 APPLICATION OF BASNEF MODEL

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Introduction: Diabetic foot as a late complication of diabetes imposes high costs to the health care system. The present study aimed to investigate combinatorial educational program based on BASNEF model on foot care in type 2 diabetic patients referred to diabetes clinic of Samirom city.

Method: This study is a semi-empirical study, in which 164 eligible patients were selected after the pre-test, and randomly assign in intervention and comparison groups. Questionnaire based on BASNEF structure was used for data collection. Post-test was obtained at three and six months after the intervention. Data were analyzed using SPSS v.11.5 and Chi-Square, T-Test, ANOVA, Paired-TTest and Repeated Measure statistical tests.

Result: Before, three months and six months after the education Knowledge, beliefs, attitude, intended behavior, enabling factors, and the performance variables were significantly different in the intervention group (P < 0.05), but not in the comparison group (P > 0.05). Subjective norms variable between the two groups was not statistically significant (P > 0.05). Also, the intervention group than the comparison group to do a better controlling behavior the blood sugar, three months and six months after the training so that HbA1c levels of %69/8 ± %2/27 before training to %7/50 ± %1/42 percent three months later, and %7/44 ± %1/34 percent, came six months after the training showed significant difference (P < 0.001).

Conclusion: The results showed that education based on BASNEF model is effective in the promotion of diabetic foot care. Thus, implementation, monitoring and follow-up such educational programs based on this model is recommended in diabetes care clinics.

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DYNAMIC CONTROL OF CARBOHYDRATE METABOLISM IN PREGNANT WOMEN WITH TYPE 1 DIABETES: THE BASIC CONDITION OF A SUCCESSFUL OUTCOME OF PREGNANCY

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Objective: to study the effectiveness of additional remote counseling (ARC) algorithm for pregnant women with DM Type1.

Subjects and Methods: 100 women (group 1) with type DM Type1 used the ARC during pregnancy: 40 used on-line clinic, 60 sent data (self-control and CGM) by e-mail once every three days; 60 used traditional counseling. The following indicators were evaluated, HbA1c, frequency of hypoglycemic episodes per week, the probability of the risk of preeclampsia, macrosomia. 80% of patients were using insulin pump (Medtronic and Roche pumps were used), 20% of the multiple injections.

Results: HbA1c was similar during I, II trimesters, in III it was significantly lower ($p < 0.01$) in group 1: $5.9 \pm 1.1\%$ VS $6.5 \pm 1.2\%$. The frequency of hypoglycemic episodes was lower 0.9 VS 1.5 in the I trimester, 0.8 VS 1.9 in II trimester, 0.6 VS 1.9 ($p < 0.0001$) in III trimester. Risk probability of preeclampsia in group 2 HR (95% CI) was 1.72 (1.27–2.3) $p < 0.001$, the probability of the risk of macrosomia was 1.75 (1.39–2, 19), $p < 0.001$ in group 2.

Conclusions: the use of ARC in the online clinic and e-mail allows to optimize the mode of insulin therapy and to improve the course and outcome of pregnancy in women with DM Type1.

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ASSESSMENT OF GLYCEMIC VARIABILITY, CHANGES IN INSULIN/CARBOHYDRATE RATIO AND INSULIN SENSITIVITY FACTOR IN TYPE 1 DIABETIC PATIENTS TREATED WITH BOLUS CALCULATOR: RESULTS AT 4 MONTHS

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Introduction: Calculation of insulin bolus is a complex process which involves several factors: carbohydrate counting, insulin/carbohydrate ratio (CarbF), insulin sensitivity (ISF). Bolus calculator (BC) is a device that can avoid mental calculations.

Table 1: First phase: Characteristics at baseline and 4 months. Glycemic variability.

|	BC (n=42)		CT (n=28)	
	basal	4m	basal	4m
HbA1c (%)	8,37*	7,7*	8,34&	7,94&
	(SD 0,87)	(SD 0,71)	(SD 0,87)	(SD 0,96)
Overall Glycemia	165,98	166,43	169,22	175,95
(mg/dL)	(SD 27,42)	(SD 34,95)	(SD 30,86)	(SD 37,12)
DE	77,68	74,88	77,9	82,63
	(SD 16,91)	(SD 17,04)	(SD 21,91)	(SD 24,44)
MAGE (mg/dL)	163,78	145,48	155,96	153,79
	(SD 50,33)	(SD 56,46)	(SD 48,95)	(SD 50,23)
CV (%)	47,12	45,5	45,92	46,67
	(SD 8,31)	(SD 8,47)	(SD 8,31)	(SD 7,76)

*, & $p < 0.05$.

Figure 1: CarbF in breakfast, lunch and dinner. At baseline and 4 months.
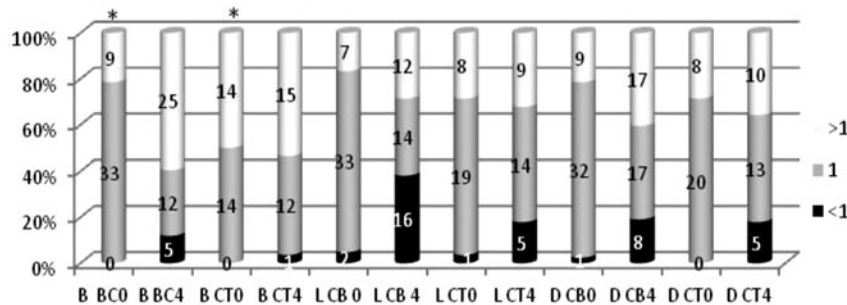
B: Breakfast, L: Lunch, D: Dinner, BC: Bolus Calculator group, CT : Control group. 0:Baseline and 4: 4 months. *p<0,05

Figure 2: ISF in breakfast, lunch and dinner. At baseline and 4 months.
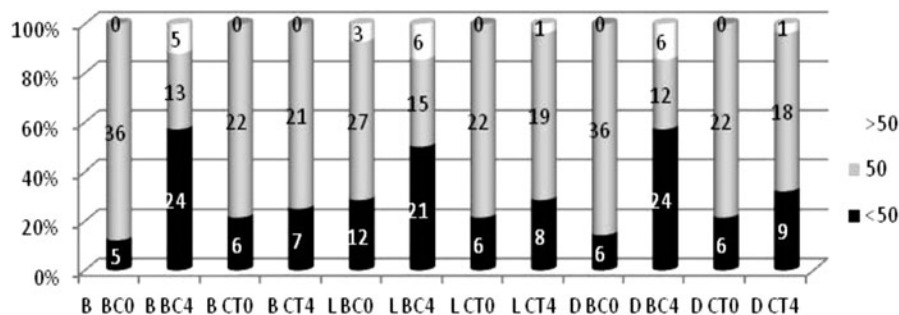
B: Breakfast, L: Lunch, D: Dinner, BC: Bolus Calculator group, CT : Control group. 0:Baseline and 4: 4 months.

Aim: To show CarbF, ISF, insulin requirements and glycemic variability in type 1 diabetic patients using BC.

Materials and Methods: Randomized, controlled, two-arms parallel, crossover study. Inclusion criteria: 18–65 years, HbA1c > 7%, basal bolus therapy. For a first phase (4 months) they were assigned either to BC use, or to control group (CT). In the second phase (4 additional months) all patients were allocated to BC. Variables: age, evolution of DM, HbA1c, CarbF, ISF, insulin doses and glycemic variability (SD, MAGE, CV).

Results: First phase: 70 patients, mean age 32.1 (SD 12.2) years, evolution of diabetes 15.3 (SD 9.2) years. BC n = 42 patients (60%), CT n = 28 (40%). Both groups had similar characteristics at baseline (age, evolution of DM and HbA1c).

We could not find any differences in glycemic variability for both groups (Tab.1). Insulin requirements did not change during the study, and CarbF and ISF were modified if needed: most patients had CarbF = 1 and ISF = 50 at breakfast, lunch and dinner at baseline; in the CB group, at the 4th month, there was an increase in CarbF for breakfast and a decrease for lunch (Fig.1). In the CB group, ISF decreased for all meals (Fig.2).

Conclusions: BC let us an improvement in the customization of CarbF and ISF. No changes in the glycemic variability or insulin requirements could be proven.

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CREATING A GAMING PLATFORM FOR ADULT DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT

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[2]*College of Nursing, New York University, New York, USA*

Our pilot work developing and testing the feasibility of a virtual environment for diabetes education and support demonstrated that this approach has the potential to improve psychosocial outcomes, self-management and metabolic control. Therefore, we are conducting an RCT to test the efficacy of this interactive online environment as compared to a traditional website format for providing education and support. We built a community on a gaming platform for adults with type 2 diabetes. The platform functionality allows for group information sharing and social networking, individual learning and behavior modification strategies. Participants attend synchronous diabetes education classes with educators and peers in the site; or visit
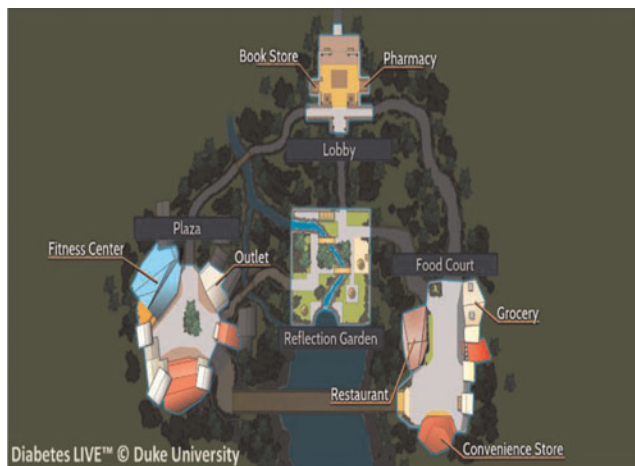
locations (i.e., grocery store or bookstore) for advice and information to support adult learning and health behaviors. Participants may practice grocery shopping and identifying healthy selections based on item-specific feedback regarding nutritional value, preparation or substitutions. Similarly, participants may practice eating out in a healthier way, even at fast food restaurants, based on nutrition information and feedback on menu selections. Placing this information within representations of real locations promotes learning transfer from the virtual community to real world behaviors. Importantly, the social networking capabilities within the community include synchronous voice conversation, text chat, forums, and sharing of experiences during classes. These aspects of the platform, along with gaming and incentives in the platform to reward positive real world behaviors (exercise, etc.) and participation in the site, are important in the design and implementation of online diabetes education and support.

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THE MOBILE DIABETES PATIENT EXPERIENCE: AN ANALYSIS OF THE MOST COMMONLY ACCESSED FEATURES OF A NEW DIABETES SMART PHONE APP

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Background: Estimates from global mobile statistics indicate that smartphone ownership will increase to 1.76 billion people by the end of 2014.[1] With the staggering growth of smartphones comes a dramatic growth of apps. According to 2013 Google Play Store data, only 1,000 of the 700,000 apps available focus on diabetes self-management support, critical skills needed by a rapidly growing patient population.[2] Additional analysis of literature shows that diabetes apps can vary in the medical value of the features offered and in the value perceived by the users.[3,4,5]

Methods: Using mobile app tracking analytics data, user behavior was reviewed to identify trends associated with key clinical components of the new Accu-Chek Connect Diabetes Management (Connect) app.

Results: Since the launch of the Connect app in August 2014, the number of 30-day active users has steadily increased with approximately 30% establishing cloud-based data sharing accounts at month three. The top two most commonly accessed clinically-relevant features are automatic transfer of glucose test results from the meter to the app and cloud and the medically-proven bolus advisor.[6] Growth of the use of each of these features is shown in Figures 1 and 2.

Diabetes LIVE™ © Duke University

Figure 1

Bolus advice use

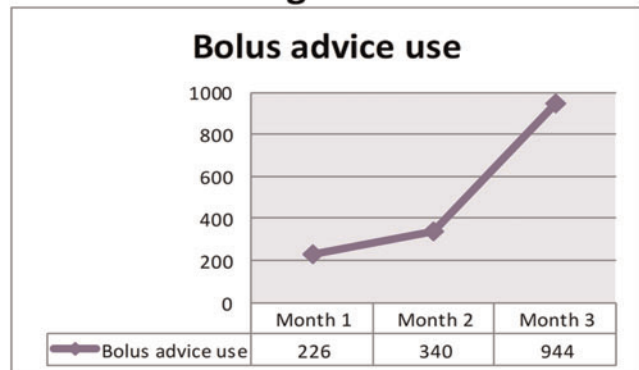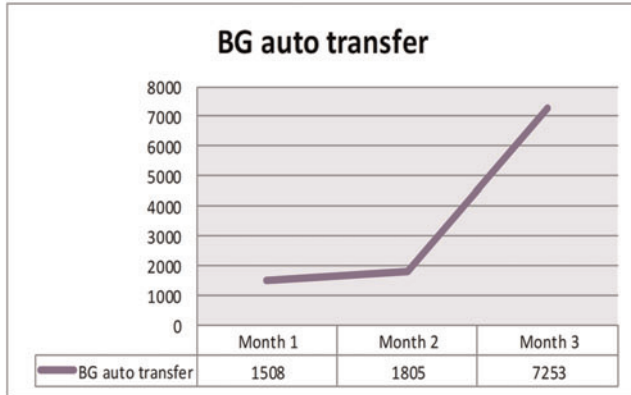|	Month 1	Month 2	Month 3
Bolus advice use	226	340	944

Figure 2

Conclusion: Using app tracking analytics, the Connect app has shown solid initial user growth and steady increases in utilization of clinically-relevant features. Developer monitoring of diabetes app feature use may aide in identifying patient preferences and usage trends, and may result in the development of diabetes management apps with more clinically-relevant features preferred and consistently used by patients.

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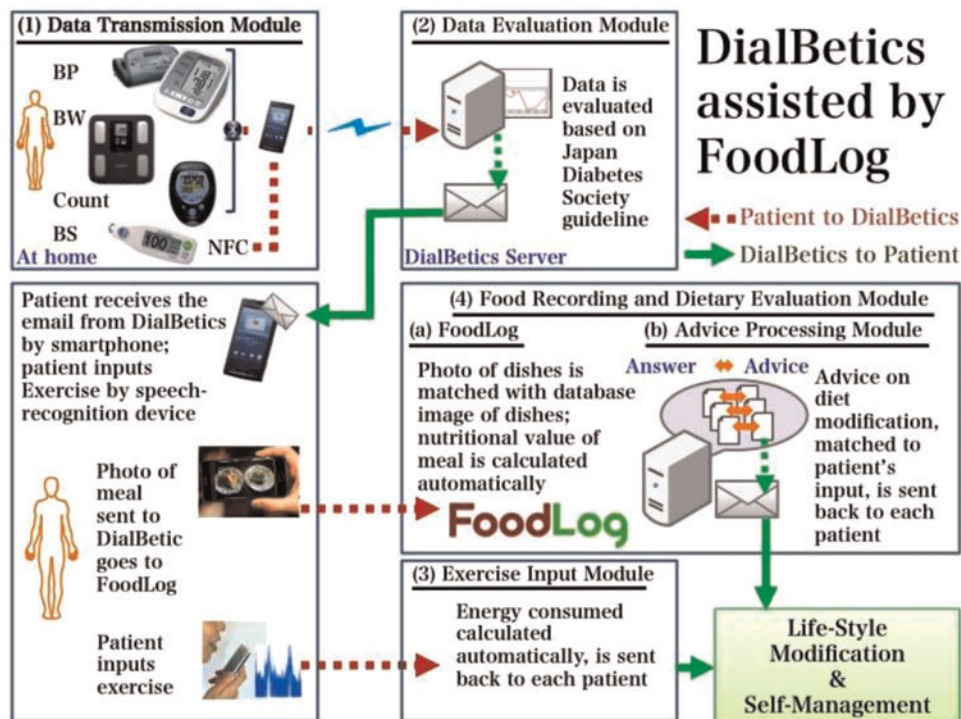### DIALBETICS WITH A MULTIMEDIA FOOD RECORDING TOOL, FOODLOG: SMARTPHONE-BASED SELF-MANAGEMENT FOR TYPE 2 DIABETES

K. Waki[1], K. Aizawa[2], H. Fujita[1], S. Kato[1], H. Lee[1], H. Kobayashi[3], M. Ogawa[4], K. Mouri[4], T. Kadowaki[5], K. Ohe[6]

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Background: Systems based on information and communication technology (ICT) for supporting self-management of diabetes have become promising tools for diabetes patients. Our aim was to test a more patient-friendly version developed from participants' feedback about the previous version of DialBetics, a smartphone-based system that helps patients improve self-managed diabetes control. This new version is the first such system – combining ICT technology and image processing – that performs real-time automated meal evaluation with diet advice to patients, all based on their meal-photo inputs.

Method: DialBetics is composed of four modules; (1) Data transmission, (2) Evaluation, (3) Exercise input, and (4) Food recording and dietary evaluation, which is assisted by FoodLog, an application that matches patients' photos of dishes with database images of dishes. After the patient inputs a photo of each dish, image retrieval proceeds, based on the color tone of each food. A one-week pilot study was designed to determine if usability and compliance improved compared with the previous system.

Results: Overall compliance was relatively high for health-data measurements, averaging over 90% in the morning and nearly 85% at bedtime for both versions. However, input of meal photos was higher than with the previous version of DialBetics ($84.8 \pm 13.2\%$ vs. $77.1\% \pm 35.1\%$). Four of the five participants thought the diet-input function improved; the fifth found input easier, but did not consider the result an improvement.

Conclusions: DialBetics with a multimedia food record—FoodLog—was shown to be a feasible and convenient tool for providing patients with real-time diabetes self-management support.

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SALIVARY ANTIOXIDANT ALTERATIONS IN DIABETIC PATIENTS

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Background: It has been noted that detection of salivary constituents in diabetic patients may be useful in the understanding and management of the oral manifestations.

Aim: The aim of this study was the comparative evaluation of saliva antioxidants in type 1 diabetic subjects with a healthy group.

Methods: In this case control study, 20 patients with diabetes type 1 and 20 healthy controls enrolled. Five milliliters of saliva from each person was collected. Enzyme activity of super oxide dysmutase, peroxidase and uric acid were measured with Randox and Santinel kits by spectrophotometric assay. SPSS software and Student's t-test were used to analyze the data.

Results: Superoxide dismutase was significantly higher in diabetics (7.67 ± 5.57 U/ml) than controls (5.02 ± 3.23 U/ml). On the other hand, peroxidase was higher in patients than in controls, but the difference was not statistically significant. There was positive relationship between HbA1c and super oxide dismutase, and peroxidase ($p = 0.005$, 0.029, $r = 0.629$, 0.442) respectively.

Conclusion: Salivary superoxide dismutase was significantly higher in diabetics, and there was positive relationship between HbA1c and superoxide dismutase and peroxidase.

Keywords: Diabetes, Saliva, Super oxide dismutase

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FEATURES OF HEART RATE VARIABILITY IN PATIENTS WITH DIABETES MELLITUS TYPE 2 DEPENDING TO THE LEVEL OF GLYCEMIA

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Estimate the effect of glycemic parameters on heart rate variability (HRV)

Was made synchronous monitoring of glycemia (CGMS) and Holter monitoring in patients with a diagnosis of diabetes mellitus type 2

Was established significant inverse relationship between the level of glycemia and frequency indicators of HRV: low-frequency component (LF) ($r = -0,49$, $p < 0,05$), a **high frequency component** (HF) ($r = -0,67$, $p < 0,05$), the total power

spectrum (TP) ($r = -0.65$, $p < 0.05$). LF/HF ($r = 0.42$, $p < 0.05$). Hyperglycemia more 15 mmol/l, in which apart from reduction in LF ($p > 0.05$) is marked decrease HF ($p = 0.044$) with an increase in the relationship ($p = 0.043$), i.e. develop relatively sympathicotonia, significantly increases the risk of arrhythmias. Also, when glycemia is over 15 mmol/l any differences glycemia led to a significant reduction in the HF level ($r = -0.71$, $p < 0.05$), the TP ($r = -0.87$, $p < 0.05$) and increase heart rate ($r = 0.74$, $p < 0.05$). Was found a linear relationship between the level of SD ($r = 0.53$, $p = 0.05$) and MAGE ($r = 0.52$, $p = 0.02$) and the number of PVCs. Patients with a history of hypoglycemia with hypoglycemia less than 3.9 mmol/l absent significant reduction of HRV. In patients without a history of hypoglycemia we noted significant decrease in HRV. There was a direct correlation between the level of the index of a hypoglycemia and the number of hypoglycemic ventricular arrhythmias ($r = 0.38$ $p = 0.01$).

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CARDIOVASCULAR RISK IN PATIENTS WITH ORTHOSTATIC HYPOTENSION

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Introduction: Cardiovascular autonomic neuropathy (CAN) is the most overlooked chronic complication of diabetes mellitus. It is associated with increased cardiovascular morbidity and also mortality.

Aim of the study: Assess the mortality in relation to the presence of orthostatic hypotension (OH) in a group of patients with DM type 1 or 2 and analyse the factors affecting survival.

Patients and Methods: We investigated 187 patients of whom 60 had DM type 1 and 127 patients had DM type 2. Average age in the first group was 42.2 years, in the second group 57.8 years. CAN was diagnosed with spectral analysis of heart rate variation during Ewing battery of cardiovascular reflexes. OH was present in case of decrease in systolic BP of at least 20 mmHg and/or diastolic BP of 10 mmHg by 3 minutes of standing up. The most severe form of CAN is the presence of OH.

Results: Orthostatic hypotension was in the group of patients with DM type 1 present in 19 patients (31.7%) and in the group of patients with DM type 2 in 41 patients (32.3%). Overall mortality in the first group without OH was 2.4% and in the group with OH was 31.6%. In patients with DM type 2 without OH was the overall mortality 8.1% and in the group with OH was 31.7%.

Conclusions: Patients with severe cardiovascular autonomic neuropathy (CAN grade 3) with orthostatic hypotension has significantly higher overall mortality. Routine examination for CAN and interdisciplinary cooperation is therefore necessary.

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DEVELOPMENT OF NON-INVASIVE METHOD FOR BLOOD MICROCIRCULATION DISORDERS DIAGNOSTICS IN DIABETES PATIENTS USING LASER DOPPLER FLOWMETRY (LDF)

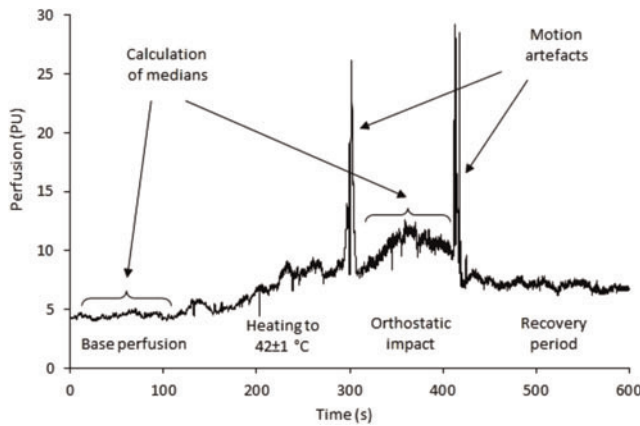*A. Dreval[1], Y. Kovaleva[1], A. Glazkov[2], D. Kulikov[2]*

FIGURE 1. Example of probe results.

TABLE 1. RESULTS

	Diabetes group Me [Q_{25}; Q_{75}]	Control group Me [Q_{25}; Q_{75}]	p-value (Mann-Whitney test)
Base perfusion	5,6 [2,8; 9,4]	3,2 [3,0; 3,7]	0,088
Combined impact	10,8 [9,1; 13,9]	18,1 [13,9; 22,4]	0,023
Relative index	2,1 [1,4; 3,3]	5,6 [4,3; 7,5]	0,001

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Aim: To provide diagnostics of microcirculatory disorders with diabetes mellitus (DM) by using LDF.

Materials and methods: On the first step we examined the condition of blood microcirculation during functional testing (occlusion, heat, cold, orthostatic) in different combinations, duration of action and created survey algorithm (Figure 1). Study included 52 patients with type 1DM and 2DM. The second step was to assess the feasibility of applying the algorithm for the
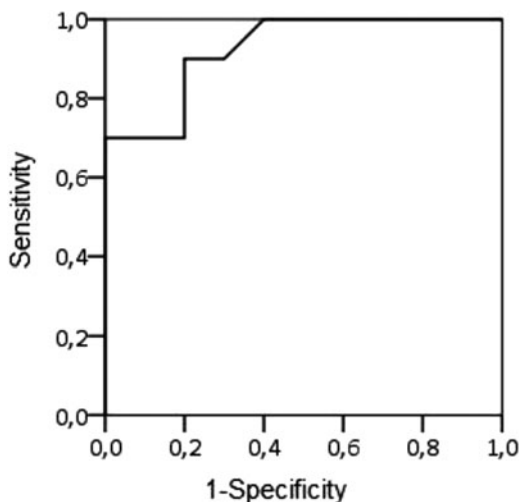
diagnosis of microcirculatory disorders in patients with diabetes. Prognostic significance of measured parameters was evaluated by using ROC-analysis. A logistic regression model was built. The study included 10 patients with type 2DM (HbA1c level – $8.9 \pm 1.2\%$), the duration of DM was more than 5 years. The control group consisted of 10 healthy volunteers. Blood microcirculation in skin was measured by using LAKK–02 system.

Results: Results of registration of the skin perfusion are shown in the table 1.

Ratio of median base perfusion to median perfusion during combined functional impact (relative perfusion index) allowed us to classify the surveyed persons by groups with or without microcirculation disorders with 80% sensitivity and specificity. Area under the ROC-curve (AUC) was 0.93, 95% confidence interval for the AUC was 0.81-1 (Figure 2).

Conclusion: The developed method has demonstrated the efficacy of detection of microcirculatory disorders in patients with diabetes. Received results can considered as foundation for the wide-scale study with the achievement of 90% power.

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EFFECT OF VITAMIN B6, VITAMIN B12, AND FOLIC ACID ON SERUM HOMOCYSTEINE LEVEL

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Background: Hyperhomocysteinemia is known risk factor of cardio-cerebrovascular Disease. We studied to evaluate the effect of vitamin B6, vitamin B12, and folic acid treatment on serum homocysteine level.

Methods: In this retrospective cohort study, we reviewed 122 suitable subjects' medical records who were measured serum homocysteine level and prescribed vitamin B complex (vitamin B1; benfothiamine 69.15 mg, vitamin B6; pyridoxine HCl 50 mg, vitamin B12; cyanocobalamine 0.5 mg) by family medicine clinic of a university hospital. Subjects were measured follow up serum homocysteine level within 1 year. Subjects were divided into two groups of vitamin B complex once daily and vitamin B complex plus folic acid once daily. We analyzed changes of serum homocysteine level in each group before and after taking vitamin B complex and folic acid.

Results: The mean follow up period was 26 weeks and mean treatment period was 18 weeks. Serum homocysteine level decreased 22.1% (p < 0.001) in vitamin B complex group (n = 92) and 23.5% (p < 0.001) in vitamin B plus folic acid group (n = 30). In two group comparison, the baseline and follow up homocysteine level showed no difference. The variation calculated (baseline homocysteine – follow up homocysteine)/ baseline homocysteine*100, also showed no difference between two groups (p = 0.578) which means adding folic acid on vitamin B complex has no additional effect.

Conclusion: Vitamin B6 and vitamin B12 lowers serum homocysteine level. Adding folic acid does not have an additional beneficial effect on serum homocysteine level lowering on those taking vitamin B6 and vitamin B12.

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RISK ASSESSMENT CALCULATOR FOR DIABETIC PATIENTS WHO FAST DURING RAMADAN

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FIGURE 2. ROC-curve for relative index.

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Diabetes mellitus is a leading public health problem with increasing incidence and long term complications. In spite of marvelous advancement in medical sciences it is still an incurable life-long disease. Worldwide 57 countries are Muslim Majority Countries with a population of about 2.02 billion people, and about one billion people fast during the month of Ramadan. For all Muslim adults, fasting during Ramadan is one of the five basic pillars of Islamic practices. Ramadan is a lunar-based month in the Hagree calendar, its duration varies between 29 and 30 days. Depending on the geographical location and season the duration of the daily fast may range from 12 to 20 hours per day.

Risk stratification tools are being used to identify and classify many disorders in the field of medical sciences. However, to our knowledge, currently no such categorization model is available to assess the risk of diabetic patients who are planning to fast during the month of Ramadan. We established a diabetes risk assessment calculator for diabetic patient who fast. This calculator can be used to grade diabetic patients into various categories by using patient anthropometric, clinical and biochemical parameters and each component has been awarded points according to the degree of risk it poses during Ramadan fasting to the diabetic patient. This calculator will be helpful to healthcare practitioners including, physicians, paramedical staff, diabetes educators, patients and their family members. On the basis of the score, patient will be categorized into low, moderate or high-risk group.

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EFFECT OF VILDAGLIPTIN ON ARTERIAL STIFFNESS IN DRUG NAÏVE PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Introduction: Arterial Stiffness (AS) is a predictor of cardiovascular (CV) events and mortality in patients with Diabetes mellitus.

Aim: We assessed the effect of a DPP-4 inhibitor Vildagliptin (V) on AS in drug naïve patients with type 2 diabetes mellitus (T2DM).

Patients and methods: Sixty-four drug naïve subjects with type T2DM and inadequate glycemic control participated in this randomized, open-label study. Half of the patients received metformin (M) 1700 mg/d (M group) and the other half M 1700 mg/d plus Vildagliptin 100 mg/d (V group) for 6 months. AS (carotid femoral pulse wave velocity, cfPWV), body weight (BW), body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), glycosylated hemoglobin (HbA1c), Albumin/Creatinine ratio (A/C ratio), C-peptide, HOMA-IR and HOMA-β were assessed at baseline and after 6 months.

Results: cfPWV, BW, BMI, SBP, DBP remained unchanged after 6 months in both groups (p = NS). V decreased HbA1c more effectively than M alone (V group: Δ (HbA1c) = $-1.7 + 0.7\%$, M group: Δ (HbA1c) = $-1.2 + 1.2\%$, p < 0.05). Moreover C-peptide and HOMA-β raised significantly in V group (V group Δ (C-peptide) = 1.3 + 3.6 ng/ml, M group Δ (C-peptide) = $-0.3 + 1.5$ ng/ml, p < 0.05, V group Δ (HOMA-β) = 22.0 + 33.8%, M group Δ (HOMA-β) = 8.1 + 55.8%, p < 0.05).

Conclusions: The addition of V to M for a period of six months had no effect on AS in drug naïve T2DM patients but V treatment improved glycemic control (HbA1c) and β-cell function (C-peptide, HOMA-β).

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CHARACTERIZATION OF SUBSTRATE UTILIZATION IN DIFFERENT GENOTYPES OF GENE POLYMORPHISM RS659366 UCP2 IN PATIENTS WITH TYPE 2 DIABETES

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Objective: to investigatethe characteristics of characterization of substrate utilization depending on the genotypes of polymorphic marker rs659366 UCP2 gene in patients with type 2 diabetes.

Materials and Methods: in 120 patients with type 2 diabetes aged 40 to 65 years were studied energy expenditure of rest and metabolic substrates (protein, fat, carbohydrates) using the method of indirect calorimetry. Genotyping was performed using allele-specific amplification, detection results in real time and using TaqMan-probes complementary to polymorphic DNA regions.

Results: in all patients with type 2 diabetes were observed metabolic disturbances in the form of reducing the rate of carbohydrate oxidation by an average of 35%. Carriers of the T allele of the gene variant rs659366 UCP2 in the heterozygous state rate of carbohydrate oxidation averaged 111 ± 12 g/day, and in the homozygous state - 48 ± 7 g/day, which is significantly lower than that in patients with type 2 diabetes with genotype C/C (on average 161 ± 18 g/d). The rate of oxidation of fat in patients with genotype C/T (average 107 ± 10 g/d), and T/T (average 123 ± 9 g/d) was significantly higher than in patients with genotype C/C (mean 87 ± 10 g/d), (p < 0.05). The rate of oxidation of the protein in all patients with type 2 diabetes was normal.

Conclusions: The genotype T/T, C/T gene variant rs659366 UCP2 in patients with type 2 diabetes is characterized by a low rate of oxidation of carbohydrates and high rate of fat oxidation in comparison with data rates in patients with genotype C/C.

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PRECLINICAL EVALUATION OF A1CARE™ ANALYZER FOR HEMOGLOBIN A1C MEASUREMENT

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The hemoglobin A1c (HbA1c) is a key glycemic control marker for type 2 diabetes treatment, which reflects the average blood glucose levels of past 2∼3 months. A1Care™ analyzer developed by i-SENS is designed for use in a physician's office laboratory (POL). The platform consists of a single-use, self-contained reagent cartridge and an optical analyzer equipped with a thermostated mechanical incubator. The cartridge takes ∼2.5 uL of whole blood, venous or capillary, and analysis time for HbA1c is approximately 4 minutes. The principle of the assay is based on a series of enzymatic reactions: multiple enzymes such as protease, FPOX and peroxidase in the cartridge consecutively act on hemoglobin and glycated hemoglobin, resulting in a redox color change in the end for optical measurements. The amount of total hemoglobin is measured prior to HbA1c measurement and the ratio between the two is calculated. The dynamic linear range of the A1Care™ HbA1c assay was from 4% to 14%. The assay exhibited little or no interfering responses to various substances such as labile HbA1c, glucose, bilirubin, ascorbic acid, and modified hemoglobins. The within-laboratory precision tests, performed following the CLSI EP-05 guidelines, were less than 2.6% (at 5.3% HbA1c, $n = 20$) and 2.2% (at 10.7% HbA1c, $n = 20$), respectively. Using 40 EDTA whole blood samples, a method comparison (CLSIEP-09) between A1Care™ and an HPLC system (Bio-Rad Variant II Turbo) showed an excellent linear correlation across the normal and elevated ranges of HbA1c ($Y = 1.022X + 0.02$, $n = 40$, $r = 0.995$). Various laboratory and validation test results on newly developed A1Care™ are to be discussed in this presentation.

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GENETIC TESTING FOR MONOGENIC DIABETES USING TARGETED NEXT-GENERATION SEQUENCING IN THE MODY REGISTRY COHORT OF POLAND

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I. Wybranska[3], P. Wolkow[2], M.T. Malecki[1]*

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Specific molecular diagnosis of monogenic diabetes mellitus is important for individualized patient care—by understanding the pathophysiology of the disease one can optimize hypoglycemic treatment and define prognosis for the entire family. Next Generation Sequencing-based exome-sequencing (NGS) might provide additional diagnostic potential as it enables simultaneous analysis of multiple genes in a single test.

Our aim was to assess feasibility of NGS usage for detection of mutations in a set of earlier described diabetic genes in a group of patients from the Polish Registry of MODY. We designed a custom Agilent Sure Select exon-capture assay with baits for 13 known MODY genes (GCK, HNF1A, HNF4A, HNF1B, NEUROD1, INS, CEL, PDX1, PAX4, BLK, KLF11, KCNJ11, ABCC8), two gene mutations of which cause lipodystrophy (LMNA, PPARG), mitochondrial genome and 20 neonatal diabetes genes.

A total of 96 DNA samples were tested. Samples were fragmented using Bioruptor (Diagenode), indexed for multiplexing and hybridisation. Sequencing was performed with an Illumina using 75 or 150 bp paired end reads.

The analysis was performed for chromosomal genes only. High or medium impact mutations were identified in 74% of the studied patient samples. We identified 16 high impact mutations: 12 of them were located in HNF1A gene, 1 in ABCC8, 1 in GCK, 1 in EIF2AK3 and 1 in LMNA. We identified 107 medium impact mutations. All known mutations in the positive control samples were detected.

Our pilot experiment using NGS for monogenic diabetes screening in the MODY cohort confirmed that its use is feasible in routine genetic testing.

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AUTONOMIC CARDIOVASCULAR NEUROPATHY IN DIABETES MELLITUS: PREVALENCE, RISK FACTORS AND METHODS OF EARLY DIAGNOSIS

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The aim of our study is to assess the prevalence, risk factors for cardiovascular autonomic neuropathy (CAN) and to investigate the most sensitive and specific methods of preclinical diagnosis in patients with diabetes mellitus.

Methods: the study involved the examination of 30 type 1 diabetes patients (15 males) with average age 40.1 ± 12.69. It employed tests of autonomic function (30:15, E/I ratio, Valsalva ratio and postural change in systolic blood pressure) and 24-h heart rate variability (HRV) spectral analysis of Holter records (VLF, LF, HF) to compare autonomic function in patients with healthy, age- and gender-matched controls ($n = 30$). Possible correlations between anamnesis data, laboratory findings, coexistent peripheral neuropathy and the occurrence of CAN were also studied. CAN was defined as the presence of at least 3 abnormalities among 7 indices.

Results: the prevalence of CAN was 43% ($n = 13$). Only 77% of them ($n = 10$) had clinical manifestations of CAN. Significant correlations were observed between CAN and duration of diabetes ($p = 0.0047$), glomerular filtration rate (GFR) ($p = 0.0077$) and resting heart rate ($p = 0.0441$). 100% ($n = 13$) of patients with CAN suffered from different types of peripheral neuropathy. The HRV spectral power indices' decrease was accompanied by at least 1 abnormal reflex test in 46% of cases ($n = 6$). Among the tests of autonomic function, E/I ratio showed the highest sensitivity and specificity.

Conclusion: the prevalence of CAN in diabetes is high. Longer duration of diabetes, peripheral neuropathy, GFR decrease are significant risk factors. E/I ratio can be used to early diagnose CAN as a screening test.

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THE ALMASED CONCEPT AGAINST OVERWEIGHT AND OBESITY AND RELATED HEALTH RISK (ACOORH) HAS STARTED

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Overweight and obesity are important factors for development of T2DM, metabolic syndrome and cardiovascular diseases. It has been recently shown that a meal replacement diet, high in soy protein is more effective in improving body composition and reducing metabolic and atherogenic risk factors than conventional lifestyle changes.

To evaluate this, ACOORH was designed as a registered 1-year-multicenter randomized controlled trial for overweight and obese patients using a low-glycemic, soy-protein-rich product (Almased). An additional aspect of this trial is the evaluation of a subgroup with pre-diabetes to demonstrate a possible intervention-induced reconversion from pre-diabetes to normoglycemia.

At least 576 non-diabetic participants (BMI 27–$35 \, kg/m^2$, 21–65 yrs) with at least one criterion of the metabolic syndrome will be randomized into a telemedically controlled lifestyle (LS) intervention or a meal replacement (MR) regimen for one year. Primary target variable is total body weight, secondary targets include body fat and lean body mass, fasting blood glucose, fasting insulin level, HbA1c, apolipoprotein B, and leptin. Tertiary outcome variables include risk factors for endothelial function, cardiovascular disease, and measure of muscle function, quality of life, activity and dietary behaviors.

All outcomes will be tested for significant differences in baseline vs. after 12 weeks values (interim analysis) as well as after 12 months as a comparison between the MR and the LS group. Stratified analysis for participants will be done with HbA1c < 5.7% and HbA1c 5.7–6.4%. The described RCT has been started in 8/2014, and final results will be presented at the beginning of 2016.

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EQUIVALENT WEIGHT LOSS BUT DIFFERENT DIABETES BENEFITS IN A MATCHED COHORT WITH AND WITHOUT METABOLIC SYNDROME IN TYPE 2 DIABETES PATIENTS WITH OBESITY AFTER LAPAROSCOPIC GASTRIC BYPASS

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Background: Metabolic syndrome (MS), a constellation of metabolic abnormalities, has an intertwined link with morbid obesity and type 2 diabetes (T2DM). Gastric bypass (GBP) is considered an effective option for the management of these patients. However, most of the diabetes patients in China have distinguishing abdominal obesity rather than severe obesity, while some patients may have MS and some may not. Otherwise, data concerning non-morbid obesity patients with MS has rarely been reported. It is important to investigate if the same principles of GBP that improve diabetes with MS could be applied to the diabetes without MS in non-obesity patients.

Objective: We sought to determine effects of laparoscopic gastric bypass on weight loss and diabetic remission in patients with MS compared with appropriately matched cohort without MS.

Methods: Retrospective analysis of 42 T2DM patients with BMI 28–35 kg/m^2, stratified by MS into two groups (group 1, MS group, group 2, non-MS group). Anthropometric, biochemical, and clinical evaluations were performed preoperatively and then at 1,3,6 and 12 months postoperatively.

Results: During the one year follow-up, all groups showed a significant reduction in BMI, waist circumference, LDL-C and HOMA-IR. However, remission of T2DM is different, higher in MS group (18/20, 90%) and lower in non-MS group (14/22, 64%), which total remission is 86% (32/42).

Conclusions: Laparoscopic gastric bypass has an independent mechanism with weight loss on non-obesity T2DM, which is associated with resolution of insulin resistance. Furthermore, BMI is not the only main inclusion criteria for gastric bypass on diabetes while metabolic disorders maybe the next important one.

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ACTIVIN A- AND LY294002-GRAFTED POLY(LACTIDE-CO-GLYCOLIDE) NANOPARTICLE/ GELATIN SCAFFOLDS TO DIFFERENTIATE INDUCED PLURIPOTENT STEM CELLS TOWARD ISLET CELLS FOR DIABETES TREATMENT

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Aim: This study investigates the capability of activin A- and LY294002-loaded poly(lactide-*co*-glycolide) nanoparticle (PLGA NP)/gelatin scaffolds to guide the differentiation of induced pluripotent stem cells (iPSCs) toward pancreatic islet cells.

Methods: Activin A and LY294002 are crosslinked in PLGA NP/gelatin scaffolds and iPSCs are encapsulated in activin A- and LY294002-grafted PLGA NP/gelatin scaffolds for endodermic and pancreatic differentiations.

Results: An increase in the weight percentage of PLGA NPs decreased the porosity and swelling ratio of PLGA NP/gelatin scaffolds. In addition, an increase in the concentration of activin A and LY294002 in the scaffolds reduced the viability of iPSCs. A higher concentration of activin A yielded a lower quantity of expressed SSEA-1 and a higher quantity of expressed SOX-17, suggesting that the activin A-grafted PLGA NP/gelatin scaffolds are triggers for endodermic differentiation. Moreover, an increase in the concentration of LY294002 in PLGA NP/gelatin scaffolds enhanced the quantity of expressed PDX-1, indicating an induction of differentiation toward pancreatic islet cells.

Conclusions: Activin A- and LY294002-grafted PLGA NP/ gelatin scaffolds are effective in guiding differentiation of iPSCs toward islet cells and can be applied to preclinical trials for diabetes treatment.

Keywords: islet cell, induced pluripotent stem cell, differentiation; activin A; LY294002; poly(lactide-*co*-glycolide); nanoparticle; gelatin.

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LONG-TERM BENEFIT OF LAPAROSCOPIC SLEEVE GASTRECTOMY ON METABOLIC PARAMETERS

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Table 1. Metabolic parameters before and 5 years after LSG

Parameter	Before surgery	5 years after surgery	p
BMI (kg/m^2)	44.02 ± 6.97	33.98 ± 5.43	<0.001
Waist circumference (cm)	123.55 ± 20.75	104.9 ± 16.97	<0.001
Glucose (mg/dl)	103.57 ± 38.71	96.11 ± 23.61	NS
Insulin (mUI/dl)	21.67 ± 15.98	9.14 ± 5.94	<0.001
HOMA-IR	5.53 ± 4.37	2.19 ± 1.72	<0.001
Total cholesterol (mg/dl)	209.5 ± 38.24	203.35 ± 35.81	NS
LDL (mg/dl)	138.25 ± 32.72	123.68 ± 32.23	<0.05
HDL (mg/dl)	43.7 ± 9.78	60.81 ± 12.92	<0.001
Triglycerides (mg/dl)	168.59 ± 137.07	103 ± 68.57	<0.01
Uric acid (mg/dl)	6.47 ± 3.82	5.39 ± 1.31	<0.05

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Background: Recent years brought into attention the concept of obesity surgery seen as metabolic surgery, considering its benefits that extend beyond weight loss, causing a dramatic improvement of type 2 diabetes, dyslipidemia, hypertension or insulin resistance. The aim of our study was to identify the long term effect of LSG regarding obesity and its metabolic complications in a group of extremely obese patients evaluated before and 5 years after surgery.

Patients and methods: 46 extremely obese patients (28 women, mean BMI = 44.02 ± 6.97 kg/m^2, mean age = 42.07 ± 10.46 years) were evaluated before and 5 years after LSG. This included complete clinical examination, as well as metabolic and hormonal tests.

Results: In all 46 patients there was an important and sustained weight loss (mean excess BMI loss = 54.44 ± 25.26%), accompanied by significant changes in metabolic parameters, as seen in Table 1.

Metabolic syndrome prevalence decreased from 67.4 to 23.9% (p < 0.05).

Excess BMI loss (%EBL) was not influenced by gender or preoperative BMI but negatively correlated with age (r = −0.302, p < 0.01).

Conclusion: Patients who suffered LSG continue to have important metabolic benefits 5 years after surgery.

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HOW WILL YOU GO ON MANIKIN? OBESITY, INSULIN RESISTANCE AND FUTURE OF OUR TEENAGERS

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Objective: the aim of this study was to evaluate association of biomarkers in the differentiation of prediabetic (obese, insulin resistant) and healthy teenagers.

Methods: 120 age- and sex-matched individuals were included in this randomized, controlled analysis. Mean age was 10.9 (3.9 SD; 33 males, 27 females) and 10.7 (3.6 SD; 34 males, 26 females). We determined metabolic changes like body composition, HbA1C, CRP, lipid values, fasting plasma glucose (FPG), glucose values during the oral glucose tolerance test (OGTT), insulin levels during OGTT, atherogen lipid values, and some derived parameters (insulin sensitivity, HOMA index, Beta-cell dysfunction in obese, insulin-resistant and healthy Hungarian teenagers.

Results: The following variables showed significant association with prediabetic state: biphasic plasma glucose curve (OR: 3.28; 95% CI: 1.21–9.32; p = 0.0133), BMI (OR: 1.83; 95% CI: 1.48–2.26, p < 0.001), insulinogenic index (OR: 1.18; 95% CI: 1.08–1.28, p < 0.001), fasting plasma insulin (OR: 1.22; 95% CI: 1.12–1.34, p < 0.001), ISI (OR: 0.84; 95% CI: 0.77–0.93, p < 0.001), AUC (logOR: 5.87, 95% CI: 0.09–11.65, p = 0.047), CRP (OR: 6.41; 95% CI: 2.56–16.06, p < 0.001), Beta cell dysfunction (OR: 1.04; 95% CI: 1.01–1.06, p = 0.001), Insulin sensitivity (log OR: −15.60; 95% CI: −24.02 to −7.19, p < 0.001), HOMA Index (OR: 2.20; 95% CI: 1.53–3.16, p < 0.001).

Conclusion: The above studied parameters give a good estimation of obesity-related risks. An ongoing longitudinal study assessment can prove whether they can be used in everyday's life settings to evaluate early intervention's efficiency.

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LOOKING BACK AT LOOKING AHEAD

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Background: Look AHEAD was the largest, longest randomized clinical trial designed to test whether improved lifestyle can prevent cardiovascular disease in adults with diabetes.

Methods: Sixteen U.S. study centers randomly assigned 5145 overweight or obese patients to Intensive Lifestyle Intervention (ILI) or a Diabetes Support and Education (DSE) comparison group. ILI goals were: sustained weight loss of ≥7% of initial weight, and increased physical activity to ≥175 minutes/week. All ILI and DSE participants were required to have: successfully passed a maximal graded exercise tolerance test; a primary care provider (to reduce cost and mirror real clinical practice); no known cardiovascular disease; BMI ≥ 25.0; glycated hemoglobin ≤11%; systolic blood pressure <160 mm Hg; diastolic blood pressure <100 mm Hg; triglycerides <600 mg/dl.

Results: By one year ILI participants showed greater improvement than DSE participants in weight loss, fitness, glycated hemoglobin, and all cardiovascular risk factors except LDL cholesterol. Smaller, still significant differences were observed by trial end. Look AHEAD was closed for futility after 10 years by the DSMB, when only 418 DSE patients and 403 ILI patients had a cardiovascular event.

Conclusions: The design and protocol were based on novel design choices to reduce costs and risks and promote retention. Eligibility criteria yielded unusually healthy patients with

diabetes, thereby reducing CVD event rates. Alternatively, it is possible that macrovascular disease cannot be prevented or slowed by weight loss within 10 years in adults, particularly those with diabetes for an average of 14 years at baseline.

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SMALL CALORIE RESTRICTION HAS BENEFICIAL EFFECTS IN TYPE 2 DIABETIC PATIENTS

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Objectives: To assess the compliance to dietary intervention and its impact on patients with type 2 diabetes mellitus (T2DM).

Methods: Thirty patients (male: 13, age = 62 ± 13, BMI = 35.6 ± 5.6) with T2DM were asked to record the quantity of foods consumed for three consecutive days. Medical and nutritional history, anthropometric measurements, blood exams and blood pressure were taken at baseline and after a month of intervention on a personalized hypocaloric diet (1400–2000 Kcal). Patients' compliance was assessed by 24-hour telephone food recalls for three random days (2 weekdays, 1 weekend day) during the intervention month and by an adherence/self-satisfaction questionnaire at the end of the intervention.

Results: According to food records, 26 patients (87%) reduced their calorie intake. The calorie restriction, although statistically significant (p = 0.001), was small (386 ± 398 kcal/day) and on average the calorie intake was decreased by 16%. Significant reduction in body weight (1.57 ± 2.3 kg, p = 0.012), BMI (0.5 ± 0.8, p = 0.009), waist circumference (1.6 ± 2.4 cm, p = 0.011), HbA$_{1c}$ (0.4 ± 0.5%, p = 0.017) and triglycerides (28 ± 38 mg/dl, p = 0.005) was observed. However, according to the adherence/self-satisfaction questionnaire there was no statistically significant difference in all the above parameters between the participants who answered that they strictly followed the provided hypocaloric diet and those who did not or partially followed it.

Conclusions: Even a small energy intake reduction for a short time-period has a great impact on body weight, triglyceride levels and glycemic control, although the majority of participants did not adhere to the provided diet.

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DIABETES EDUCATION PROGRAM WITH EMPHASIS ON PHYSICAL EXERCISE PROMOTES SIGNIFICANT REDUCTION IN BLOOD GLUCOSE, HBA1C, AND TRIGLYCERIDES IN PEOPLE WITH TYPE 2 DIABETES

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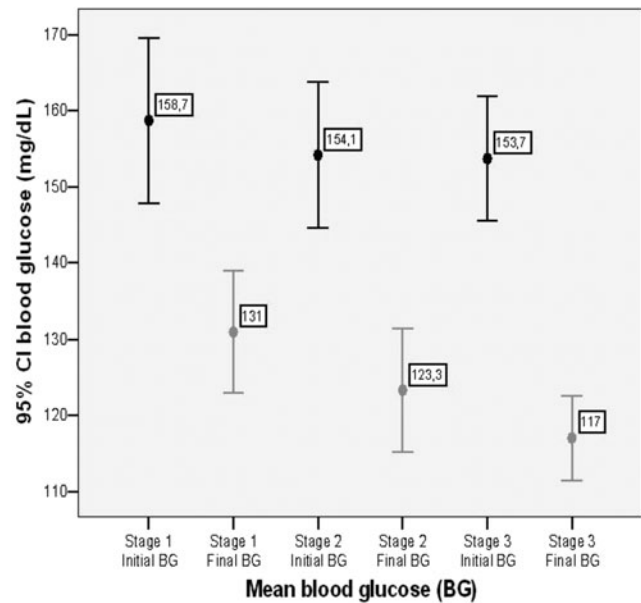
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Objective: To investigate effects of continuous educational intervention program with exercise on health of overweight people with type 2 diabetes (T2DM).

Method: A quasi-experimental study with 103 people with T2DM (age 64.1 ± 10.8 years, 73% women, 23% on insulin therapy, BMI 27) participants in the program over 8 months. At the beginning and end were measured glycated hemoglobin (HbA1c) and lipid profile, and capillary blood glucose (BG) before and after each session (education and exercises, 120 minutes, 2x/week). Statistical analysis used chi-square tests (Pearson), paired t, MANOVA, p < 0.05.
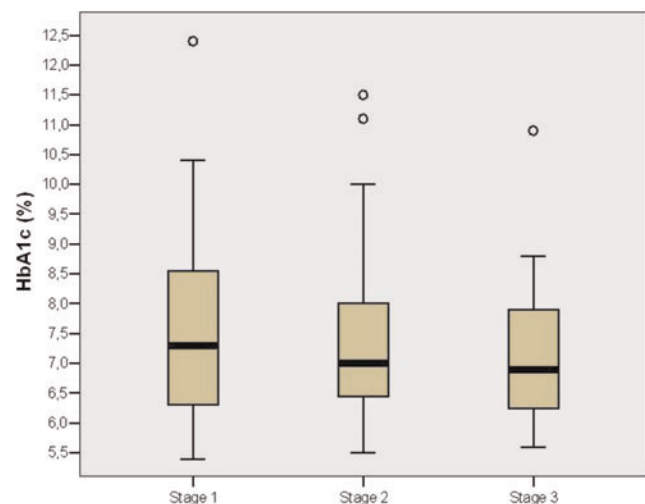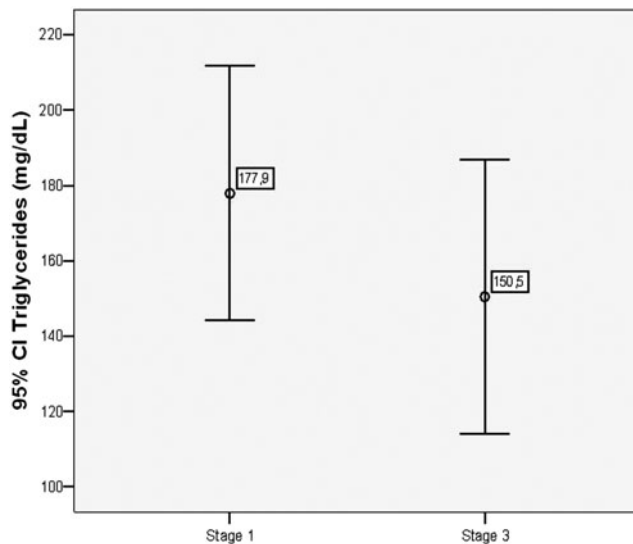
Results: Acute effect: BG increased significantly ($p < 0.001$) from 158 ± 62 to 129 ± 48 mg/dL. Prevalence of normoglycemic BG improved (44% to 68.5%). Chronic effect: significant reduction ($p < 0.05$) of BG from beginning to end of the study (145 ± 5 to 135 ± 3 mg/dL), HbA1c (7.3 ± 1.3 to 7.1 ± 1.0%) and triglycerides (177.9 ± 121.3 to 150.4 ± 130.9 mg/dL).

Conclusion: Diabetes education associated with supervised exercise improved glycemic control and triglycerides in type 2 diabetics.

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DRAMATIC CHANGES OVER 30 YEARS IN THE JAPANESE DIABETIC PATIENTS WITH END-STAGE RENAL DISEASE: A SINGLE CENTER RETROSPECTIVE ANALYSIS

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Aim: To analyze the causes of the tremendous increase of diabetes in Japan.

Methods: Using the medical records of our hospital from 1985 to 2010, the characteristics of diabetic patients who entered RRT were analyzed for the years 1985, 1995, and 2005.

Results: In 1985, more than 70% of the 75 patients did not receive any treatment just before the start of RRT. The average age was 60 ± 2 years and males were predominant (75%). In 1995, more than 20% increases in body weight between the ages of 20 to 35 years involved 82% of 112 patients. The average age was 56 ± 8 years and 60% of patients were males. In 2005, more than 90% of the 135 patients were treated as diabetic patients and the age distribution was scattered from the low 20's to over 80 years old.

Discussion: These dramatic changes in the diabetic population with end-stage renal disease (ERSD) were closely associated with life style changes in Japan. Before 1985, both physicians and patients did not recognize the disease entity 'diabetes'. Besides, the economy of the Japanese society was undergoing a remarkable resurgence at a rapid pace and many people had little concerns about their health. During subsequent decades, life style especially in the diet changed dramatically from Japanese rice to the western diet. During the final 15 years, the changes in life style were spread to every corner of Japan.

Conclusion: Disease morbidity and mortality may be largely determined by social status.

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DIABETES AND EATING DISORDERS

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People with the combination of diabetes and an eating disorder have a drastically increased risk of developing both the acute and the chronic complications of diabetes more rapidly, especially when the eating disorder presents as insulin restriction for the purpose of weight management. Severe complications in diabetics with an eating disorder is not uncommon in people in their early to late twenties. Traditional treatment for a diabetic in DKA due to insulin restriction typically involves hospitalization with the goal of normalizing blood glucose levels, re-education about diabetes management, and discharge to the environment in which the eating disorder originally developed. The common result of this approach is return to the eating disorder and extremely poor diabetes management. Dietary recommendations which may be helpful for the diabetic without an eating disorder can be dangerous for the individual with one, as they often trigger the eating disorder thoughts and behaviors. The mindful eating approach often used to treat people with eating disorders can be extremely effective in treating people with type 1 or type 2 diabetes. This approach leads to decreased pre-prandial, post-prandial, and random blood glucose levels, significantly decreased A1c levels, and normalization of food behaviors with minimal or no weight gain, and sometimes actual weight loss. It is critical that endocrinologists and diabetes educators become more effective in diagnosing eating disorders in their diabetic patients and that they develop an approach to treatment which considers the impact of an eating disorder on diabetes management.

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ASSOCIATION OF RESISTIN $-420C > G$ POLYMORPHISMS AND TYPE 2 DIABETES MELLITUS IN TAIWAN

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The incidence of type 2 diabetic mellitus (T2DM) is rapidly increasing globally. T2DM patients comprise more than 95% of all diabetic patients in Taiwan. Although evidence shows that elevated resistin levels and the polymorphisms located at gene encoding resistin (*RETN*) are associated with diabetic pathogenesis, the correlation between *RETN* genotypes and T2DM is still controversial since discrepancies among different studies exist. For clarifying whether *RETN* genotype contributes to Taiwanese diabetic incidence, the resistin levels and the most widely studied *RETN* $-420C > G$ genotypes were examined in Taiwanese control and T2DM subjects in the present study. In

addition, the genetic polymorphism of *RETN* −420C > G and resistin levels, as well as between *RETN* −420C > G and subjects' clinical characteristics was statistically analyzed. Our results indicate that not only the distribution of *RETN* −420C > G genotypes but also G allele is significantly different between diabetic and control subjects. Nevertheless, no significant association between the subjects' biochemical data and *RETN* −420 SNPs is found. Investigation of *RETN* polymorphisms in T2DM patients from various ethnic populations are crucial and will contribute to the understanding of this gene in the diabetic etiology. We hope the present results may provide clues to elucidate the contribution of genetic heterogeneity for diabetic development.

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EVALUATION OF TYPE 2 DIABETES REMISSION 2 YEARS AFTER BARIATRIC SURGERY

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Introduction: Obesity is the main risk factor for type 2 diabetes (T2D). Improved glycemic control is expected in T2D patients after bariatric surgery associated weight loss.

Methods: Retrospective cohort of 69 patients submitted to bariatric surgery, with previous history of T2D. Demographic, clinical and analytical characteristics were evaluated. A comparative analysis of T2D remission at 2 years of follow-up was made, based on Model A – ADA consensus 2009 (partial remission (PR): fasting glucose 100–125 mg/dL and HbA1c < 6.5%; complete remission (CR): fasting glucose < 100 mg/dL and HbA1c < 6.0%), Model B – HbA1c criteria for T2D diagnosis (PR: HbA1c 5.7–6.5%; CR: HbA1c < 5.7%) and Model C (PR: fasting glucose 100–125 mg/dL or HbA1c < 6.5%; CR: fasting glucose < 100 mg/dL or HbA1c < 6.0%). In each model, the patient was assumed to have stopped antidiabetic drugs for at least a year.

Results: Female gender 85.5% (n = 59), 50.0 ± 7.8 years, BMI 47.7 ± 7.4 Kg/m^2, fasting glucose 137.4 ± 50.1 mg/dL and HbA1c 7.4 ± 1.6%. Before surgery, 88.4% (n = 61) were on antidiabetic therapy (1.6 ± 0.7 drugs per patient and 64.4 ± 31.6 UI of insulin). The most common surgical procedures were: gastric banding 30.4% (n = 21) and gastric bypass 58% (n = 40). At 6 months, 1 and 2 years, there was a significant reduction (p < 0.05) in HbA1c (5.94 ± 1.12%; 5.87 ± 1.20%; 5.86 ± 1.47%), fasting glucose (99.4 ± 34.4 mg/dL; 96.3 ± 32.1 mg/dL; 125.7 ± 130.1 mg/dL) and excess body weight loss (40.3 ± 18.2%; 46.2 ± 18.5%; 44.0 ± 18.6%), respectively. On models A, B and C there was PR in 11.1%, 30.0% and 9.8% and CR in 38.9%, 33.3% and 56.1%, respectively.

Conclusion: Bariatric surgery was effective in improing glycemic control (reduction of fasting glucose and HbA1c).

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PREDICTORS OF QUALITY OF LIFE AND GLYCEMIC CONTROL IN SAUDI ADULTS WITH DIABETES

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Introduction: Diabetes mellitus remains one of the most complex disorders worldwide impacting Quality of Life (QOL). Because of the chronic nature of diabetes, the goal of medical treatment and lifestyle modifications. is not only to prolong life but also to maintain a high level of QOL The aims of the present study are; (i) to assess the QOL and glycemic control (GC) among diabetic patients at king Abdulaziz Medical City (KAMC), KSA, and (ii) to determine the significant predictors of QOL and GC.

Methods: A cross sectional survey was conducted to assess the QOL and glycemic control in 420 Saudi adults diabetics at outpatient clinics of KAMC using a previously validated Arabic version of Diabetes QOL Brief Clinical Inventory. Personal characteristics (age, gender, education, occupation, etc.), disease characteristics (age at onset, duration, type of diabetes, treatment regimen, complications) and lifestyle characteristics (dietary habits, smoking behavior, exercising) were obtained, as well as extracted medical chart data of the duration of diabetes, and most recent HbA1c levels. Logistic regression analysis was applied to identify the significant predictors of good QOL. Significance limits were set at P < 0.05.

Results: The overall percentage mean score of QOL was 74.1 + 11.6, with good QOL in 29.8% of all patients. Diabetics reported lack of satisfaction of : exrcise (49.1%), burden on family (31%), and sex-life (28%) due to diabetes, and reported worry of: physical illness (31%), bad night sleep (26%), pain by treatment (24%), and limitation of career (22%) due to diabetes. After adjusting for possible confounders, higher QOL score was significantly associated with male gender (t = 3.26, p = 0.001), treatment with oral pills (2.14, p = 0.03), healthy diet (t = 2.63, p = 0.009), physical inactivity (t = 2.28, p = 0.023) and absence of diabetic complications (t = 3.47, p = 0.001). Two-thirds (68.8%) of all patients showed poor glycemic control (PGC). Presence of diabetic complications was the only significant predictor of PGC (OR = 1.66, p = 0.024).

Conclusion: Changing the lifestyle of Saudi diabetics is necessary to improve their QOL. Avoidance of complications is a safeguard against possible deterioration in QOL and glycemic control. Future research on transcultural aspects, and effects of lifestyle interventions is recommended.

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POTENTIAL BENEFITS OF CONTINUOUS GLUCOSE MONITORING IN PREDICTING FETAL OUTCOMES IN PREGNANT DIABETIC WOMEN

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Background: Infants born to mothers with diabetes mellitus are more likely to be large-for-gestational age (LGA: ≥ 90th centile) and are at greater risk of birth-related injuries, physiological, and metabolic sequelae. Poor glycaemic control

contributes and transient hyperglycaemia may exacerbate. There exists little evidence on the association between glycaemic variability and fetal overgrowth in women with pre-gestational diabetes.

Methods: 33 pregnant diabetic women attending a multidisciplinary antenatal clinic underwent 72–120 hours of blinded continuous glucose monitoring (CGM) in the 2nd-3rd trimesters. Markers of glycaemic variability (mean glucose, SD, CONGA, LI, JINDEX, LBGI, HBGI, GRADE, MVALUE and MAG) were calculated using EasyGV software (v9.0). Women who delivered LGA infants (Group 1; n = 12) were compared to those who delivered appropriate-for-gestational age infants (Group 2; n = 22).

Results: There were no significant differences in maternal age mean(SD), BMI and booking HbA1c (31.3(5.7)yrs vs. 33.3(5.3)yrs; 27.6(6.4)kg/m^2 vs. 30.7(6.0)kg/m^2; 62.9(10.8)mmol/mol vs. 55.1(16.6)mmol/mol in Groups 1 and 2 respectively). Similar proportions of women were of non-caucasian ethnicity and had Type 2 Diabetes (58.3% vs. 52.4%; 50.0% vs. 61.9%). Mean glucose, SD, CONGA, JINDEX and HBGI were significantly higher in Group 1. LI correlated significantly with fetal birthweight ($r^2 = 0.12$) and SD and JINDEX with fetal birthweight centile ($r^2 = 0.13$ and 0.14 respectively).

Conclusions: Markers of glycaemic variability (mean glucose, SD, CONGA, JINDEX and HBGI) were significantly associated with fetal overgrowth. LI correlated with fetal birthweight and SD and JINDEX with fetal birthweight centile. This suggests a potential role for CGM in pregnancy and implicates glucose excursions in the pathogenesis of fetal overgrowth.

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HYPOGLYCEMIA ADVERSELY AFFECTS SHORT-TERM CARDIOVASCULAR OUTCOMES IN NON-CRITICALLY ILL PEOPLE WITH TYPE 2 DIABETES INITIATING INSULIN THERAPY

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Background: Hypoglycemia is associated with adverse health outcomes and could result in vascular events in patients with diabetes. The impact of hypoglycemia on cardiovascular outcomes in non-critically ill people with diabetes is not well determined. So, we examined short term cardiovascular outcomes of hypoglycemic events in people with type 2 diabetes treated with insulin during their routine clinical care.

Table 1. Demographic and background characteristics of the participants according to gender

	All participants (n=1104)*	Female (n=413)	Male (n=654)	P-value
Age (yrs.)	41.22±9.80	37.05±7.76	43.83±9.98	< 0.001
Clinical practice (yrs.)	12.72±9.27	9.33±6.99	14.65±9.77	< 0.001
Practice location (%)				
Urban	84.2	84.9	83.7	0.61
Rural	15.8	15.1	16.3	
CME* (yes) (%)	39.8	41.2	38.7	0.43

* Thirty-seven participants did not mention their gender.

**CME: Continuous Medical Education

Table 2. Diabetes related knowledge distribution of the participants in relation to taking part in CME programs.

	All participants (n=1104)*	CME Programs Yes (n=422)	CME Programs No (n=637)	P-value
FPG (70-130 mg/dl)	56.9%	66.4%	50.4%	< 0.001
PPG (<180 mg/dl)	51.1%	61.4%	44.7%	< 0.001
HbA1c < 7.0% (< 53 mmol/mol)	52.1%	57.6%	48.2%	0.003
Systolic BP (< 130 mmHg)	60.3%	68%	55.7%	< 0.001
Diastolic BP (<80 mmHg)	50.5%	55%	48%	0.03
TG (< 150 mg/dl)	30.8%	38.4%	26.5%	0.08
LDL (<100 mg/dl)	41.8%	51.4%	35.9%	< 0.001
HDL (>40 mg/dl)	35.5%	41.5%	32.5%	0.003

*Forty-five participants did not mention whether they had participated in CME programs or not.

FPG: Fasting Plasma Glucose

PPG: Post-Prandial Glucose

HbA1c: Glycosylated Hemoglobin

BP: Blood Pressure

TG: Triglyceride

LDL: Low Density Lipoprotein

HDL: High Density Lipoprotein

Table 3. Patients-care parameters depending on CME programs

	All participants (n=1104)	CME Programs Yes (n=422)	CME Programs No (n=637)	P-value
Physical activity				
Duration (≥180min/Wk)	47.2%	50.0%	45.1%	0.12
Distribution (≥ 3 times/Wk)	98.35%	98.5%	98.3%	1.00
Metformin (Primary treatment)	41.5%	45.6%	38.9%	0.03
ACEI/ARB	76%	73.5%	79.7%	0.03
Statins (always)	51.7%	57.9%	47.6%	0.001
Add basal insulin	27.9%	31%	25.8%	0.06
CVD risk assessment (≥50%)	84.7%	87.7%	82.7%	0.03

*Forty-five participants did not mention whether they had participated in CME programs or not.

ACEI/ARB: Angiotensin Converting Enzyme Inhibitors / Angiotensin Receptor Blockers

CVD: Cardiovascular disease

Methods: One hundred and twenty non-critically ill people with type 2 diabetes on oral glucose lowering drugs were enrolled in this study. Insulin therapy was initiated due to uncontrolled diabetes. The patients were educated to perform self-monitoring of blood glucose on a daily basis. In addition, they were asked to record the results if they experienced any symptom indicative of hypoglycemia during the 24 week of the study. The occurrence of any major cardiovascular event including unstable angina, fatal or non-fatal myocardial infarction, fatal and non-fatal stroke, or death from cardiovascular cause was also evaluated based on the patients' hospital records.

Results: There were 210 hypoglycemic episodes and 31 major cardiovascular events. Forty four percent of the patients who had documented hypoglycemic episodes developed cardiovascular events compared to 15.6% of those who did not experience any hypoglycemia (P = 0.001). The odds ratio for occurrence of major cardiovascular event relating to hypoglycemia was 6.75 (CI = 2.4–18.58) with a risk ratio of 2.65.

Conclusions: Hypoglycemia is a major risk factor for occurrence of the first major cardiovascular event in non-critically ill people with type 2 diabetes initialing insulin therapy.

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DIABETES A&E ATTENDANCES AND ADMISSIONS PRE AND POST IMPLEMENTATION OF AN OUT OF HOURS TELEPHONE SERVICE

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Introduction: During working hours the diabetes team provides support to patients and their families. Out of hours (OOH) less support exists and diabetes related attendances to A&E pose a potential avoidable burden on acute services. In 2013 our three institutions created an OOH paediatric diabetes consultant delivered telephone support service. The result of its impact on A&E attendances and admissions to wards is shown.

Methods: Diabetes related attendances to A&E out-of-hours and ward-admissions were retrospectively analyzed in the year before and after the implementation of the OOHS. Unavoidable attendances ie: New onset diabetes, were excluded along with patients not registered with our diabetes service.

Results: A&E attendances: Evelina: 23 pre-OOHS, 16 post-OOHS (−30%); Lewisham: 28 pre-OOHS, 25 post-OOHS (−11%); King's: 70 pre-OOHS, 54 post-OOHS (−33%).

Admissions to ward: Evelina: 12 pre-OOHS, 13 post-OOHS (+8%); Lewisham: 3 pre-OHHS, 11 post-OOHS (+266%); King's: 30 pre-OHHS, 22 post-OOHS (−27%).

Conclusions: The effect of the OOH service on A&E attendances showed a reduction across all sites. However, the effect of OOH on admission was inconsistent. A possible explanation is poor patient engagement with the OOH service. Review of those patients presenting to A&E on more than one occasion within the Evelina cohort found them to have poor diabetes control reflected by high HbA1c and poor compliance with their treatment regimen (reflected in clinic letters). One family did not speak English. Thus advocating the use of the OOH service more actively to these families and providing leaflets advertising the service in different languages.

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THE AVERAGE VALUE OF GLYCEMIA AND INDICATORS OF SLEEP IN PATIENTS WITH TYPE 1 DIABETES

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Objective: To evaluate the effect of glycemia during the day on the performance of sleep in patients with type 1.

Methods: daily monitoring of glucose - 'CGMSGold', 'Medtronik MINIMED' (average glucose (AG) and the duration of hyperglycemia, hypoglycemia, euglycemia during the day before bedtime «b» and after sleep «a»; polysomnographic monitoring - «SOMNOlab 2 (PSG) Polysomnography». Group 1

Indicator	Group 1 Mean (min-max)	Group 2 Mean (min-max)
Number of patients	**13**	**20**
Age (years)	**34.5(25.0–54.0)**	**35.9(20.0–56.0)**
HbA1c (%)	7.5(5.0–9.4)	8.0(5.6–12.0)
AG «b» (mmol/l.)	6.6(3.2–8.0)*	10.0(8.1–16.6)
Hyperglycemia «b» (%)	11.5(0.0–22.0)*	43.5(10.0–86.0)
Hypoglycemia «b» (%)	14.4(0.0–80.0)*	3.7(0.0–25.0)
Normoglycemia «b» (%)	74.1(20.0–92.0)*	52.7(0.0–77.0)
AG «a» (mmol/l.)	7.7(4.5–12.2)	8.5(3.6–17.0)
Hyperglycemia «a» (%)	23.2(0.0–74.0)	28.0(0.0–100.0)
Hypoglycemia «a» (%	12.3(0.0–63.0)	10.9(0.0–77.0)
Normoglycemia «a» (%)	63.2(26.0–99.0)	61.0(0.0–100.0)

* p < 0.05

consisted of patients with a level of AG < 8.0 mmol/l, group 2 - with the index AG > 8.0 mmol/l.

Results:

AG 10.0 mmol/l prolongs latency of REM, increases the rate of change of the phase of sleep (r = −0.56), increases of S4 (r = 0.50), the efficiency of sleep phases 3 (r = 0.45). Hypoglycemia are accompanied by an increase of SWS (r = −0.68), S3 and S4 (r = −0.56 and r = −0.56), change the phase of sleep (r = −0.56).

In patients with AG «b» 6,68 mmol/l noted elongation REM (r = 0.76), increasing sleep efficiency 3 (r = 0.63); AG affect duration SWS (r = 0.73), the overall cycle time (r = −0.84), sleep efficiency 1 (r = −0.72) and 2 (r = −0.61). Sleep latency increases the frequency of hypoglycemia 'a' (r = 0.64).

Conclusion: fluctuations in blood glucose before bed affect the performance of night sleep, regardless of HbA1c.

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HOSPITAL-USE GLUCOSE METER WITH CONNECTIVITY IN AN EYE CENTER AS A TOOL FOR GLYCEMIC CONTROL IMPROVEMENT

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Background and aims: Blood glucose (BG) control is required to safely perform ocular surgery in patients with diabetes. The aim of this study was to evaluate the efficiency of a hospital-use point-of-care (POC) glucose meter with connectivity for optimizing BG control in patients undergoing ocular surgery.

Methods: Prospective study in a National Eye Center. BG was determined through a hospital-use POC glucose meter, allowing online real-time access to a BG database by diabetes team which could track patients with uncontrolled diabetes. Serial BG testing measurements and hypo- or hyperglycemic interventions were both performed according to a written protocol in all inpatients with diabetes.

Results: Among the 9735 hospital stays between February and August 2014, 1949 (20%) were registered in 1383 patients with diabetes (68 ± 13 yrs, 50% cataract and 19% retinal surgery). A total of 5213 BG measurements were analyzed. Mean BG was 152 ± 63 mg/dl (57% in the range: 100–180 mg/dl) and

43 (0.8%) BG measurements < 60 mg/dl were recorded in 33 patients and 22 (0.4%) > 400 mg/dl in 16. Half of these events were linked to prescription and/or management errors with a change in hypoglycemic treatment at discharge in one third of patients.

Conclusion: While BG profile was acceptable in most patients in our Eye Center, events occurring during the perioperative period leading to diabetes intervention were easily and effectively detected by the diabetes team through the use of an online real-time access to the BG database. This tool can contribute to improve the quality of inpatient glycemic management.

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COMPARATIVE EFFICACY OF SECOND LINE OADS: PREFERABLE AGENT AFTER METFORMIN FAILURE: CROATIAN PILOT STUDY

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The aim of this study was to review the efficacy of different second-line agents with respect to HbA1c, glycemic profile, body weight and occurrence of hypoglycemia in T2DM patients. This is the first pilot study exploring the efficacy of second-line treatment in Croatia. Research included 200 patients not reaching ADA glycemic targets on metformin alone. Patients were followed for 6 months. There were no significant differences in age and BMI among patients at baseline. Second-line treatment for most (38%) was sulphonylurea (Su), followed by DPP-4 inhibitor (25.5%), repaglinide (11.5%), human basal insulins (HBI) (10%), biphasic insulin analogues (IA) (8%), thiazolidinediones (TZD) (6%) and acarbose (1%). All therapies, except acarbose and HBI significantly (p < 0.01) increased proportion of patients reaching target HbA1c after 6 months; DPP-4 inhibitors and Su significantly (58.8% and 27.6% respectively, p < 0.01) increased proportion of target HbA1c patients after 3 months. After 6 months all therapies, except acarbose, significantly (p < 0.01) increased the proportion of patients reaching target fasting blood glucose (FBG), and all except acarbose and TZDs significantly (p < 0.01) increased proportion of patients with target postprandial blood glucose. After 3 months target FBG and postprandial blood glucose levels were reached with DPP-4 inhibitors, Su and IA. There were no registered hypoglycemic episodes during analyzed period. During 6 months body weight gain was observed for patients on HBI (+3.3 kg), and IA (+2.4 kg), while other therapies were weight neutral. To conclude, glycemic targets are concivable with DPP-4 inhibitors, Su and insulins, but the latter is associated with weight gain.

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DIFFERENT EFFECTS OF GLYCEMIC EXCURSION ON OXIDATIVE STRESS DEPEND ON DURATION OF DIABETES

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The stability and fluctuation of glycemic excursion may cause the oxidative stress, resulting in one of the pathogenic factors of diabetic complications. This study aimed at investigating relationships between the degree of hyper- and hypoglycemia and oxidative stress. Methods: T2DM (n = 34) and T1DM (n = 17) were subjected to the CGM. The oxidative stress markers such as total free radical derived from reactive oxygen species (ROS), urinary output of 8-hydroxy-2'-deoxyguanosine (8-OHdG), and 15-isoprostane F2t (isoprostane), and glucosylated products such as HbA1c and pentosidine were measured. The lipid profiles and high-sensitivity (hs)-CRP were also measured. The glucose instability was expressed as the mean glucose plus SD (mG + SD) and the combined percentages of hyper- plus hypoglycemia (Hyper + hypo). The stability and duration of hyperglycemia were classified by the cut-off of mG + SD and HbA1c. The continuous hyperglycemia presented by high values of mG + SD and HbA1c were classified as HH, while both low values were classified as LL.

Results: The values of total ROS were correlated with the values of mG + SD, Hyper + hypo or hsCRP in T2DM. The urinary output of isoprostane were correlated with the values of mG + SD, Hyper + hypo or 8-OHdG in especially T2DM with short duration (< 2 yrs). The production of total ROS in HH was higher than those in LL. The mG + SD or Hyper + hypo were correlated with the values of pentosidine in T2DM with long duration (> 2 yrs).

Conclusion: The short-term fluctuation of blood glucose may affect markers for oxidative stress such as isoprostane, while long-term one influences AGE such as pentosidine.

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RAMADAN FASTING AMONG ALGERIAN TYPE 2 DIABETES PATIENTS—A REAL CHALLENGE

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Background and aims: Ramadan fasting constitutes a real challenge, for people with diabetes, their health care providers (HCP) and even for their families. The aim of the current study was to evaluate the attitude and practices of a group of Algerian type 2 diabetes patients towards Ramadan fasting.

Materials and methods: 165 outpatients with diabetes type 2 aged of 55 ± 16 years were selected before Ramadan 2012 in Sidi-Bel-Abbes city (West of Algeria). The food consumption was measured using the 3-days food record. Fasting (FSG) and postprandial serum glucose (PPG), HbA1c, total cholesterol, HDL-c, LDL-c were measured before, during, and after fasting month.

Results: Our results showed that the decision to fast was always discussed with relatives (85%), while the Imam (religious leader) was consulted for advice (15%) and HCPs (13%). 73% of investigated patients undertook fasting with no diet and medication guidance. There was a significant increase (p < 00.5) in the total number of hypoglycemic events (< 3.3 mmol L-1) comparing to non-Ramadan fasting days. FSG levels decreased non-significantly during Ramadan (day 15 and 28), however, a significant increase in PPG was recorded. Lipid metabolism showed non-significant change during fasting days.

Conclusion: The current study revealed a gap between HCPs and their patients. The therapeutic strategy should be individualized and patients who want to fast Ramadan safely should be previously informed and educated to avoid diabetes complications during this period.

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GLYCEMIC VARIABILITY ANALYSIS DURING HOSPITALIZATION IN PATIENTS WITH TYPE 1 DIABETES

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Type 1 diabetes (T1D) is characterized by complete destruction of insulin secreting β cells, significant glucose variability, and significant morbidity often resulting in hospitalization for various reasons during its natural history. Limited data are available on glucose control in patients with T1D during hospitalization, despite the challenges faced by hospital teams. We electronically retrieved in hospital glucose measurements in patients with T1D during the years 2006–2010 to assess the current state of glycemic control and glucose variability. A total of 788 patients were hospitalized a total of 1541 times (mean 2.5 stays/person; range 1–27) during the study period. GC was highly variable in the study sample with the mean (range for mean) BG for patients (over multiple stays) of 183 (75–347) mg/dl. Accordingly, the mean (range) average daily risk range was 35 (0.3 to 118), with only 16% of patients being classified as low risk (ADRR < 20). The reason for the poor control appears to be related to hyperglycemia as illustrated by the lack of concordance in the low blood glucose index (LGBI) and the high blood glucose index (HGBI). Approximately 22% and 65% of the patients meet the HBGI criteria for 'Moderate' or 'high' risk for hyperglycemia, respectively, whereas only 14% and 5% of the patients were at 'Moderate' or 'High' risk for hypoglycemia. These data suggest the need to improve algorithms to manage these patients while in the hospital.

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EFFECTS OF INTERMITTENT SEQUENTIAL COMPRESSION (ISC) OF LEGS ON BLOOD OXYGENATION AND GLUCOSE METABOLISM OF THE BRAIN DURING PNEUMOPERITONEUM

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Background and objectives: Hyperglycemia with simultaneous hypooxia has detrimental effects on patient clinical outcome. Tissue ischemia interferes with local metabolism and influence tissue glucose utilization. Oxygen saturation of mixed venous blood from internal jugular vein $SjvO_2$ is an indirect indicator of brain oxygenation and metabolism. Various methods of improving brain oxygenation during pneumoperitoneum have been established. Aim of this study is to evaluate the effect of Intermittent Sequential Compression (ISC) on brain oxygenation and glucose during pneumoperitoneum.

Method: Study included 100 patients, ASA i/II, scheduled for laparascopic cholecystectomy. Patients were randomized in two groups: Group ISC, where ISC was applied and control group n-ISC- without ISC. Samples for gas analysis of $SjvO_2$ and glycemia were obtained from right internal jugular vein (main drainage vein from brain), before creation of pneumoperitoneum, during pneumoperitoneum and after ending of pneumoperitoneum.

Results: Baseline measurment for $SjvO_2$ and blood glucose were not statistically different in both groups. Average values of

$SvjO_2$ were significantly higher (p < 0.05) in group ISC during and after pneumoritoneum compared to group n-ISC (86.4% vs 77.8%; 85.3% vs 80.6%). Glycemia was lower and within the range of 4.6–7.4 mmol/l in group ISC, compared to control group 4.7–8.2 mmol/l. Coefficient of regressional analysis was 0.461 and saturation of the blood have statistically significant influence (p = 0.0000) on brain oxygenation and glucose metabolism while haemodynamic parameters don't.

Conclusion: ISC of the legs is not an expensive method and improves brain oxygenation and local glucose metabolism in patients who are at risk of developing local hypoperfusion during pneumoperitoneum.

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NEW ONSET DIABETES AFTER CORONARY ARTERY BYPASS GRAFT AND IMPACT OF HYPERGLYCEMIA ON HOSPITAL STAY

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Context: Hyperglycaemia in diabetics or nondiabetics during hospital admission is associated with adverse outcomes. The risk of subsequently developing Type 2 diabetes is not known. We hypothesize that CABG poses a strong stress leading to new development of Type 2 diabetes.

Aims: To evaluate the hypothesis that CABG can produce de novo Type 2 diabetes in post-op period. Whether this glycemic disruption has any impact on hospital stay.

Methods: Data of 1559 patients (1355 males, 254 females) who underwent CABG between 2012 – 2013 at a single tertiary center was retrospectively analyzed after ethical clearance.

Results: Out of 933 nondiabetics, 57 patients developed diabetes de novo, all these patients were discharged at least after seven days on basal-bolus insulin. There was strong correlation between the duration of ICU stay and development of diabetes (r = 0.138, P < 0.001) and overall hospital stay and development of diabetes (r = 0.163, P < 0.001). Interestingly, family history of diabetes, smoking, and alcoholism was present in very few of these 57 patients.

Discussion: Derangement of glucose metabolism after surgery can also occur in nondiabetic patients due to various surgical stresses. 57 new cases of Type 2 diabetes were detected after CABG which is 6.1% of the nondiabetics who underwent CABG. Considering the colossal numbers of diabetics this new diabetes though in a small fraction of people, has enormous economic impact.

Conclusion: CABG per se can produce Type 2 diabetes. The stress of surgery, inotrope usage are some of the factors responsible for CABG induced Type 2 diabetes in 6.1% of non-diabetic patients undergoing CABG.

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THE USE OF CONTINUOUS GLUCOSE MONITORING (CGM) TO FACILITATE THE SAFE CESSATION OF INSULIN IN PEOPLE WITH GENETIC FORMS OF DIABETES

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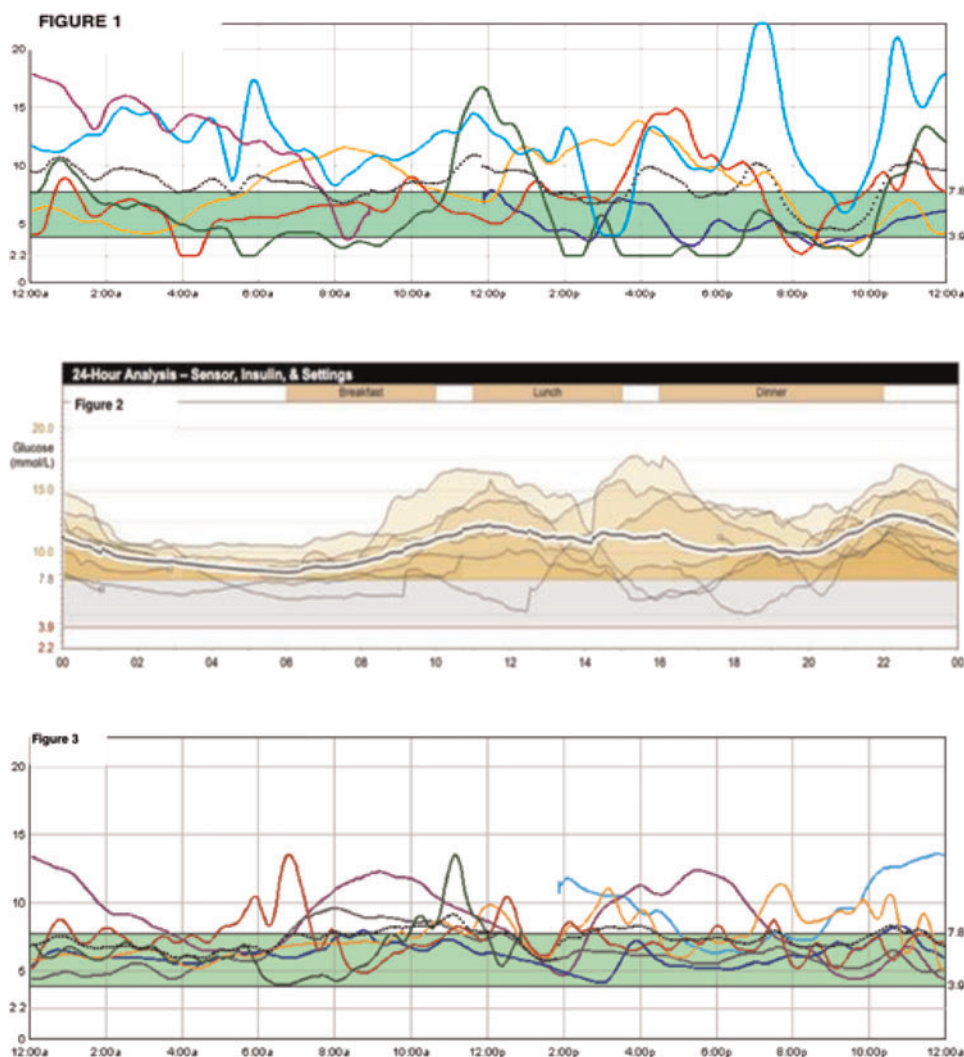
FIGURE 1

24-Hour Analysis -- Sensor, Insulin, & Settings

Figure 2

Figure 3

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Introduction: Monogenic diabetes results from mutations in genes associated with insulin production and may present as neonatal diabetes or maturity onset diabetes of the young (MODY). Some mutations are sulphonylurea sensitive, but cases may be misdiagnosed as type 1 diabetes (T1DM). Transfer from insulin to sulphonylurea therapy can be challenging due to hypoglycaemia risk and unknown underlying beta-cell function as baseline C-peptide levels are low due to the mutation.

Methods: Two cases are reported where CGM facilitated down-titration of insulin and sulphonylurea initiation.

Results: Case 1: 21-year-old woman diagnosed as T1DM aged 6 weeks and treated with insulin pump, C-peptide 11 pmol/L. Genetic testing confirmed KCNJ11 mutation. Retrospective CGM (iPro 2, Medtronic) revealed hypoglycaemia and increased glycaemic variability (standard deviation 4 mmol/L, figure 1). After initiation of high-dose glibenclamide and reduction in basal rates, sensor-augmented pump (Medtronic) demonstrated resolution of hypoglycaemia and improved variability (standard deviation 2.9 mmol/L, figure 2), enabling glibenclamide dose-escalation (C-peptide now 413 pmol/L).

Case 2: 48-year-old man with HNF1-alpha MODY (C-peptide 168 pmol/L), managed on insulin with frequent hypoglycaemia. Low-dose glibenclamide initiated with 50% insulin reduction. Retrospective CGM (figure 3) revealed resolution of hypoglycaemia with postprandial hyperglycaemia, allowing glibenclamide dose escalation and insulin cessation (C-peptide increased to 628 pmol/L).

Conclusion: Stopping insulin risks ketonaemia and significant hyperglycaemia in people with uncertain underlying beta cell function. Initiation of glibenclamide risks hypoglycaemia where awareness may already be impaired. The use of CGM may provide reassurance about hypoglycaemia, objective data informing treatment changes and allow safe down-titration of insulin in these complex cases.

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EFFECT OF COLOR DISPLAY ON THE SMBG METER: ANALYSIS OF DATA FROM THE COLOR IMPACT STUDY

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Background: We conducted a clinical research study to evaluate the effect of two color-indication methods used in SMBG, color record (CR) and color display (CD), on glycemic control in insulin-treated type 2 diabetes patients.

Methods: This was a prospective, 24-week, comparison study. One hundred twenty outpatients were randomly allocated to four groups with 2×2 factorial design: CR or non-CR and CD or non-CD. Blood glucose levels more than 160 mg/dl or less than 70 mg/dl were recorded in red or blue pencil in the CR arm, and red or blue indicator light on SMBG meters was lit in the CD arm, respectively. The primary endpoint was HbA1c reduction. The secondary end points were self-management performance change and psychological state change. Written informed consent was obtained from all subjects (IRB approval No.E1332, CTR No.UMIN00006865).

Results: HbA1c levels were significantly decreased in CR arm by -0.31% compared to those in non-CR arm (p = 0.044) because of improvement in diet and exercise scores. Contrarily, HbA1c levels were not different between CD arm and non-CD arm. However, as compared with non-responders to CD method, HbA1c levels were significantly reduced by -0.99% in responders (p < 0.001) because of improvement in exercise score. Change in psychological states were not altered between the groups.

Conclusions: Active usage with color-indication methods by patients has a favorable effect on self-management performance and glycemic control. Color, especially red, motivates type 2 diabetes patients to exercise, and to recognize their blood glucose levels as high or low optimizes self-management, resulting in improved glycemic control.

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A CASE OF USING AN ARTIFICIAL ENDOCRINE PANCREAS WITH CLOSED-LOOP GLYCEMIC CONTROL SYSTEM IN CARDIAC SURGERY

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Hyper- and hypoglycemia are associated with increased mortality of cardiac surgery. In past reports, conventional intensive insulin therapy with open loop system resulted in hypoglycemia. To avoid hyper- and hypoglycemia, accurate continuous blood glucose monitoring device and closed loop system for computer-assisted blood glucose control are proposed. We reported a case of using an artificial endocrine pancreas (AP) with closed-loop glycemic control system in cardiac surgery.

A 73 year-old Japanese man was scheduled to coronary artery bypass graft surgery. He had diabetes. He has received multiple insulin injection therapy. Total daily insulin dose was 30 units. Body height was 155.5 cm, body weight was 50.1 kg. After the patient entered intensive care unit, AP (STG-55, Nikkiso Co. Ltd, Tokyo, Japan) was started. Target blood glucose level (BG) was 110 mg/dl. Duration of using AP was 18 hours and 13 minutes. BG was measured 1094 times. Maximum BG was 154 mg/dl, minimum BG was 60 mg/dl, average BG was 113.6 mg/dl in using AP. Total insulin dose was 36.25 units.

AP may save a lot of time and provide hypoglycemia-free glucose control in perioperative glycemic control.

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BLOOD GLUCOSE METER PERFORMANCE IN PATIENTS WITH END-STAGE RENAL FAILURE

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Patients with diabetes and end-stage renal failure may require frequent dialysis. The procedure induces major changes in the protein and electrolyte composition of human blood and influences blood viscosity. The purpose of our study (Clin.Trial. Reg.No. DE/CA99/00008198) was to investigate the impact of the dialysis procedure on the performance of glucose meters for patient self-testing (BGStar andiBGStar, Sanofi; Contour XT, Bayer; FreeStyle InsuLinx, Abbott; OneTouch Verio IQ, LifeScan).

Capillary blood was obtained before and after dialysis from 40 patients with end-stage renal failure (19 male, 11 non-diabetic subjects, 24 type 2, 5 type 1, age: 73 ± 11 yrs., mean diabetes duration: 13 ± 9 yrs., mean dialysis duration: 3.1 ± 2.8 yrs.). The glucose concentration was immediately measured within 5 min with the comparative meters. The YSI analyzer served as reference method. As this setting is not appropriate for a valid accuracy analysis, we analyzed the pre- vs. post-dialysis MARD changes as an indicator for the sensitivity of the devices to changes induced by the procedure and made an additional Parkes-Error-Grid Analysis.

The observed differences between pre- and post-dialysis MARDs were $+1.6\%$ for iBGStar and $+2.5\%$ for BGStar (InsuLinx: -0.1%, Contour XT: -0.6%, Verio IQ: $+6.0\%$). Parkes-Error-Grid resulted in the following % values in zones A/B/Conly: iBGStar: 96.3%/3.7%/0%, BGStar: 96.3%/3.7%/0%, InsuLinx: 97.5%/2.5%/0%, ContourXT:98.7%/1.3%/0%, Verio IQ: 100%/0%/0%.

In this study, the changes induced by the dialysis procedure did not seem to have a substantial influence on the performance of the investigated blood glucose meters.

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CAN PREOPERATIVE AMINO ACID INFUSIONS IMPROVE BLOOD GLUCOSE AND C-PEPTIDE LEVELS IN SURGICAL PATIENTS?

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Background and objectives: Surgical patients have induced stress response which affects glucose metabolism. Preoperative fasting emphasizes stress and promotes stress hyperglycemia. In diabetic patients, protein rich food has positive impact on insulin secretion and glycemia. Preoperative change of metabolism from 'hunger' to 'fed' with amino acids may be beneficial for patients who have risk of developing stress hyperglycemia. Aim of this study was to analyse the influence of amino acid on glycemia and C-peptide levels in surgery patients.

Material and method: In prospective clinical study 13 patients, scheduled for elective surgery were included and randomized in two groups. Inclusion criteria were BMI < 35 m^2, ASA I/II and preoperative glycemia < 6.1 mmol/l. Prior surgery group AA (n = 6), received amino acid infusion with 12 ml/kg/120 min whereas group RL (n = 7) received Ringer Lactate with same regime. C-peptide and glycemia were measured in both groups prior the infusions, after ending of infusions and 24 hours postoperatively.

Results: Both groups showed increase of glycemia from baseline, after infusions. Postoperative average blood glucose levels decreased in group AA (5.26–4.65) whereas they increased in RL group (5.31–5.7) and difference was statistically significant (p = 0.007). Hyperglycemia occurred postoperatively only in group RL in 42.86% of patients. C-peptide values increased progressively from baseline in group AA (1.33–1.63) while in RL decreased (1.31–1.1) respectively. Between the groups, C-peptide values were not statistically different (p > 0.05).

Conclusion: Preoperative amino acid infusions in surgical patients improve blood sugar levels and increase C-peptide levels. Our results should be validated in larger study.

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USE OF CONTINUOUS GLUCOSE MONITORING, COMPUTERIZED THERAPY RECOMMENDATIONS, AND AUTOMATED DATA PROCESSING IN A PEDIATRIC TRIAL OF TIGHT GLYCEMIC CONTROL

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Background: Tight glycemic control (TGC) reduces morbidity and mortality in certain, but not all, populations of critically ill patients, with the possibility that specific subpopulations or age groups may still benefit. The Heart and Lung Failure Insulin Titration Trial (HALF-PINT) is a clinical trial that randomizes critically ill children with cardiovascular and/or respiratory failure to tight glycemic control (TGC) in two BG ranges (80–110 mg/dL vs. 150–180 mg/dL). The purpose is to compare mortality-adjusted ICU length of stay.

Methods: Planned enrollment is 1,880 subjects; 32 US centers are participating. An explicit computerized insulin titration algorithm and continuous glucose monitoring (DexCom G4 Platinum) are used to maintain BG concentrations in the assigned TGC ranges. Subjects receive standardized intravenous glucose at age-appropriate rates to provide basal calories and mitigate

hypoglycemia. A website was developed to randomize subjects and capture data in near real-time.

Results: To date, 245 subjects have been randomized into the trial at 22 sites. The data capture system has notified study staff of hypoglycemia and other events on an hourly basis, allowing ongoing analysis of algorithm performance (time in target range), CGM performance (MARD of 12.7% in 16,801 paired samples), and protocol compliance (rate of therapy recommendation overrides).

Conclusion: Use of a centralized data management system in a multi-center trial of TGC allows near real-time monitoring of algorithm and CGM performance, adverse events, and protocol compliance. This, together with an explicit algorithm for titrating insulin, improves standardization across sites and generalizability of the research findings.

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RANDOMIZED EVALUATION OF GLYCEMIC CONTROL AND VARIABILITY IN THE MEDICAL INTENSIVE CARE UNIT USING REAL-TIME CGM (REGIMEN TRIAL)

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Context: Hyperglycemia occurs in 50–85% of patients admitted to a medical intensive care unit (MICU).

Objective: To study whether real-time continuous glucose monitoring (RT-CGM) improves glycemic control and variability, and reduces hypoglycemia risk in MICU patients with an APACHE-II score ≥ 20.

Design and Patients: Thirty-five patients (age 66 ± 10 y; non-diabetic/diabetic patients 27/8; APACHE-II-score 28 ± 6) were randomly assigned to RT-CGM (n = 16) using the GlucoDay®S device or to blinded CGM. Insulin infusion was performed using a modified Yale protocol.

Main Outcome Measures: Percentage of time in normoglycemia and in hypoglycemia, glycemic variability, and CGM accuracy.

Results: During 96-h of monitoring, glycemia reached target (80–110 mg/dl) in 36 ± 11% of time, was between 70–180 mg/dl in 92 ± 2%, and < 60 mg/dl in 2 ± 2% of time. In the RT-CGM group glycemia averaged 119 ± 17 mg/dl vs 122 ± 11 mg/dl in the control group; the percentage of time at target glycemia were 37 ± 12% vs 34 ± 10% respectively (NS). The percentage of time in hypoglycemia was similar between groups. Glucose variability was low (SD: 31 ± 13 mg/dl, MAGE: 53 ± 28 mg/dl and MODD: 37 ± 17 mg/dl) and similar between groups. The number of arterial glucose measurements was 5 ± 7 in the RT-CGM group versus 8 ± 8 in the control group. GlucoDay®S values and arterial glycemia correlated well with 98.6% of data falling in regions A and B of error grid analysis.

Conclusion: RT-CGM did not ameliorate glucose control and variability, nor reduce hypoglycemic events, but our insulin infusion protocol led to overall tight glucose control without a significant hypoglycemia risk, leaving little space for improvement.

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A MODEL FOR HYPOGLYCEMIA ALARM: ADAPTIVE GLUCOSE PREDICTION

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Objective: An adaptive plasma glucose prediction model and hypoglycemia early alarm method were proposed based on continuous glucose monitoring system (CGMS).

Methods: An glucose prediction model was established based on an autoregressive model (AR) due to the non-stationary characteristics of plasma glucose concentration signal. While Kalman filter was used to reduce background noise of the glucose data from CGMS and the adaptive forgetting factor least square was used to estimate the model parameters to adapt to the inter/intra-subject variation; then a prediction model was proposed to early warning of clinical hypoglycemia.

Results: The proposed AR model outperforms the traditional AR, for both the root mean square error (RMSE) and the sum of squares of the glucose prediction error (SSGPE) of predictions using the proposed AR model are smaller. Also, the alarm method could effectively forecast hypoglycemia.

Conclusions: The proposed model whose parameters are determined by the adaptive forgetting factor least square does very well in the prediction of future glucose, and its application in the hypoglycemia warning technology can help patients reduce the likelihood of the occurrence of hypoglycemic events.

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EVALUATION OF BLOOD GLUCOSE LEVELS ON ADMITTING TO INTENSIVE CARE UNIT AFTER SURGERY AND RELATIONSHIP TO MECHANICAL VENTILATION

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Background and objectives: Blood glucose control (BGC) during surgery and in Intensive Care Unit (ICU) has positive impact on patients outcome. Macedonia is middle income country where protocols for BGC in surgical patients are still not well established. The aim of this study was to evaluate blood glucose levels of surgical patient on admission in ICU and its relationship to the need for mechanical ventilation.

Material and method: The retrospective study was done on records of 982 patients admitted in surgical ICU in University clinical Center–Skopje from December 2012 to December 2013. Data collected included age, gender, glycemia, APACHE II score and duration of mechanical ventilation.

Results: Total of 982 patients' records were analyzed. After surgery, 53.77% (528) patients were admitted in ICU. Out of the total, hyperglycemia (blood glucose levels higher than 6.1 mmol/l) on admitting in ICU was found in 73.1% and normoglycemia in 26.9%. Need for mechanical ventilation (in days) was significantly higher in patients with hyperglycemia (7.2 vs 4.7 days $p < 0.05$) compared to patients with normoglycemia. Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were significantly higher ($p < 0.05$) in patients with hyperglycemia and other data measures did not significantly differ between the two groups.

Conclusion: Surgical patients develop higher blood glucose levels during surgery. Hyperglycemia on entering in ICU prolongs the need for mechanical ventilation in surgical patients. Introducing protocols for BGC during and after surgery may shorten the days of mechanical ventilation in surgical patients. This relationship should be validated by larger randomized study.

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JNK SIGNALING PATHWAYS IS REQUIRED FOR MITOCHONDRIAL DYSFUNCTION-INDUCED IINSULIN RESISTANCE IN WRL-68 HUMAN LIVER CELL

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Mitochondrial dysfunction and metabolic inflammation have emerged as the key events underpinning the development of obesity-related insulin resistance and type 2 diabetes. Accumulating evidence indicates that c-Jun NH(2)-terminal kinase (JNK) signaling pathways are among the regulatory pathways responsible for oxidative stress linked inflammation in the development of hepatic insulin resistance. So far, little is known about the upstream roles of JNK signaling pathways in maintaining adequate energy balance relative to mitochondrial functions in hepatocytes. Therefore, the aim of this study was to investigate the therapeutic roles of JNK signaling pathways inhibition upon mitochondrial dysfunction-induced insulin resistance in WRL-68 human liver cells. We found that JNK inhibitor (SP600125) exhibits ameliorative properties in cells treated with rotenone, mitochondrial complex I inhibitor via enhancement of insulin stimulated-glucose uptake activity. The increased phosphorylation of insulin signaling activities via IRS1, Akt/PKB and AS160 was observed. The augmented level of oxidative DNA damage, protein carbonylation and lipid peroxidation in hepatocytes with mitochondrial dysfunctions was prevented by JNK inhibitor. In addition, rotenone caused massive production of pro-inflammatory mediators IL-6, TNF-α and IL-1β by altering inflammatory signaling pathways whereas JNK inhibitor counteracted all these parameters in insulin-resistant cells. In summary, we showed that JNK inhibitor could prevent mitochondrial dysfunction and insulin resistance via inhibition of JNK signaling pathways.

Together, these discoveries for the first time identify JNK signaling pathways as one of the therapeutic regulators of mitochondrial dysfunction in hepatic tissue insulin resistance and inflammation.

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GENERAL PRACTITIONERS' KNOWLEDGE AND CLINICAL PRACTICE IN MANAGEMENT OF PEOPLE WITH TYPE 2 DIABETES IN IRAN: THE IMPACT OF CONTINUOUS MEDICAL EDUCATION PROGRAMS

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Aims: To obtain information related to the knowledge and clinical practice of general practitioners (GPs) in management of

Table 1. Demographic and background characteristics of the participants according to gender

	All participants (n=1104)*	Female (n=413)	Male (n=654)	P-value
Age (yrs.)	41.22±9.80	37.05±7.76	43.83±9.98	< 0.001
Clinical practice (yrs.)	12.72±9.27	9.33±6.99	14.65±9.77	< 0.001
Practice location (%)				
Urban	84.2	84.9	83.7	0.61
Rural	15.8	15.1	16.3	
CME* (yes) (%)	39.8	41.2	38.7	0.43

* Thirty-seven participants did not mention their gender.

**CME: Continuous Medical Education

Table 2. Diabetes related knowledge distribution of the participants in relation to taking part in CME programs.

	All participants (n=1104)*	CME Programs Yes (n=422)	CME Programs No (n=637)	P-value
FPG (70-130 mg/dl)	56.9%	66.4%	50.4%	< 0.001
PPG (<180 mg/dl)	51.1%	61.4%	44.7%	< 0.001
HbA1c < 7.0% (< 53 mmol/mol)	52.1%	57.6%	48.2%	0.003
Systolic BP (< 130 mmHg)	60.3%	68%	55.7%	< 0.001
Diastolic BP (<80 mmHg)	50.5%	55%	48%	0.03
TG (< 150 mg/dl)	30.8%	38.4%	26.5%	0.08
LDL (<100 mg/dl)	41.8%	51.4%	35.9%	< 0.001
HDL (>40 mg/dl)	35.5%	41.5%	32.5%	0.003

*Forty-five participants did not mention whether they had participated in CME programs or not.

FPG: Fasting Plasma Glucose

PPG: Post-Prandial Glucose

HbA1c: Glycosylated Hemoglobin

BP: Blood Pressure

TG: Triglyceride

LDL: Low Density Lipoprotein

HDL: High Density Lipoprotein

Table 3. Patients-care parameters depending on CME programs

	All participants (n=1104)	CME Programs Yes (n=422)	CME Programs No (n=637)	P-value
Physical activity				
Duration (≥180min/Wk)	47.2%	50.0%	45.1%	0.12
Distribution (≥ 3 times/Wk)	98.35%	98.5%	98.3%	1.00
Metformin (Primary treatment)	41.5%	45.6%	38.9%	0.03
ACEI/ARB	76%	73.5%	79.7%	0.03
Statins (always)	51.7%	57.9%	47.6%	0.001
Add basal insulin	27.9%	31%	25.8%	0.06
CVD risk assessment (≥50%)	84.7%	87.7%	82.7%	0.03

*Forty-five participants did not mention whether they had participated in CME programs or not.

ACEI/ARB: Angiotensin Converting Enzyme Inhibitors / Angiotensin Receptor Blockers

CVD: Cardiovascular disease

people with type 2 diabetes, and to explore the impact of formal continuous medical education (CME) programs.

Methods: A cross sectional survey was conducted in 2011. A total of 1104 GPs completed a self-administered questionnaire. The questionnaire focused on demographic and background characteristics, diabetes related knowledge, and patient care.

Results: The majority of the participants worked in large cities and 39.8% had taken part in CME programs in diabetes management. Overall, 52% of the GPs knew the treatment goal for HbA1c. The rate was slightly higher for those who had taken part in CME. Considering patient care, more than half of the participants answered correctly to the questions on duration and distribution of physical activity recommended by the guidelines, with no differential effect by taking part in CME programs.

Conclusions: This study shows that the knowledge and clinical practice of Iranian GPs in management of type 2 diabetes were not satisfactory. Furthermore, traditional CME programs in diabetes management are not effective in changing the GPs' clinical practice. Consequently, designing and implementing more effective strategies are necessary for improving patient health related outcomes.

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INSULIN RESISTANCE AND LIVER FAT CONTENT ARE STRONGLY CORRELATED IN TYPE 2 DIABETIC PATIENTS TREATED WITH MULTI-DAILY INJECTIONS (MDI) USING GOLD-STANDARD METHODS

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Type 2 Diabetic patients show both altered insulin secretion and insulin resistance (IR). They often have also steatosis. Gold-standard methods for assessment of IR and liver fat content are glucose clamp and spectroscopy RMN respectively. The aim of this work was to present preliminary data of a cohort of MDI treated diabetic patients who underwent gold-standard methods to assess IR, liver fat content and a CGM registration. Patients and Methods: We performed in MDI treated type 2 diabetic patients a BOTNIA test (which evaluates both insulin secretion and IR with glucose clamp), a spectroscopy RMN and a CGM

during one week. Results: for all patients (N = 12) we found significant negative correlations between M value (reflect IR) (N = 9), Si (ratio of M value and the mean steady-state insulin levels during the last 60 min of the clamp) (N = 7) and degree of steatosis (N = 9) (p = 0.03 and p = 0.023 respectively); there was a positive correlation between mean CGM glycaemia values, AUC over 180 mg/dl/day and degree of steatosis (p = 0.009 and p = 0.003 respectively). Conclusions: the suspected correlation between liver fat and IR from studies using simple methods to assess liver fat content and IR is demonstrate in our preliminary results using gold-standard methods. During CGM measures, mean hyperglycaemia and AUC over 180 mg/dl/day are also strongly correlated with liver fat content in type 2 diabetic patients treated with MDI.

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AN INCIDENT AND HIGH RISK TYPE 1 DIABETES COHORT - ADDRESS-2: CLINICAL PRESENTATION OF A MULTI-ETHNIC COHORT IN THE UK AND EFFECTS OF HUMORAL AUTOIMMUNITY

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Aims: Describe a multi-ethnic cohort of volunteers with incident Type 1 diabetes (T1D) and their siblings, recruited with a view to participating in aetiopathogenesis and early intervention studies.

Methods: Patients with T1D, 5–60 years were recruited in the UK within 6 months of diagnosis. Clinical and demographic data were stored; serum, extracted DNA and peripheral blood lymphocytes were frozen for later analysis.

Results: Between September 2011 and February 2014, 1,580 patients were recruited (1,453 North European; 127 non-European) from 134 sites in England and Wales. 58% were male. One or more of osmotic symptoms, weight loss, fatigue were present in 1,555. Symptoms were present for a median of 3 weeks (IQR 2–6). Symptom duration increased with age at diagnosis (p < 0.001), female gender (p < 0.001), European ethnicity (p = 0.002). Ketoacidosis was the presenting feature in 42% (European-43%, non-European-38%; p > 0.05) and was independent of gender or age. Recruited siblings had similar age, BMI and birth weight.

84% of 926 patients that donated serum had evidence of humoral autoimmunity. AAb positive(AP) patients were younger (AP:median age 19 y, (IQR 12–31); AN:median age 30.5 y, (IQR 20.5–40); p < 0.001). Rate of humoral autoimmunity decreased with age (p < 0.001) and was higher in European than non-European patients (85% vs 67%; p < 0.001). Rate of ketoacidosis at presentation was comparable (AP-43%; AN-39%; p > 0.05).

Conclusions: This is a registry-based recruitment study of representative patients with clinical diagnosis of T1D and their siblings, over a wide age-range. A high proportion had ketoacidosis at presentation, irrespective of ethnicity, gender, age. Humoral autoimmunity was absent in 16% and did not affect ketoacidosis rate.

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ASSOCIATION BETWEEN SELF-MONITORING BLOOD GLUCOSE (SMBG) AND QUALITY OF LIFE IN A NATIONAL COHORT OF PATIENTS WITH TYPE 1 DIABETES MELLITUS

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Objective: To determine the relationship between the daily frequency of SMBG and quality of life among patients with T1D in routine clinical care in Brazil.

Research Design and Methods: This was a cross-sectional, multicenter study conducted between December 2008 and December 2010 in 28 public clinics in 20 Brazilian cities. Data were obtained from 1,813 adult patients (56.7% females, 57.9% Caucasians), aged 29.6 ± 9.9 years with diabetes duration of 14.1 ± 8.4 years. Quality of life was evaluated by EuroQol (EQ-5D).

Results: The prevalence of SMBG was 84.7%. The mean number of SMBG performed daily was 3.25 ± 2.0. 25.5% of patients performed at least three BG daily. No difference was noted in EuroQol between patients who performed SMBG and those who did not. Considering the group of patients who performed SMBG, EuroQol analysis did not show association between the daily frequency of SMBG and mobility, personal self-care and usual activities. An association was found with pain/ discomfort (p = 0.0001), anxiety/depression (p = 0.0001) and the health status punctuation (p = 0.02). No correlation was found between the number of SMBG /day and health status punctuation (r = − 0.04, p = 0.09).

Conclusions: In conclusion, despite the known advantages of SMBG over glycemic control, the majority of T1D patients did not measure glycaemia as recommended. The frequency of SMBG can influence some aspects of quality of life mainly those related to pain, discomfort and anxiety. These aspects have to be taken into account to overcome the barriers and guarantee the increase of SMBG in order to get a better metabolic control.

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REVIEW OF SELF-MONITORING OF BLOOD GLUCOSE USE IN PHASE III CLINICAL STUDIES OF INSULIN ANALOGUES

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Objectives: Safe and efficacious insulin therapy of diabetes mellitus requires initial dose titration and regular dose adjustments based on blood glucose (BG) monitoring. Our objective was to explore the use of BG-measurement in phase-III clinical trials of insulin analogues, as these studies provide essential safety and efficacy information for regulatory authorities and are the base for insulin analogues' marketing approval.

Methods: A systematic review of phase-III trials of rapid-acting insulin analogues (Insulin-Lispro, -Aspart and -Glulisine) and pre-mixed insulin analogues (Biphasic Insulin-Aspart, and Insulin Lispro-Mix) was conducted. Trials were identified through manufacturers' databases. Search for reports was performed in Medline and registry of clinical trials (clinicaltrials.gov). The European Medicines Agency was contacted to provide available Clinical Study Reports.

Results: In total 46 trials were included. BG measurement was reported in 98% of the studies. BG was measured by self-monitoring of blood glucose (SMBG) alone in 84%, by laboratory alone in 7%, and both SMBG and laboratory in 9% of studies. In total, 91% of the studies reported utilization of SMBG. Majority of studies (98%) reported insulin therapy adjustments based on BG measurements.

Conclusions: The findings suggest that BG monitoring in general and SMBG specifically are co-dependent technologies with insulin analogues, as BG measurement is used in most phase-III registration trials to establish safe and efficacious administration and is furthermore recommended in the labels of insulin. The indispensable role of SMBG in treatment of insulin-dependent patients should receive the attention of payers to consistently assess and reimburse SMBG along with insulin.

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EFFECTS OF FLUOXETINE ON E-CADHERIN DISTRIBUTION IN PANCREATIC BETA CELLS

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Background: Major depressive disorder (MDD) is a common psychiatric illness and it affects as many as 840 million people. MDD and Type 2 diabetes (T2D) are disorders with mutual risk factors identified in prevalence study reports. Antidepressant treatment could be another critical factor affecting the bidirectional associations between MDD and T2D. Long-term use of selective serotonin reuptake inhibitors (SSRIs), the most commonly prescribed class of antidepressants, is associated with an increased risk of developing T2D. However, the mechanism(s) underlying this association remains elusive.

Methods: Here we examine the effects of the SSRI fluoxetine (Prozac®) on beta cell function employing MIN6 cells, a mouse beta cell line, to elucidate the underlying molecular mechanisms.

Results: We showed that Fluoxetine treatment significantly reduced glucose stimulated insulin secretion (GSIS). Fluoxetine-treated cells formed smaller colonies of loosely packed cells. We discovered that there is a reduction of cell-cell adhesion. Moreover, we found accumulation of E-cadherin appears in cytoplasm. Cell cycle analysis revealed that Fluoxetine induced the percentage of sub-G1 population, subsequently leading to apoptosis. The characteristic of apoptosis was also confirmed by the presence of active caspase-3. Fluoxetine treatment significantly reduced ERK activity. Taken together, our results suggested that use of SSRI antidepressants may increase the risk of new-onset T2D by increasing beta cell dysfunction concomitant with a reduction of cell-cell adhesion which may which may contribute to cell apoptosis in pancreatic beta cells.

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HYPOGLYCEMIA-RELATED HEALTHCARE COSTS AMONG U.S. PATIENTS WITH TYPE 2 DIABETES

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Background: Hypoglycemia is a major complication in patients with diabetes and is associated with significant reduction in quality of life. While tight glycemic control remains the goal of diabetes management to reduce further complications, the barrier of hypoglycemia is a limiting factor of maintaining glycemic control.

Objective: To estimate the healthcare costs of hypoglycemia among U.S. privately insured Type 2 diabetes patients.

Methods: Type 2 diabetes patients with a minimum of 1-year of continuous enrollment to commercial plans from index date, defined by first fill date for oral antidiabetics (OADs) or insulin were followed until the patients experienced hypoglycemia requiring medical intervention; reached the end of study period (12/31/2012); or had lapse in insurance coverage. Diabetes-related complications were identified within 90 days from the index date. Pharmacy claims were evaluated for diabetes treatment regimens. Healthcare costs were defined as the amount paid to providers plus patient cost share, adjusted to 2012 dollars.

Results: The average cost of a hypoglycemic inpatient visit was higher for patients on one OAD compared to patients on at least two OADs ($22,913 vs. $20,574) with the highest average cost of $24,155 incurred by the youngest group (ages 18–34). The average costs of outpatient visits including emergency and non-emergency settings for monotherapy and combination therapy were $426 and $471, respectively. The total cost of hypoglycemia borne by payers and these patients over the 5-year period was $148,744,959.

Conclusion: Considerably high costs of hypoglycemia were observed among type 2 diabetes patients in a large U.S. claims database.

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HEALTH RELATED QUALITY OF LIFE OF ADOLESCENTS WITH TYPE 1 DIABETES FOR TURKISH POPULATION

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Purpose: The purpose of the study was to evaluate whether the health related quality of life (HRQOL) of adolescents with type 1 diabetes was associated with adolescents' gender, HbA1C values, frequency of testing blood glucose in a day and received diabetes education and, whether the teen and parent proxy reports were consistent.

Method: 104 adolescents aged 13–18 with type 1 diabetes and their parents from a diabetes center participated in this descriptive study. The Pediatric Quality of Life Inventory 4.0 Generic Core Scales (PedsQL 4.0) and PedsQL Diabetes Module 3.0

were teen and parent proxy reports were administered to the adolescents and their parents for data collection.

Results: Mean ages of participants were 14.65 ± 1.51. The parents reported lower diabetes-specific HRQOL than adolescents themselves ($p < .01$). Also parents reported that their children had more difficulties regarding Treatment ($M = 66.65 \pm 17.80$; 78.23 ± 16.65, respectively; $t = 5.50$; $p < .01$), Worry ($M = 70.11 \pm 25.64$; 75.72 ± 24.33, respectively; $t = 2.12$; $p < .05$) and Communication ($M = 60.33 \pm 32.19$; 80.60 ± 24.14, respectively; $t = 4.70$; $p < .01$). Scales were compared with what the children experienced. There were no significant effects for gender, HbA1C values, received diabetes education for diabetes-specific HRQOL. However adolescents reported that they were worried when they tested their blood glucose more than 4 times a day with respect to Worry Scale ($t = 2.51$, $p < .05$).

Conclusion: Based on the research results, development of diabetes-related technologic devices can help improve the HRQOL of adolescents with type 1 diabetes. These kinds of devices may facilitate in treatment adherence and reduce worry about treatment.

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USE OF BOLUS CALCULATOR DURING CARBOHYDRATE COUNTING IMPROVE GLYCEMIC CONTROL AND FACILITATE LEARNING IN ADULT WITH TYPE 1 DIABETES

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Background: In type 1 diabetes carbohydrate counting allows to get better control and it is recommended in the management of the disease.

Aim: To investigate the effect of carbohydrate counting course using automatic bolus calculator in adult with type 1 diabetes.

Material and Methods: We enrolled 12 type 1 diabetic patients (age: 40 ± 14; HbA1c: $8.2\% \pm 0.9$; blood glucose, BG: 182 ± 36 mg/dl) who participated at an educational group course with healthcare team, made up of medical doctors, nurses and dietitian, followed for 6 months.

Patients were trained about carbohydrate counting and use of a bolus calculator for management of insulin therapy. From self-monitoring BG we downloaded some indices of glycemic variability, included HBGI, LBGI, SD of BG at baseline and re-evaluated after 6 months. A questionnaire to check their learning was administered at the beginning and during follow up.

Results: After 6 months we observed a significant improvement of HbA1c (8.2 ± 0.98 vs 7.6 ± 0.7 p 0.02) without any difference in LBGI (p: 0.203). HBGI and SD of BG have not undergone significant change. At baseline correct answers in the questionnaire were 30%, while at follow-up were 71%.

Conclusions: Educational group care that considered use of a bolus calculator for application of carbohydrate counting improved glycemic control without risk of hypoglycemia in patients with type 1 diabetes. The course had improved learning of

patients, probably by enhancing the sense of efficacy in relation to their ability to manage the disease.

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GENETIC AND RISK FACTORS FOR DYSGLYCAEMIA IN THE FAMILIES OF TYPE-2 DIABETES PATIENTS: THE DESCENDANCE SURVEY

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Type-2 diabetes (DT2) is a familial disease involving transmission of genetic susceptibility and environmental factors. Some 70 genetic markers for DT2 have been identified. Although accounting for only 10% of inheritability, they may be involved in disease development over several generations.

We aim to determine familial DT2 inheritability (environmental/genetic) by studying families over at least 2 generations, with each generation (G1 parents, G2 children) having at least one member with DT2 and one without dysglycaemia >35 years (confirmed by glucose tolerance test [GTT] and HbA1c). Polymorphisms of 70 genes associated with DT2 in genome-wide association studies are genotyped or attributed using Illumina Infinium HumanCore BeadChips and familial transmission disequilibrium tests are then performed.

We have analysed 54 families comprising 113 diabetic/prediabetic subjects (G1 = 57; age = 75.2 ± 8.6; BMI = 30.1 ± 5.1/G2 = 56; age = 50.7 ± 8.5; BMI = 30.7 ± 5.5) and 95 subjects non-dysglycaemic on GTT (G1 = 18; age = 68.9 ± 8.1; BMI = 26.8 ± 4.9/G2 = 77; age = 48.7 ± 8.4; BMI = 27.1 ± 5.4). Five genetic variants (P < 0.05) were nominally associated with familial DT2 transmission (SPRY2, CILP2, HNF1A, GCK and MTNR1B). Statistical power at this preliminary stage is only 23.5%, but would increase to 80% with 350 cases and 350 control subjects in generation G2.

These preliminary data demonstrate a trend towards association of certain genetic factors with familial DT2 transmission. Participation of pharmacists in the Paris region in the Descendance survey will ensure inclusion of the requisite number of families. The ultimate goal is to obtain an equation allowing prediction of adult onset of diabetes in the children of parents with DT2, based on familial genetic, epigenetic and environmental data.

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EFFECT OF SIMULTANEOUS KIDNEY–PANCREAS TRANSPLANTATION IN PATIENTS WITH TYPE 1 DIABETES TO STABILIZE/PROGRESSION OF COMPLICATIONS

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Objective: To evaluate the effect of successfully simultaneous kidney- pancreas transplantation (SPK) in patients with type 1 diabetes mellitus (T1DM) to stabilize/progression of complications.

Materials and Methods: The study included 15 patients on standard immunosuppressive triple therapy. The average duration of T1DM 22 years [20;31], the duration of diabetic nephropathy (DN) -8 years [6;10]. All patients remained in the study for at least 24 months [8;36] after the transplantation.

Results: The mean level of glycated hemoglobin (HbA1c) in the group before the study was 8.65% [8.4;9.1], then decreased to individualising glycemic targets- 5.7% [5.5;5.8] after SPK. According to a continuous glucose monitoring system using «iPRO2» marked euglycemia during the day (glycemia 3.9–8.9 mmol/l-89%, to lower than 3.9 mmol/l-11%, higher than 8.9 mmol/l-0% of the time of day). The examination determined normoalbuminuria, GFR 74 [67;89]. All patients had normal levels of hemoglobin 120 [112;130], parathormone 77.3 [60.4;92.5], phosphorus 1.2 [1.05;1.4], blood pressure110 [100.0;120]. In the post-transplantation period the progression proliferative diabetic retinopathy (DR) was observed in 20% of patients, followed by performing a vitrectomy and additional sessions of laser panretinal photocoagulation. At 86% (13 people) identified nonstenotic atherosclerosis of the lower extremities, 1 patient- significant stenosis of the popliteal, posterior tibial artery to the right, requiring holding endovascular balloon angioplasty. In 33% (5 people) developed ulcerative defects in the lower limbs and 3 people observed the progression of the chronic stage of osteoarthropathy.

Conclusions: In addition to the recovery of renal function and euglycemia in patients with T1DM undergoing SPK, noted the progression of DR and diabetic foot syndrome, which bear witness to the genesis of multivariate diabetic complications requiring verification and timely therapy.

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UNDERSTANDING THE CONSTRUCT OF FAMILY COMMUNICATION USING THE FAMILY COMMUNICATION SCALE (FCS) IN ADOLESCENTS WITH TYPE 1 DIABETES (T1D) AND THEIR PARENTS

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The impact of family communication on health behaviors and glycemic control in youth with T1D is largely understudied. This study aimed to assess psychometric properties of a newly developed questionnaire the Family Communication Scale (FCS) and the relationship between family communication and division of responsibility, conflict, and glycemic control. A unique feature of the FCS is that it measures both frequency and tone (positive vs. negative) of communication.

As part of an outpatient Artificial Pancreas remote monitoring study, 110 youth (50% female) with T1D between 12–18 years (14.47 ± 1.78) and their parents completed the FCS during a clinic visit. They also completed division of responsibility, diabetes management, and family conflict questionnaires.

Internal reliability of the FCS for both youth and parent communication frequency was good (a = .843, a = .809 respectively), and reliability for youth and parent communication tone was excellent (a = .934, a = .976 respectively). Negative correlations were found between communication tone and glycemic control for youth (p < .000). Negative correlations were also found between communication frequency and division of responsibility for parents and youth (p < .142, p < .133 respectively), suggesting that more frequent communication is correlated with parents taking more responsibility.

The FCS appears to be a reliable instrument for assessing frequency and tone of parent-youth communication in T1D. In addition, frequency and tone of family communication is associated with HbA1c, division of responsibility and family conflict. It is important to understand the impact of family communication on diabetes management and HbA1c, particularly as we advance into diabetes technology with parental monitoring capabilities.

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HYPOGLYCAEMIA, ENDURANCE EXERCISE, PEER SUPPORT AND CONTINUOUS GLUCOSE MONITORING: TEAM BLOOD GLUCOSE CYCLING RESEARCH

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Introduction: Hypoglycaemia is a significant obstacle for people with type 1 diabetes undertaking physical activity, with excursions both during and after the period of exercise. Continuous glucose monitoring (CGM) and peer support may mitigate this risk. The impact of endurance exercise on hypoglycaemia during a multi-day event was studied.

Methods: Team Blood Glucose cycled from Barcelona to Vienna in 2014. The event comprised three five-day stages (mean

TABLE 1. PERCENT (%) OF TIME SPENT HYPOGLYCAEMIC
IN RIDERS WITH DIABETES (TISSUE GLUCOSE)

	Tissue glucose <4.0 mmol/L			Tissue glucose <3.3 mmol/L			Tissue glucose <2.8 mmol/L		
	Stage 1	Stage 2	Stage 3	Stage 1	Stage 2	Stage 3	Stage 1	Stage 2	Stage 3
Participant 1	5	7	6	2	3	3	2	2	1
Participant 2	2	3	4	0	1	1	0	0	1
Participant 3	10	8	8	5	3	3	1	1	1
Participant 4	5	7	3	2	2	1	0	0	0
Participant 5	2	2	4	1	1	2	0	1	0
Participant 6	1	9	0	0	5	0	0	2	0
Participant 7	8	6	12	3	1	5	2	0	2

distance 159 km/day) with a rest day between each stage. Volunteers wore Dexcom G4 continuous glucose monitoring devices and self-adjusted their insulin dosage with peer-support.

Results: We recruited 7 volunteers with diabetes (age 26–47 years) who cycled all stages. Continuous subcutaneous insulin infusion (n = 5) and multi-dose injections (n = 2) were used. Data showing the percent time hypoglycaemic (<4.0 mM, <3.3 mM and <2.8 mM) are shown (Table 1). There were no significant differences in hypoglycaemia between stages within individuals or across the group.

Discussion: Despite long duration exercise and significant energy expenditure hypoglycaemia frequency and severity did not change as the cycling event progressed. This may be due to peer-support and education, with further benefit from CGM. Further work to delineate mechanisms underlying this are required.

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SPECTRUM—A NEW PEDIATRIC QUALITY-ASSURED STRUCTURED EDUCATION PROGRAM FOR CONTINUOUS GLUCOSE MONITORING (CGM)

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CGM is a useful tool to optimize glycemic control and to reduce hypoglycaemia, offering an important impact on long term metabolic control.

Current limitations of CGM include economic and behavioural barriers, sensor accuracy and the lack of a quality-assured structured education program for children, adolescents and their parents.

Therefore we develop together with the Adult Spectrum Group (leadership: B. Gehr) of the Working Group for Diabetes-Technology (AGDT) of the German Diabetes Association (DDG) an education and treatment program for real-time CGM called **Spectrum** ('**S**chulungs- und Behandlungs**p**rogramm für **e**igenständiges **c**ontinuie**r**liches Gl**u**cose-**M**onitoring').

In several modules all aspects of CGM use will be discussed. Module 0 (introduction) will inform the patients about positive and possible negative experiences in long-term CGM use so that they will get a realistic view of this technology beforehand. The main modules cover basic knowledge about CGM, alarm-settings, glucose trend arrows, CGM in everyday life and CGM software. In an additional module particularly adapted for pediatric patients, children, adolescents and parents are trained how to assess CGM data, improve CGM use and implement it in their daily life. In addition emotional coping with unexpected fluctuation of glucose values and feelings of helplessness are addressed to prevent young people from surrender and resignation.

Spectrum provides patients and diabetes-teams the opportunity to optimize CGM use in an independent and effective way. Important conditions of this new education program are independency of manufacturers and product-neutrality allowing certification after evaluation with the goal of reimbursement from third party payers as further steps.

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LEPTIN:ADIPONECTIN RATIO—PREDICTOR OF METABOLIC RISK IN POSTMENOPAUSAL WOMEN

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Background: Adipokines secreted from adipose tissue including Interleukin-6, Tumor necrosis factor-alpha, Resistin, Adiponectin, and Leptin may contribute to the development of visceral obesity mediated adverse effects on glucose and lipid metabolism. Adiponectin and leptin are pro-insulin and play a protective role in metabolic syndrome. However increase adiposity leading to leptin resistance also contributes to high circulating leptin that may increase the risk for metabolic syndrome. So increase in Leptin:Adiponectin (L:A) ratio may be a predictor for cardiometabolic risk.

Methods: In the present cross sectional case-control study, 380 postmenopausal women were enrolled. Out of which 178 postmenopausal women with metabolic syndrome according to NCEPATP guidelines and 202 healthy control postmenopausal women without metabolic syndrome, anthropometrical measurements, lipid profile, glucose estimation were done and insulin, leptin and adiponectin level were determined by ELISA.

Results: Waist circumference, waist-to-hip ratio, body mass index, lipid profile, glucose and fasting plasma insulin were significantly higher in postmenopausal women with metabolic syndrome than in postmenopausal women without the syndrome ($p < 0.001$). Furthermore, L:A ratio was significantly correlated to WC, WHR, SBP, glucose, TC, TG HOMA-IR (r = > 0.5, p < 0.001) and negatively correlated with HDL (r = −0.65, p < 0.001) in pre- and postmenopausal women. No significant correlation of L:A ratio was found with BMI and insulin in pre- and postmenopausal women.

Conclusions: L:A ratio may act as an independent predictor for cardiometabolic syndrome in postmenopausal women.

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ASSOCIATION OF LEPTIN 2549C/A GENE POLYMORPHISM WITH METABOLIC RISK MARKERS IN PREMENOPAUSAL WOMEN

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Introduction: Leptin gene is one of potential candidate genes for metabolic syndrome. The present study was attempted to investigate whether the leptin gene polymorphism is associated with metabolic syndrome in Indian population.

Design: Totally 615 subjects were enrolled for the study, 305 women were with metabolic syndrome and 310 women were without metabolic syndrome according to NCEP-ATP III criteria. Anthropometric measurements were done in all the subjects. Fasting circulatory level of leptin, insulin, plasma glucose and lipid profiles were estimated along with calculation of insulin resistance. Leptin- 2549C/A promoter region polymorphism was done by RFLP method.

Results: Homozygous mutant genotype (AA) (CC v/s AA) (p = 0.03: OR = 1.68: 95% CI = 1.06–2.68) and mutant allele (A) (p = 0.02: OR = 1.30: 95% CI = 1.04–1.63) of the 2549 C/A leptin polymorphism were significantly observed in study population. The presence of the A allele were significantly associated with systolic blood pressure (p = 0.01), diastolic blood pressure (p = 0.03), LDL (p = 0.01), TC/HDL (p = 0.03) and LDL/HDL (p = 0.04) in study population.

Conclusion: This study concludes that leptin 2549 C/A gene polymorphism was significantly associated with cardiometabolic risk in premenopausal women

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GLYCEMIC CONTROL AND CLINIC ATTENDANCE OF EMERGING ADULTS WITH TYPE 1 DIABETES AT TRANSITION CARE CLINIC

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Background: Emerging adulthood is a challenging period for diabetes management with increased risk of poor glycemic control and loss of clinical follow-up. Our aim was determining if dedicated transition clinic for emerging adults with T1DM can improve glycemic control and visit attendance.

Methods: Observational study of 53 emerging adults (30 males) treated between 2010 and 2014 in a newly established transition clinic. The clinic is operated jointly by pediatricians and adult endocrinologists and treatment was provided by a multi-disciplinary team including a transition coordinator. Data collected included HbA1c levels, frequency of visit attendance, acute complications and quality of life. For 27 patients who previously attended the pediatric clinic in the same hospital, HbA1c levels and visit attendance in 3 years preceding the transition were also collected.

Results: Age at the transfer to the transition clinic was 22.1 ± 2.7 years and disease duration at the transfer 8.4 ± 5.0 years. Follow up duration at the clinic was 1.2 ± 1.1 years (range 0–3.5 years). Mean HbA1c levels decreased from $8.3 \pm 0.2\%$ at transfer to $7.3 \pm 0.2\%$ after a year ($p < 0.001$). Median number of visits in the year prior to transfer was 1 (range 0–5) and 4 (range 1–8) in the year post transfer ($p < 0.001$). The negative impact of diabetes on quality of life, disease-related worries and life satisfaction didn't change significantly after a year.

Conclusions: A dedicated transition clinic for emerging adults can facilitate good glycemic control and visit attendance. Diabetes care providers should be sensitive to the developmental aspects of emerging adulthood and tailored support is required.

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MANAGING PSYCHOLOGICAL STRESSES IN CHILDREN WITH TYPE 1 DIABETES—A CHALLENGE ON TOP OF INSULIN THERAPY!

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Children with type 1 diabetes often experience psychological stresses associated with their condition. We present a case, who with multiple stress factors and subsequent progression of manifestations from tics to pseudo seizures, posed a challenge to the multidisciplinary team to manage her diabetes.

This 8 year old girl was diagnosed with diabetes and hypothyroidism simultaneously. She was initiated on basal bolus regime and her initial control was good.

Seven months later, feeling lonely and miserable, she began to engage in psychological therapies. Her stress increased when her mum was diagnosed with chronic illness with her dad already suffering from one! This, in conjunction with coping with her conditions and complex medication regime, compounded her personal stresses.

Four years post diagnosis, at twelve years of age; she experienced fainting episodes at school. There was no associated hypoglycaemia or focal neurology and an electroencephalogram was normal. Shortly after, she developed severe motor tics resulting in injury, absence from school and sleep deprivation. These progressed into tonic-clonic pseudo seizures.

Currently her diabetic control remains challenging. Her tics and pseudo seizures are debilitating, have necessitated admission to the local paediatric ward and further psychotherapy.

Childhood diabetes is frequently diagnosed during a challenging transitional phase from childhood to adolescence. With additional stresses, patients may develop complex behaviours, which can interfere with daily activities. Therefore, we recommend an early multidisciplinary team approach with psychotherapy intervention and effective communication to optimise patient's quality of life.

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DEVELOPMENT OF A NEW MEASURE TO ASSESS PATIENT TREATMENT SATISFACTION WITH GLUCOSE MONITORING DEVICES

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Currently, there is no well-accepted, validated method to assess treatment satisfaction with glucose monitoring devices or the impact of such devices on patient-reported outcomes. We developed and validated a new, comprehensive instrument to address these needs.

Items were developed from interviews with 15 T1D and T2D adults and 8 healthcare professionals, leading to an initial set of 42 items reflecting positive and negative aspects of glucose monitoring systems (5-point scale, agree to strongly disagree).

460 patients (254 T1Ds, 206 T2Ds), recruited from an online research registry, completed the initial 42 items plus measures assessing quality of life (WHO5), diabetes distress (DDS), self-care behaviors (SDSCA), attitudes towards blood glucose monitoring (A-BGM), and a previously developed measure of blood glucose device satisfaction (BGMSRQ). Each participant received a $10 gift card.

For T1Ds and T2Ds respectively, mean age was 47/60, % female was 52/61, mean years since diagnosis was 27/16. Multiple factor analyses of the 42 items yielded overlapping but separate scales for T1Ds and T2Ds. Each Glucose Monitoring Satisfaction (GMS) scale contained 15 items, each with 4 subscales (GMS-T1D alpha = .86; GMS-T2D alpha = .90). Both GMS scales share subscales of Emotional Burden, Behavioral Burden and Openness. T1Ds have an additional subscale for Trust, and T2Ds for Worthwhileness. GMS-T1D and GMS-T2D total score and subscale scores were significantly correlated with WHO5, DDS, SDSCA, A-BGM and BGMSRQ, indicating good concurrent validity.

GMS-T1D and GMS-T2D are reliable, valid measures of glucose device satisfaction and impact for use with adults with diabetes.

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ASSOCIATION OF PLASMA OMENTIN-1 LEVEL WITH INSULIN RESISTANCE IN CHRONIC KIDNEY DISEASE PATIENTS

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Introduction: The early prediction and prevention of cardiovascular disease risk factors in chronic kidney disease (CKD) patients are very important. The plasma level of omentin was found to be associated with different conditions such as insulin resistance, diabetes mellitus, obesity, endothelial dysfunction and atherosclerosis. The aim of the study was to clarify the influence of changes in levels of circulating omentin-1 on the insulin resistance in CKD subjects with and without type 2 diabetes mellitus.

Subject and methods: Seventy eight patients were enrolled in this cross-sectional study. They included 23 patients with CKD on conservative treatment, 35 patients on maintenance Hemodialysis and 20 healthy volunteers. Serum concentrations of omentin-1 was determined by an enzyme-linked immunosorbent assay (ELISA) kit.

Results: Significant difference in plasma omentin-1 level between diabetic patients and non-diabetic patients in either predialysis group or HD group was noticed. There was also a significant difference in plasma omentin-1 level between non diabetic patients in predialysis group and HD group and between diabetic patients in predialysis group and hemodialysis group. There was a significant positive correlation between Plasma omentin-1 level and fasting insulin level, HOMA-IR, IL-6 and CRP and significant negative correlation with eGFR.

Conclusion: plasma omentin-1 concentration was higher in CKD patients. In addition, there is an association between omentin-1 and insulin resistances in hemodialysis patient which may considered as a cardiovascular risk factor in CKD patients.

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FACTITIOUS HYPOGLYCEMIA IN TYPE 1 DIABETES (T1D): CLINICAL CASES AND EXPERIMENTAL TEST

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T1D adolescents who advisedly induce false Low Blood Glucose (LBG) readings registered in the meter's memory are presented and the mechanism is elucidated. Subject 1, HbA1c 9.6%, presented high truancy justified by frequent fasting LBG. An asymptomatic LBG (14 mg/dl) was immediately repeated by an adult showing 170 mg/dl. Although the meter was replaced, frequent LBG persisted. Subject 2, HbA1c 12.6%, presented with persistent nocturnal polyuria and polydipsia, associated with intriguing frequent fasting LBG (10–20 mg/dl), resulting in skipped insulin and high carbohydrate breakfast. No LBG was confirmed in ward.

Objective: to check the prevalence of factitious LBG readings and to elucidate the mechanism.

Method: Computer records of 84 subjects using Accu-Chek Active meter (photometric BG determination by oxidoreductase) were analyzed. Twenty-six subjects exhibited events of LBG (10–20 mg/dl), with instant replay and discordant results. Two healthy subjects performed 25 consecutive BG tests varying the location and size of the blood drop.

Results: Eight BG results were recorded in the meter (7 within normal range, and one false LBG), 17 error alerts (E4, E7 and ERR) were not recorded. Consecutive BG of 93, 14 and 94 mg/dl separated by 3 and 4 min were obtained. The false LBG (14 mg/dl) was induced depositing a small blood drop on the center of the strip test area.

Conclusion: An insufficient blood drop results in false LBG readings. Most parents react properly repeating the test, however, patients must be aware to avoid wrong decisions and it is a fact that some adolescents advisedly manipulate the results.

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MODELLING GLUCOSE KINETICS DURING EUGLYCAEMIC CLAMP FOLLOWING ADMINISTRATION OF RAPID ACTING INSULIN ANALOGUE

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The euglycaemic clamp technique may be used to determine time-action profiles of modern insulin analogues. We use mathematical modelling to describe the relationship between the dextrose infusion rate on the input and blood glucose levels on the output, to reconstruct the time-action profile independent of oscillations induced by automated delivery of dextrose during the clamp. We developed a three-compartment model to describe glucose kinetics combined with (i) a Fourier series description of the net glucose disposal and (ii) a transit compartment model to estimate the time-delay in the appearance of intravenously infused dextrose in plasma. The model was identified using data collected during eight clamp studies in four healthy subjects [male/female 3/1, age 43(16) years, BMI 26(2.8) kg/m^2, mean(SD)] following administration of a subcutaneous bolus of rapid acting insulin analogue aspart [25.0(1.5) U]. Satisfactory model fit and physiologically plausible parameter estimates of the glucose kinetics model were observed. The time-delay and the distribution volume of the central compartment were estimated accurately at 3.2 ± 0.1 minutes and 0.054 ± 0.007 l/kg, respectively (mean $\pm$ SE). The fractional transfer rates estimates showed distinction between a rapid-equilibrating compartment and a slow-equilibrating compartment. The eight reconstructed insulin time-action profiles derived by the model show a high degree of smoothness and physiological plausibility. In conclusion, the model represents well the glucose kinetics during euglycaemic clamp studies and a physiologically plausible time-action profile can be obtained to assess pharmacodynamic attributes of the studied insulin analogue.

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THE ROLE OF TCF7L2 GENE POLYMORPHISM IN THE DEVELOPMENT OF TYPE 2 DIABETES

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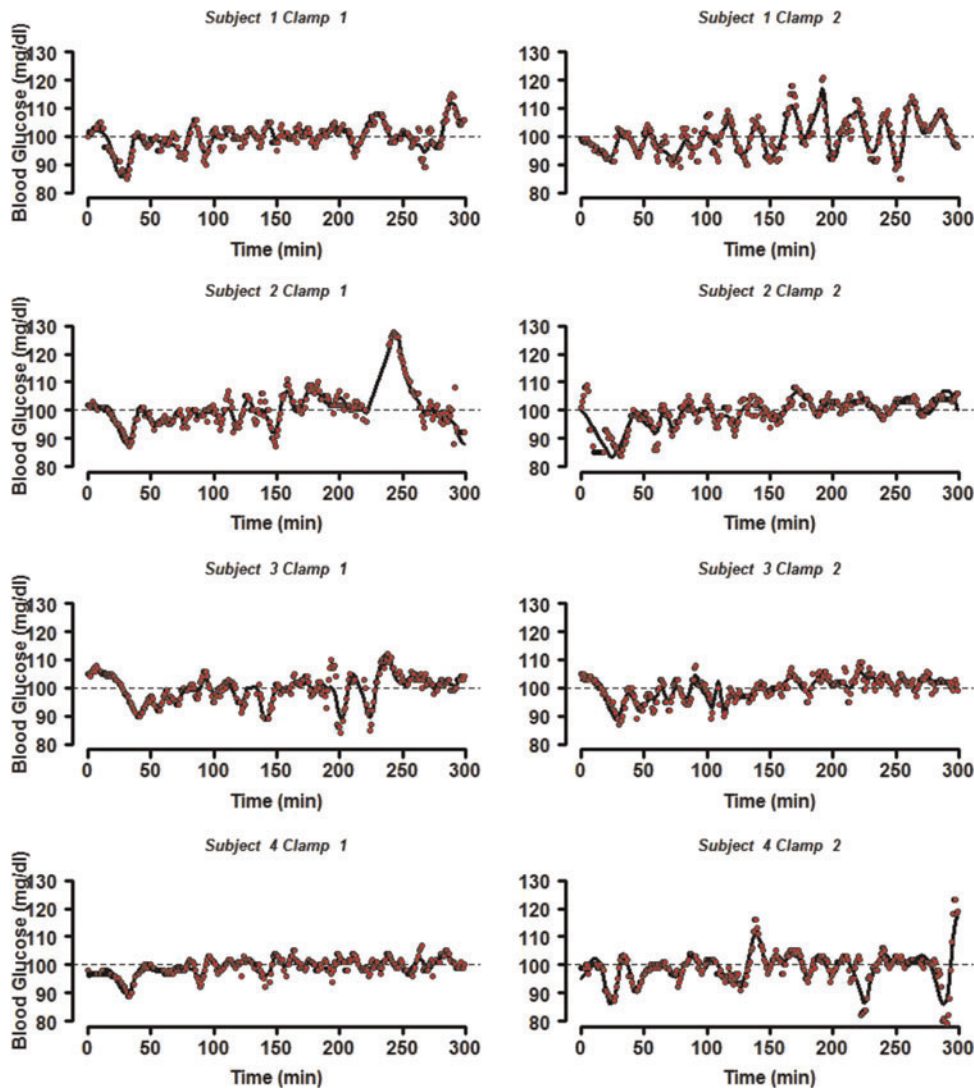
FIGURE. Model fit.

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Nowadays one of the worldwide popular medical studies is the study of the genes responsible for the development of insulin resistance, which is an important part in the formation of type 2 diabetes (DM2). Meanwhile the role of heredity in another pathogenetic link of DM2 - genetic defects in β-cells of the pancreas is still less studied. It is believed that gene polymorphism TCF7L2 affects the amount and functional activity of the β-cells.

The aim of the study was to investigate the gene polymorphism TCF7L2 and its associations with indicators of carbohydrate and lipid profiles in patients with DM2 and essential hypertension (EH). The main group of our study consisted of 252 patients with DM2 in combination with EH. The group of comparison consisted of 70 patients with EH without DM2.

Thus 63,9% of patients with DM2 were considered as the patients with presence of the allele T, what is associated with the progression of DM2; 54,3% of patients without DM2 were diagnosed with genotype CC, that reduces the risk of DM2 progression. In both groups the presence of the allele T led to higher glucose levels and HbA1c at lower HOMA. The patients with DM2 and genotype TT were diagnosed with a lower BMI and higher levels of triglycerides than other genotypes.

Conclusion: We established the association of allele T polymorphic marker rs7903146 TCF7L2 gene with the progression of DM2. The genotype TT in patients with DM2 inversely correlated with BMI and directly correlated with the levels of triglycerides.

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THYROID PEROXIDASE AUTOIMMUNITY AND THE EFFECT ON THYROID FUNCTION IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES

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Objective: To investigate thyroid peroxidase autoimmunity and the effect on thyroid function in a large cohort of type 1 diabetes children and adolescents.
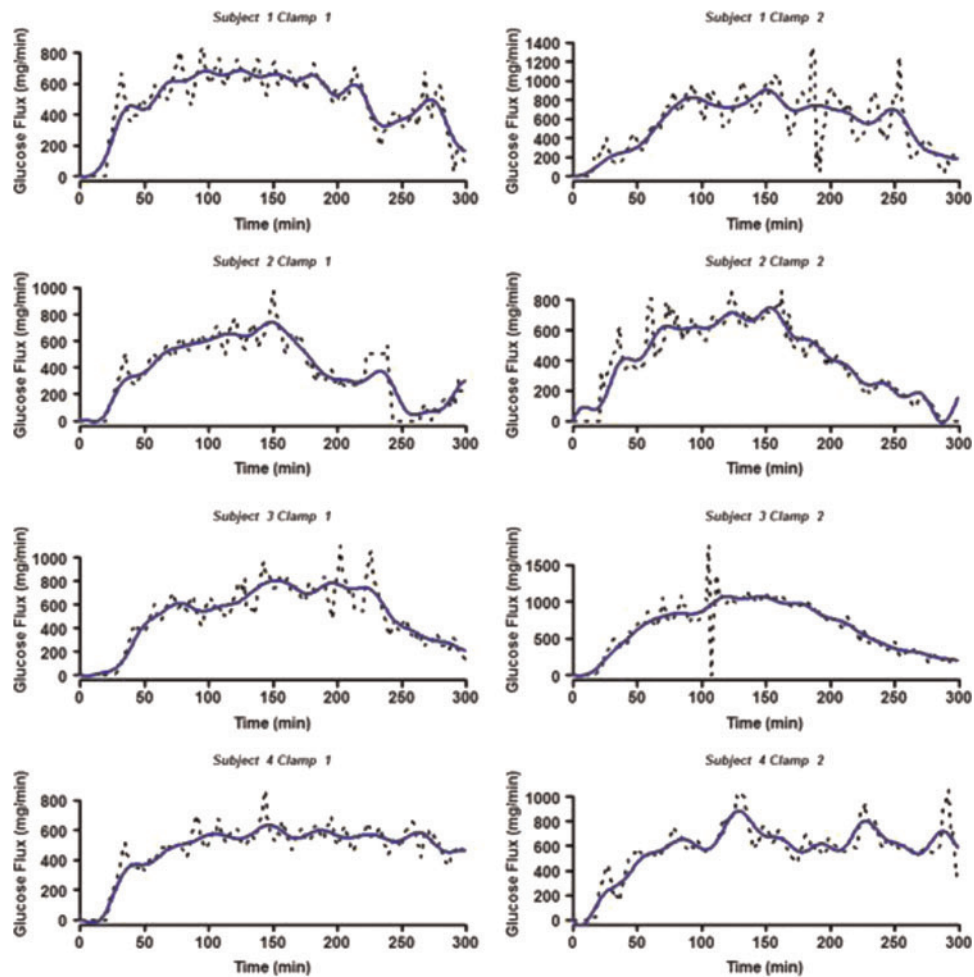
FIGURE. Insulin action (blue).

Methods: Retrospective analysis of data from 1404 type 1 diabetes patients (1 < 25 years of age, 49.3% males) treated between January 1993 and December 2013 in our diabetes center. In total 3893 antibodies to thyroid peroxidase(ATPO) values were documented, 1927 values of males at median age 13.9 years (IQR 10.0–17.3) and 1966 of females at median age 14.6 years (IQR 11.0–18.0). ATPO values ≥60 U/ml and TSH values > 4 mU/l were considered significantly elevated. Statistical evaluation: ANOVA, Student's t-test.

Results: ATPO values were elevated at least once in 185 patients (13% of all patients). Females were 2.4 times more frequent affected compared to males (18.5% vs 7.7%) and ATPO values were significantly higher in females with median 257 U/ml(IQR 76–795 U/ml) vs median 191 U/ml(IQR 58–508 U/ml) in males, irrespective of age ($p = 0.014$). They were cause for hypothyroidism in 20 males(38%) and in 39 females(30%). Maximal ATPO values of patients with hypothyroidism were significantly higher than of those with no thyroid impairment, mean 962 U/ml (IQR 373–1865 U/ml) vs 292 U/ml (IQR 123-853 U/ml) ($p = 0.039$).

Conclusion: Incidence of thyroid peroxidase autoimmunity was found substantially more often in female patients and their ATPO values were significantly higher. However, consecutive hypothyroidism occurred similarly in about one third of the male and female patients. We present a rational approach for the evaluation of thyroid autoimmunity and function.

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STRUCTURED GLUCOSE MONITORING AS PREDICTOR OF EFFECTIVENESS AND SAFETY OF INSULIN TREATMENT IN T2DM PATIENTS

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Results obtained by SMBG can be used to predict results of insulin treatment when initiated in patients with T2DM. This paper compares results of non-structured vs. structured SMBG using Accu-Check 360 View protocol during one month after start of insulin.

Design as approved by IRB: 80 T2DM patients who first started insulin treatment were randomized to standard education and care or to structured SMBG group and were followed for 3 months with monthly visits. HbA1c, body weight change and number of hypoglycemic episodes were assessed. Patients SMBG results for first month were used for assessment of glucose means, quartiles, SD. In structured SMBG group separate evaluation of variability was performed for 3-days 7-points values taken before scheduled visit.

Results: HbA1c in standard care group only mildly correlated with SMBG results ($R = 0.35$ $p = 0.02$ for mean glucose),

similar results for lower and upper quartiles and no correlation with SD. Number of hypoglycemic episodes had highest correlation with glucose lower quartile (R = −0.55 p = 0.0001) followed by mean glucose and SD (R = −0.41 p = 0.007 for both).

Structured SMBG demonstrated higher correlation of HbA1c with mean glucose (R = 0.56 p < 0.0001) and upper quartile (R = 0.55 p < 0.0001) and similarly no connection between SD and HbA1c. Number of hypoglycemic episodes correlated also more strongly with SMBG – for lower quartile and mean (R = −0.7 and −0.64 p < 0.0001). Then only View360 values were taken for evaluation these correlations persisted with similar strength.

Conclusion: Structured SMBG during first month is more reliable in predicting HbA1c and hypoglycemia risk in T2DM patients starting insulin treatment.

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THE PREVALENCE OF METABOLIC SYNDROME IN PATIENTS WITH DIAGNOSED TYPE 2 DIABETES, AND ITS CORRELATION WITH METABOLIC CONTROL

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Background and aims: The identification of metabolic syndrome (MS) is important for the appropriate management of associated cardiovascular risk factors. The aim of our study was to determine the prevalence of the MS in a selected population of type 2 diabetes.

Patients and methods: We randomly selected 500 patients with T2 diabetes in different cities of Albania. 321/500 (64.2%) responded, 158 (49.2%) males. All the patients had completed anthropometric measures and lipid profile after 12-hours fast. The patients having two more criteria except diabetes, were defined as having MS.

Results: The prevalence of the MS was 64.5%, Males 56.8% and Females 75.7%. The prevalence increased with age, from 16% before 40 years of age to 78% at 70 years. Diabetes duration was not different in patients with or without MS (M: 6.7±3.4 vs. 6.9±3.7; F: 7.2±3.8 vs. 6.8±3.6 yrs). The number of components of the MS was related to the age (ANOVA p < 0.05) but not to diabetes duration. Central obesity was present to Males 36% Females 85.4%, HTA 49.6 and 60.2%, low HDL 52 and 90%, high triglycerides 70.9 and 66.7% respectively. HbA1c was higher in persons with MS (9.6±2.2 vs. 8.7±1.4%, p < 0.01).

Conclusions: The results show that MS is two-fold more prevalent in type 2 diabetes, compared with the general Albanian population (64.5 vs. 32%). The levels of cardiovascular risk factors are increased in type 2 diabetics and urged immediate efforts directed at controlling the components of MS (mainly obesity, physical inactivity and lipid control).

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EVALUATING THE QUALITY OF THE INTERNET HEALTH RESOURCES IN DIABETES

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Background: Diabetes imposes an increasing economic burden on national healthcare systems worldwide, but patient involvement in decision-making and diseases management can reduce this burden. To do so, many patients try to find information from internet, but quality of online health information varies greatly. Therefore,the aim of the present study is to evaluate the quality of online health information concerning the diabetes.

Methods: We used three search engines Google, Yahoo and Bing and performed the search using the selected keyword 'diabetes'. The first 30 results reported by each search engine were selected and after excluding duplicate URLs, 66 out of 90 websites were eligible for examination. The quality of retrieved websites was evaluated by using the HON code of conducts quality rating tool. We conducted a cross-sectional assessment and simple descriptive statistics to analyze the data.

Results: Our research showedthat quality of websites considering diabetes information is low as only 21 websites achieved all the eight HON code of conducts principles. Results show thatpatients will encounter with low quality information when trying to use onlinehealth information, which could influence their decision-making and diseases management.

Conclusion: Physicians should be aware of thequality of information available on the Internet and guide patients to websites with quality information. Moreover, they should encourage patients to use quality rating tools like HON to choose the high-quality health websites to use. This will lead to help patients to better understand their disease and will empower them to make informed decisions.

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BACK TO THE BASICS - HISTORY, HISTORY AND HISTORY!

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MODY (maturity onset diabetes of the young) accounts for around 2% of paediatric diabetic cases. Mutation in hepatocyte nuclear factor 1-beta (HNF1-β) gene is rare (accounting for approximately 6% of MODY diagnoses in the UK) and is associated with RCAD (renal cysts and diabetes) syndrome. Owing to the common clinical features of both type 1 and type 2 diabetes, the diagnosis of MODY proves to be a paediatric challenge.

A 7 year old girl presented with history of polydipsia, polyuria and weight loss. On examination, weight was above the 99.6[th] centile and height on the 91st centile. There was an impaired oral glucose tolerance test, raised HbA1C, raised plasma insulin and a normal plasma C-peptide, collectively suggesting a probable diagnosis of type 2 diabetes.

Follow up consultation revealed her to be Glutamic Acid Decarboxylase (GAD) and Islet cell antibody positive, changing the diagnosis to be Type 1 diabetes, most likely MODY. Detailed history taking revealed a past medical history of left-sided nephrectomy due to congenital multicystic, dysplastic kidney. A renal ultrasound demonstrated showed a cyst in the remaining kidney.

Given the background of renal development disease and positive antibodies, the possible diagnosis of MODY, in particular RCAD, was postulated. Specialists at the Exeter University genetic centre have echoed the high probability of this and the HNF1-β gene mutation result is currently pending.

This case highlights the fundamental importance of thorough history taking to ensure a timely diagnosis of MODY to optimize both treatment and prognosis.

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A STOCHASTIC MODEL OF SELF-MONITORING OF BLOOD GLUCOSE MEASUREMENT ERROR: TOWARD A SIMULATOR OF DIABETIC PATIENT THERAPEUTIC DECISIONS

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Objective: Continuous glucose monitoring (CGM), despite becoming more and more reliable, is approved to support traditional self-monitoring of blood glucose (SMBG) but not to substitute it. The final aim of this work is to develop a simulator of diabetic patients taking SMBG- or CGM-based therapeutic decisions, in order to test *in silico* if CGM can effectively substitute SMBG. A first step toward this simulator is the development of a model of SMBG measurement error.

Methods: The database comprises blood glucose concentration samples measured in 72 patients by both a state-of-art SMBG device (One Touch Ultra 2, LifeScan Inc.) and high-accuracy and precision laboratory instruments (YSI, YSI Life Science Inc.). Glucose concentration ranges where constant-SD or constant-CV error distributions could be assumed were identified. A skew-normal distribution, whose parameters have been estimated by maximum-likelihood, was fitted for each zone. Model validation was performed via Monte Carlo sampling and visual predictive check (VPC).

Results: Two zones, labelled as 1 (glucose $< = 75$ mg/dl) and 2 (glucose > 75 mg/dl), were identified, where a constant-SD and constant-CV measurement error descriptions are valid, respectively. In particular, the estimated error distribution presents mean equal to 2.0 and SD equal to 6.5 in zone 1, mean equal to 4.8% and CV equal to 10.1% in zone 2. The VPC validation on 5th, 50th and 95th distribution percentiles confirmed the goodness of derived models.

Conclusion: The proposed model accurately reproduces the observed SMBG measurement error distribution, and represents the first step to create a simulator of diabetic patient taking SMBG-based therapeutic decisions.

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STREAMLINED MEDTRONIC TRAINER AND PATIENT EDUCATION TOOLS AND PROCESSES TO IMPROVE PATIENT SUCCESS ON INSULIN PUMP AND CGM THERAPY

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Patients who receive diabetes self-management training are more likely to comply with prescribed regimens and incur lower costs than those who do not. Collaboration between diabetes educators and patients results in favorable clinical outcomes and cost savings (Duncan et al., The Diabetes Educator 37:638, 2011). In preparation for releasing its new insulin pump system, the MiniMed 640G with predictive low glucose management, Medtronic Diabetes has redefined its approach to identifying, training, and managing Certified Product Trainers (CPTs). To ensure patient success with this new technology, a simple, modular, and comprehensive approach to education and training was necessary. A team of Medtronic employees in collaboration with diabetes educators from multiple countries developed a structured onboarding and management program for existing and new CPTs. The process is comprised of 5 certification phases (Figure 1) and training materials related to CPT identification, CPT and patient training, and CPT and patient follow-up (Figure 2). This ensures that CPTs receive comprehensive and consistent training on the use of Medtronic technologies in diabetes management, ultimately benefiting the patients they initiate on pump and CGM therapies. CPTs certified by this process will be prepared to deliver a locally-adapted training that utilizes tools and modules tailored to patients' prior diabetes technology experience, an approach and style that optimize patient engagement, and a standardized patient checklist to ensure traceability for quality assurance purposes. Effectiveness will be measured through patient feedback surveys on educational experience, patient therapy retention rates, and regularly-scheduled CPT interviews and re-certifications.

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RESTORING IMPAIRED AWARENESS OF HYPOGLYCAEMIA IN TYPE 1 DIABETES THROUGH TECHNOLOGY: A SYSTEMATIC REVIEW

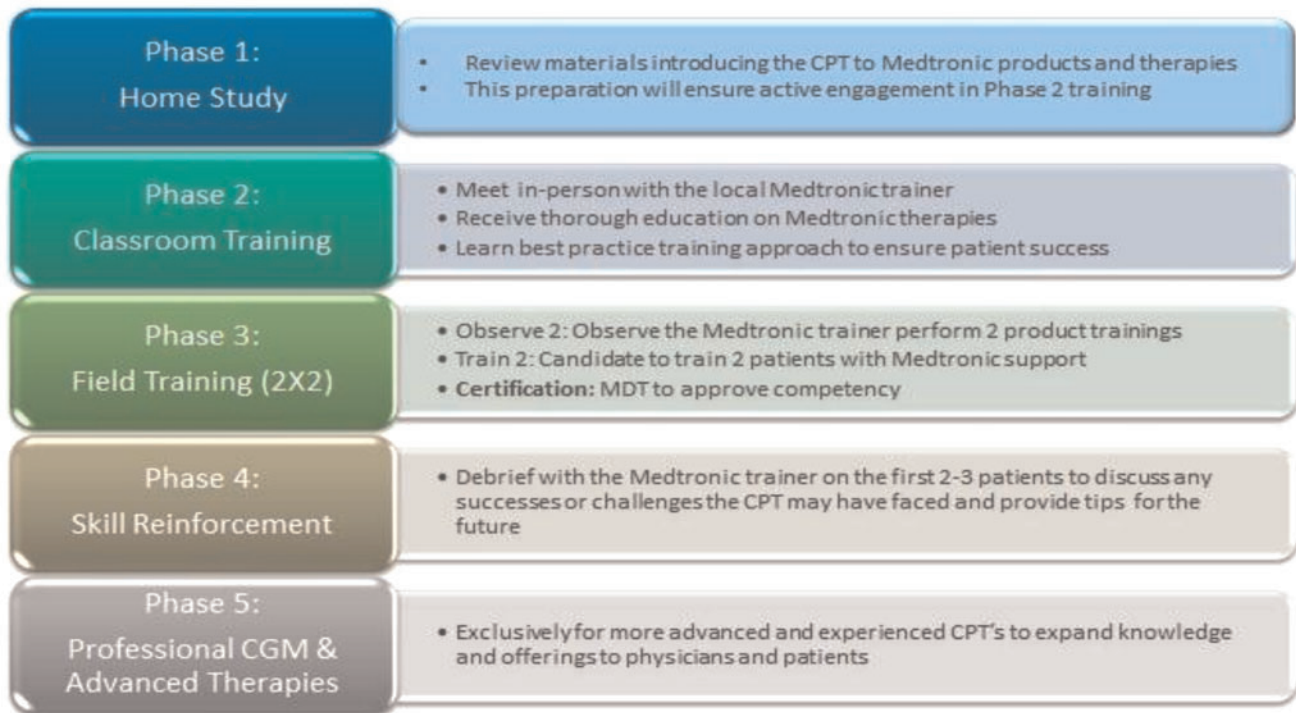*E.C.K. Yeoh[1], M. Nwokolo[2], S.A. Amiel[2], P. Choudhary[2]*

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[2]*Diabetes Research Group, King's College London, London, United Kingdom*

Background and aims: Hypoglycaemia remains a major limiting factor towards achieving good glycaemic control in adults with type 1 diabetes (T1D). Recurrent hypoglycaemia increases risks of impaired awareness of hypoglycaemia (IAH), predisposing to severe hypoglycaemia (SH).

Methods: A systematic review of technological interventions on restoring hypoglycaemia awareness (HA) in T1D patients with ≥ 5 subjects followed for ≥ 1 month. Outcomes were SH rates, HA, counter-regulatory hormone responses (CRR) and glycaemic control by HbA1c.

Results: From 1684 abstracts retrieved, 11 studies [6 randomized-controlled trials (RCTs), 5 observational] met inclusion criteria. Three (1 RCT) were insulin pump (CSII) studies; 3 used continuous glucose monitoring (CGM); 1 RCT used sensor-augmented pump; 2 RCTs (Thomas and HypoCOMPaSS) compared CSII against optimized multiple daily injections (MDI) and education, with additional real-time (RT-CGM) against self-monitoring of blood glucose (SMBG) in Hypo-COMPaSS; 1 RCT used a hand-held device providing feedback on HbA1c, hypoglycaemia risk and glucose variability.

Phase 1: Home Study	• Review materials introducing the CPT to Medtronic products and therapies • This preparation will ensure active engagement in Phase 2 training
Phase 2: Classroom Training	• Meet in-person with the local Medtronic trainer • Receive thorough education on Medtronic therapies • Learn best practice training approach to ensure patient success
Phase 3: Field Training (2X2)	• Observe 2: Observe the Medtronic trainer perform 2 product trainings • Train 2: Candidate to train 2 patients with Medtronic support • **Certification:** MDT to approve competency
Phase 4: Skill Reinforcement	• Debrief with the Medtronic trainer on the first 2-3 patients to discuss any successes or challenges the CPT may have faced and provide tips for the future
Phase 5: Professional CGM & Advanced Therapies	• Exclusively for more advanced and experienced CPT's to expand knowledge and offerings to physicians and patients

All except 1 study reduced SH frequency and improved HA. One CSII observational study showed development of IAH in 43.8% of CSII patients. Four studies investigating CRR showed no restoration of CRR. Seven studies showed no deterioration of glycaemic control despite SH rate reduction; 4 studies showed improved HbA1c. HypoCOMPaSS showed no differences between CSII or MDI, and RT-CGM or SMBG.

Conclusion: Use of technology in diabetes can reduce SH rates and improve HA without worsening glycaemic control, but does not restore CRR. Notably, structured education and optimized insulin therapy without new technologies may also be effective.

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HYPERTRIGLYCERIDEMIC WAIST PHENOTYPE AND CARDIOMETABOLIC RISK IN BRAZILIAN ADULTS: COMMUNITY-BASED STUDY

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Objectives: This study aimed to identify the prevalence of hypertriglyceridemic waist (HW) phenotype, and evaluate its association with metabolic abnormalities in Brazilian adults.

Material and Methods: A cross-sectional community-based study was performed, with 900 adults aged 20 to 59 years, living in urban area of Southeast Brazil. Participants underwent anthropometric and biochemical measurements and information about demographics, socioeconomic status and behavioral aspects was obtained. The HW phenotype was defined by simultaneous increased waist circumference (WC) (≥ 80 cm for women and ≥ 90 for men) and serum triglyceride (≥ 150 mg/dL). All analyses were adjusted for sample design effect and weighted by gender, age, and schooling. A multinomial logistic regression analysis was used to evaluate the associations of interest. Significance level was 0.05.

Results: HW prevalence was 17.33% (males 17.8%, females 16.8%). Multivariate analysis indicated that the HW was inversely associated with high level of physical activity. HOMA-IR values in the highest tertile were positively associated with high levels of TG and HW. Alcohol intake above 8 doses/week was associated with a greater chance of increased WC and HW. Low plasma levels of HDL and uric acid in the highest tertiles, were associated with increased odds of HW present. High Body mass index was positively associated with increased odds of HW phenotype and altered WC.

Conclusions: This study had demonstrated that HW was associated with an atherogenic lipid profile, and it has been suggested as a screening tool to identify metabolic alterations.

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TYG INDEX PERFORMS BETTER THAN HOMA-IR INDEX TO PREDICT METABOLIC SYNDROME IN BRAZILIAN ADULTS

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Objectives: To compare the ability of triglycerides and glucose (TyG) index and HOMA-IR to identify individuals with Metabolic Syndrome.

Material and Methods: A cross-sectional community-based study was performed, with 789 adults aged 20 to 59 years, living in urban area of Southeast Brazil. Participants underwent anthropometric and biochemical measurements and information about demographics, socioeconomic status and behavioral aspects was obtained. Comparison of the predictive ability was done using Receiver-Operating Characteristic (ROC) curves for each marker (TyG and HOMA-IR indexes) with respect to identification Metabolic Syndrome according to International Diabetes Federation criteria. For comparison of the area under the ROC curves of TyG and HOMA-IR indexes chi-square test was used. The significance level (α) was 0.05. The optimal cutpoint was determined for each marker with respect to predicting Metabolic Syndrome as the value that showed better balance between sensitivity and specificity.

Results: A total of 789 individuals were studied (44.3% were male). The area under the curve for the TyG index was 0.93 (95% CI 0.89–0.97) and for HOMA–IR index was 0.79 (95% CI 0.73–0.84). The ROC scatter plot revealed that the best value of the TyG and HOMA–IR indexes to identify Metabolic Syndrome corresponded to 5.28 and 1.73, respectively. Comparing the curves the TyG index showed better predictive ability than the HOMA–IR ($p < 0.001$). The 5.28 cutpoint showed 89.5% and 80.7% values of sensitivity and specificity, respectively. Considering the cutpoint 1.73 for HOMA–IR index, the sensitivity was 70.2% and specificity of 70.9%.

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386 SITAGLIPTIN IMPAIRS HEALING OF EXPERIMENTALLY INDUCED GASTRIC ULCERS VIA INHIBITION OF INOS AND COX-2 EXPRESSION

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387 MANAGING DIABETES IN THE VIEW POINT OF RESIDENTS OF SHIRAZ UNIVERSITY OF MEDICAL SCIENCES (S.U.M.S)

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[3]Azad Kazeron University, Kazeron, Iran

388 HEMORHEOLOGICAL APPROACH FOR EARLY DETECTION OF CHRONIC KIDNEY DISEASE AND DIABETIC NEPHROPATHY IN TYPE 2 DIABETES

S.H. Lee[1], S.H. Cho[1], M.Y. Lee[1], H.R. Baek[1], S.H. Kim[1], H.C. Kyung[1], J.S. Nam[1], S. Kang[1], C.W. Ahn[1], K.R. Kim[1]
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389 APPLICATION OF BASNEF EDUCATIONAL MODEL FOR NUTRITIONAL EDUCATION AMONG ELDERLY PATIENTS WITH TYPE 2 DIABETES: IMPROVING THE GLYCEMIC CONTROL

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390 FEAR OF HYPOGLYCEMIA AND ANXIETY RELATED EMOTIONAL DISORDERS AMONG SAUDI ADOLECENTS WITH TYPE 1 DIABETES TREATED WITH INSULIN PUMP

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391 NON-ALCOHOLIC FATTY LIVER DISEASE IN TYPE 2 DIABETES, IS THIS TIME TO CHANGE ALT VALUES FOR EARLY DETECTION OF NAFLD

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392 EFFECTS OF HAWTHORN ON HBA1C AND LIPIDS LEVELS IN DIABETIC PATIENTS (TYPE2)

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393 RESISTIN GENE POLYMORPHISMS + 299 (G > A) IN EGYPTION TYPE 2 DIABETICS

U. Khalil[1], A. Alnahal[1], M. Ghonium[1], M. Fawzy[2], M. Ibrahem[2], N. Raafat[2], W. Samy[2]
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394 CORRELATION BETWEEN CYTOMEGALOVIRUS INFECTION AND DIABETES TYPE 1 AMONG CHILDREN IN SOUTHEAST SAUDI ARABIA

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395 STRICT GLYCEMIC CONTROL IN CCU AND RCU

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396 INSULIN SENSITIVITY ENHANCEMENT BY THE MIXTURE OF SYNTHESIZED SILVER NANOPARTICLES FROM TINOSPORA CORDIFOLIA AND SORGHUM ON STREPTOZOTOCIN-INDUCED DIABETIC RATS—A PRELIMINARY STUDY

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397 NOVEL URINARY BIOMARKERS FOR EXPERIMENTAL DIABETIC NEPHROPATHY IN TYPE 2 DIABETIC RATS

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[3]ELISA-department, St.Petersburg national research University of Information Technologies Mechanics and Optics, Saint-Petersburg, Russia

398 THE ACTIVATION BY GLUCOSE OF LIVER MEMBRANE NITRIC OXIDE SYNTHASE IN THE SYNTHESIS AND TRANSLOCATION OF GLUT-4 IN THE PRODUCTION OF INSULIN IN MICE HEPATOCYTES

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399 EFFECTIVENESS OF INTERNET GROUPS FOR MORBIDLY OBESE OLDER WOMEN

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400 AN OPTIMAL CONTROL APPROACH TO PREVENT PRE-DIABETES AND DIABETES WITH AND WITHOUT COMPLICATIONS

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401 MATHEMATICAL MODEL: THE CONTROL AND REDUCTION OF OVERWEIGHT/OBESITY IN MOROCCO USING HUMAN BIOMASS

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402 THERAPEUTIC EDUCATION, COUNSELING AND ACTIVE SUPPORT THROUGH ICT FOR THE EMPOWERMENT OF INSULINIZED DIABETIC PATIENTS

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403 NONINVASIVE CONTINUOUS BLOOD MONITORING USING OPTICAL TECHNIQUES

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404 PREGNANCY OUTCOME IN WOMEN WITH TYPE 1 DIABETES ON CONTINUOUS SUBCUTANEOUS INSULIN INFUSION AND GLYCEMIC CONTROL

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405 THE COST OF DIABETES CHRONIC COMPLICATIONS AMONG IRANIAN PEOPLE WITH TYPE 2 DIABETES MELLITUS

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406 EFFECT OF GASTRIC BYPASS ON TYPE 2 DIABETES PATIENTS IN OBESITY VS NON-OBESITY IN CHINA DURING 3 YEAR FOLLOW-UP

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407 AMEROLIATE EFFECT OF NIGELLA SATIVA OIL ON INFLAMMATORY RESPONSE DURING TYPE II DIABETES MELLITUS

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408 PIVOTAL ROLE OF MICRORNA-33 IN METABOLIC SYNDROME

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409 INFLUENCE OF DIFFERENT MODES INSULIN ON CARBOHYDRATE METABOLISM, STATE TRANSPLANT, CONTROL OF METABOLIC AND HEMODYNAMIC FACTORS IN PATIENTS WITH TYPE 1 DIABETES AFTER KIDNEY TRANSPLANTATION

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410 ACTION OF METFORMIN PLEIOTROPIC EFFECT IN THE THERAPY OF TYPE 2 DIABETES PATIENTS

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411 PROTECTIVE EFFICACY OF B-SITOSTEROL IN DIABETES INDUCED OXIDATIVE DAMAGE IN PANCREAS

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412 ASSOCIATION OF CIRCULATING OREXIN-A LEVEL WITH METABOLIC RISK FACTORS IN NORTH INDIAN PRE-MENOPAUSAL WOMEN

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413 ONCE DAILY SELF-MONITORING OF BLOOD GLUCOSE (SMBG) IMPROVES GLYCEMIC CONTROL IN ORAL HYPOGLYCEMIC AGENTS (OHA)-TREATED DIABETES: SMBG-OHA FOLLOW-UP STUDY

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414 RELATIONSHIP BETWEEN MYOCARDIAL INFARCTION UNDER 55 YEARS AND ABOVE 55 YEARS WITH DIABETES MELLITUS AND TC/HDL-C RATIO SUBGROUPS IN MULTIPLE RISK FACTOR MODELS IN IRAN

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415 DESIGN AND IMPLEMENTATION OF AN OPEN ARCHITECTURE INSULIN PUMP – A RESEARCH PROPOSAL

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416 PROPOLIS ACCELERATES DIABETIC WOUND HEALING THROUGH MODULATION OF PI3K/AKT, SMAD2/SMAD3, P38 AND STAT3 SIGNALING IN A STREPTOZOTOCIN-INDUCED DIABETIC MOUSE MODEL

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418 GLIFIX/METFORMIN FIXED-DOSE COMBINATION COMPARED WITH UP TITRATED METFORMIN ALONE IN TYPE 2 DIABETES MELLITUS

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419 DIABETES SMARTPHONE APPS: A PILOT SURVEY OF REAL WORLD EFFECTS

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420 PHTHALATE EXPOSURES AND METABOLIC PARAMETERS IN KOREAN GIRLS

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421 ANTIOXIDANT STATUS OF TWO ETHNIC GROUPS' ADOLESCENT GIRLS WITH DIABETES MELLITUS TYPE 1

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422 CIRCADIAN HEART RATE VARIABILITY FOR RISK EVALUATION IN DIABETES MELLITUS PATIENTS WITH PERMANENT ATRIAL FIBRILLATION

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423 FISH CONSUMPTION: A WAY TO REDUCE THE RISK OF CORONARY HEART DISEASE MORTALITY

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424 THE CONCEPT OF "CONTROL OVER DISEASE" IN DIABETIC PATIENTS

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425 PREVALENCE OF TYPE 2 DIABETES IN ARAB WORLD

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426 DAY SURGERY BONE BIOPSY FOR CHRONIC DIABETIC FOOT INFECTION: HOW TO ACHIEVE FEASIBILITY AND RELIABILITY FOR ALL PATIENTS WITH NO MORBI-MORTALITY

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427 ADHERENCE WITH INSULIN PUMP THERAPY IN SAMARA REGION, RUSSIA

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428 PROBIOTIC POTENTIAL OF LACTOBACILLUS RHAMNOSUS RSI 3 ISOLATED FROM TRADITIONAL CEREAL-BASED FERMENTED DAIRY PRODUCT (RAABADI)

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429 GLYCEMIC AND VITAMIN D CHANGES AFTER LAPAROSCOPIC SLEEVE GASTRECTOMY

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430 SOCIAL AND HEALTH FACTORS ASSOCIATED WITH PHYSICAL ACTIVITY AMONG KUWAITI COLLEGE STUDENTS

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431 LOW INCIDENCE OF ADHERENCE TO ANTIOSTEOPOROTIC TREATMENT IN WOMEN WITH TYPE 2 DIABETES MELLITUS (T2DM)

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432 A NOVEL NIR BASED NON-INVASIVE GLUCOSE MEASUREMENT SYSTEM

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433 TITLE: ELLAGIC ACID INTERACTS SYNERGISTICALLY WITH PIOGLITAZONE TO ENHANCE INSULIN STIMULATED 2-NBDG UPTAKE IN 3T3L1 ADIPOCYTES

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434 ORIGANUM MAJORANUM MODULATES GENE EXPRESSION, HEPATIC AND RENAL CHANGES IN A RAT MODEL OF TYPE 2 DIABETES

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435 EVALUATION OF SERUM VITAMIN B12 IN ELDERLY INDIVIDUALS WITH TYPE 2 DIABETES, WITH AND WITHOUT DEMENTIA, RELATED TO METFORMIN USE OR NOT

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436 EVALUATION OF A NUTRITION EDUCATION PROGRAM TO REDUCE OVERWEIGHT AND OBESITY IN A MEXICAN HEALTH CLINIC, AS STRATEGY TO PREVENT THE TYPE 2 DIABETES MELLITUS

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437 TYPE II DIABETES MELLITUS RISK AMONG MEXICAN CHILDREN WITH OBESITY AND METABOLIC SYNDROME

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**438 EFFECTS OF PHYSICAL ACTIVITY
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**439 EFFECT OF INFORMATION TECHNOLOGY
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OF CHILDREN SUFFERING FROM DIABETES
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**440 ASSOCIATION OF SERUM 25-HYDROXYVITAMIN
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**441 THE EFFECT OF METFORMIN ON
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**442 THE CORRELATION BETWEEN THE
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IN THE THIRD TREMESTER OF PREGNANCY**

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**443 METABOLIC CONTROL AFTER YEARS OF
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**444 EFFECTS OF VITAMIN E SUPPLEMENTATION
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(A) IN TYPE 2 DIABETICS**

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**445 A TAXONOMY OF THE SAFETY ISSUES TO
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**446 FROM HUMAN BONE MARROW-DERIVED
MESENCHYMAL STEM CELLS TO INSULIN
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**447 NATURAL LATEX-DERIVED INSOLES
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**448 INDIVIDUALISED DIABETES CARE
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**449 ROLE OF IRISIN PEPTIDE IN PREVENTION
AND CORRECTION OF DIABETES MELLITUS TYPE 2
AND OBESITY: EXPERIMENTAL STUDY**

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**450 THE EFFECT OF EDUCATIONAL PROGRAM
ON PREDICTING SELF-CARE BEHAVIORS
ON GLYCEMIC CONTROL IN PATIENTS
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**451 ULTRASENSITIVE C REACTIVE PROTEIN
SERUM LEVELS AND CHRONOTROPIC RESPONSE
IN NONDIABETIC HYPERGLYCEMIC PATIENTS**

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**452 MEMORY RECALL DEFICITS AMONG
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453 ANALYSIS OF THE EFFICACY, SAFETY AND COST EFFECTIVENESS OF DULOXETINE AND TRAZODONE TO TREAT NEUROPATHIC DIABETIC PAIN

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454 CHANGES IN TRIDOSHA, TRIGUNA AND MEDICATION SCORE IN TYPE 2 DIABETICS AFTER INTEGRATED APPROACH OF YOGA THERAPY – A PILOT STUDY

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455 ANESTHESIOLOGICAL ASPECT OF FACTORS AND PERFORMANCES INFLUENCING GLYCEMIC CONTROL IN SURGICAL DIABETIC AND NON-DIABETIC PATIENTS

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456 INSULIN SENSITIVETY AND INSULIN RESISTANCE CHANGES IN SURGICAL PATIENTS WHO PREOPERATIVELY HAVE CALORIC LOAD WITH AMINO ACID INFUSIONS

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457 PREVALENCE OF DIABETIC RETINOPATHY AND RELATED RISK FACTORS IN DIABETIC PATIENTS TIRANA DISTRICT / ALBANIA

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458 MOTOR-EVACUATION FUNCTION OF THE STOMACH IN PATIENTS WITH TYPE 1 DIABETES ON THE CONTINUOUS SUBCUTANEOUS INSULIN INFUSION BY WEARABLE DISPENSER

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459 DIAGNOSIS OF DIABETIC GASTROPATHY BY THE ULTRASOUND IN TYPE 1 DIABETES

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460 IMPLEMENTATION OF EVIDENCE-BASED NURSING PRACTICE BASED ON CLINICAL GUIDELINE IN CARING FOR DIABETIC FOOT PATIENTS

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461 COMPARATIVE ANALYSIS OF EFFECTS OF RICINUS COMMUNIS FLOWERS AND GLIBENCLAMIDE ON GENETIC EXPRESSION OF ANTIOXIDANT ENZYME MARKERS IN DIABETIC MALE SWISS ALBINO MICE

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462 INTEGRATED SUBCUTANEOUS CONTINUOUS INFUSION SYSTEM AND CONTINUOUS GLUCOSE MONITORING IN PREGNANCY

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463 THE ROLE OF BONE MARROW STEM CELLS IN PHENOTYPIC CHANGES OF DIABETIC NEPHROPATHY

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464 THE VALIDATION OF PATHOGENIC MECHANISMAS OF GASTROPARESIS DIABETICORUM

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465 THE EFFECTIVENESS OF MEDICAMENT CORRECTION OF OVERWEIGHT IN ADOLESCENCE WITH OBESITY AND INSULIN RESISTANCE

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466 SENSOR AUGMENTED PUMP CAN BE EFFECTIVE IN PATIENT WITH TYPE 1 DIABETES RUNNING MARATHON: A CASE REPORT

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467 IS HEAT SHOCK PROTEIN 70 SNP ASSOCIATED WITH FOOT ULCER IN A NORTH INDIAN DIABETIC POPULATION?

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BASAL RATES PREDICTS LOW INDEX AND HYPOGLYCEMIA RISK IN PATIENTS WITH TYPE 1 DIABETES ACCUCHEK COMBO PUMP USERS

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Introduction: new challenges have begun in type 1 diabetes patients' treatment according to technological development. Hypoglycemia is one of the acute complications most feared of and many times decides motivation and treatment adherence.

Objetives: to analyze basal rates (BR) predictive values (Bayes' theory) with glycemic low index and, to evaluate its impact related with hypoglycemic risk and metabolic control.

Materials and Methods: 95 pumpers users were recruited (66 female), between 15–73 years old, from different clinical center across the country. Cross sectional study was performed. To process results we used EPIDAT 4.0. p < 0.05 was considered significant. Data were get from Smart Pix, considering the last 3 month. Low index ≥ 2.5 was consistent with hypoglycemia risk. We evaluated basal rates $\geq 50\%$ and optimal metabolic control was A1C $\leq 6.5\%$. Ethical disclosure was added to the protocol.

Results: Female probability pretest 71.2%, posttest 72.2%; positive predictive value (PPV) 72.2%; OR 1.3 (0.34–4.9). Accuracy 65.2%; Sensitivity 83%. A1c (BR ≥ 50) $7.7 \pm 0.4\%$ (BR < 50%) $6.4 \pm 0.3\%$. **Male** probability pretest 57.6% posttest 75.6%; PPV 63%; OR 3.4 (0.5–22). Accuracy 62.6% Sensitivity 89.5% A1c (BR ≥ 50) $7.8 \pm 0.1\%$ (BR < 50%) $6.5 \pm 0.6\%$.

Conclusions: basal rates above 50% of insulin diary dose are associated with poor metabolic control and increase low index with high hypoglycemia risk in pump user's type 1 diabetes patients. Different resources as bolus calculator, temporary basal rates adjustments, and systematic educative training probably reduce the hypoglycemia risk. Further trials must be performed to determine appropriately pumps settings.

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BIRTH OUTCOME RESULTS OF WOMEN WITH TYPE 1 DIABETES: 10 YEARS OF INSULIN PUMP THERAPY

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Objective: To evaluate the effectiveness of insulin pump therapy (PI) in pregnant women with DM Type 1 for the reduction of perinatal complications.

Subjects and Methods: The dynamic frequency changes of pregnancy complications, childbirths and of neonatal morbidity in women with DM Type 1 were analyzed. The databases before using of the PI and during ten years using (2004–2014) were compared. Pregnant women with DM Type 1 (170 childbirths) used Medtronic pump and Accu-Chek.

Results: The incidence of severe preeclampsia was 49% vs 9.6%; incidence of preterm delivery 38% vs 24.4%; operative vaginal delivery rates of 87% vs 90% (due to uterine scar after repeated births), the incidence of congenital malformations (CM) was 7% before the application of PI, at the implementation stage it was 4%, in 2013 the incidence of CM was 0. The incidence of macrosomia in infants from mothers with DM Type1 in 2003 was 40%, in those using PI in 2013 was 23%, newborn hypoglycemia was 31% vs 14%.

Conclusion: The use of insulin pump therapy reduces the incidence of complications of pregnancy and childbirth and reduces neonatal morbidity in women with type 1 diabetes.

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GLYCAEMIC VARIABILITY AND HYPOGLYCAEMIC RISK CHANGES DURING FOUR MONTH AFTER SENSOR AUGMENTED PUMP THERAPY INITIATION WITH STRUCTURED GROUP EDUCATION

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Aim: To assess glycaemic variability (GV) and hypoglycaemic risk changes in type 1 diabetes mellitus (T1DM) patients within four month after sensor augmented insulin pump (SAP) therapy initiation.

Patients and methods: The 4 months observation study included 18 T1DM patients (9 female, age 27.4 ± 6.5 years, diabetes duration 10.3 ± 5.5 years). All participants were transferred from MDI to SAP (Medtronic Paradigm MMT-722 and MMT-754) under the specialized diabetes school with educational program for pump users. The study include only T1DM patients with HbA1c > 7.0%. All patient used CGM on the long-term basis (> 6 day/week) and came for supervision every month. We assess GV and hypoglycaemic risk by SD, CONGA, J-index, M-value, LI, HBGI and LBGI, MAG. As native data source we use raw CGM data (Medtronic CareLink Pro, easyGV software).

Month	SD	CONGA	LI	J-index	LBGI	HBGI	M-value	MAG
1	2.53	7.56	4.06	37.78	2.22	6.26	5.75	0.90
2	2.71	7.57	4.71	39.17	2.44	6.75	6.67	0.46
3	2.64	7.31	4.65	37.11	2.76	6.51	6.65	0.37
4	2.68	7.41	4.45	38.13	3.0	6.69	7.06	0.25

Results: After four month of SAP therapy initiation all patients had better glycaemic control (HbA1c $7.4 \pm 0.9\%$ vs $8.9 \pm 1.4\%$), 33% of participants finished with HbA1c $\leq 7.0\%$, Mean HbA1c different was $1.4 \pm 1.1\%$. Despite glycaemic control improvement glucose variability (based on 425719 data points analysis) stay stable (tab.1), except MAG (p = 0.02). No one severe hypo-episode was observe.

Conclusions. SAP therapy initiation in T1DM patients with group structured education program can improve glycaemic control without increase of GV and hypoglycaemic risk in nearest future.

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ELITE STUDY CLINICAL RESULTS — A FIRST IN HUMAN STUDY FOR A NOVEL OPTOENZYMATIC CGM

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Objective: To demonstrate the safety, accuracy, and comfort of a novel CGM developed by Metronom Health in a first in man human clinical study. The CGM comprises an optoenzymatic disposable containing an arrayed enzymatic hydrogel and an optoelectronic durable component.

Method: 20 subjects with Type 1 or Type 2 diabetes were enrolled in the study, consisting of a 7 day observation phase with three in clinic visits, and a subsequent follow up visit. Up to four devices were worn by each subject during the observation period. A wide glycemic range was achieved by administration of insulin and oral carbohydrate. CGM measurements were compared with reference YSI glucose measurements from venous blood samples (15 minutes). Sensor insertion and wear comfort were assessed, along with the tissue response to the sensor implant and housing.

Results: Using a constant calibration for each sensor visit, CGM data were compared with YSI plasma glucose concentrations. The Mean absolute relative difference (MARD) was 9.3%, with a mean absolute difference (MAD) below 80 mg/dL of 7.7 mg/dL. Between 40 and 80 mg/dL 94% of the data were within the 20/20 criteria. 92% of the paired measurements were within the 20/20 criteria. 87% of the subjects reported an average insertion pain score of 0.7/10. For the skin response, the median Draize Score was zero.

Conclusion: A novel CGM was developed with an arrayed optoenzymatic approach. The CGM achieved high accuracy from 50 mg/dl to 300 mg/dl in a first in human clinical study with high comfort.

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QUANTITATIVE ANALYSIS OF COLONIC TRANSIT IN DIABETES

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The primary functions of the colon are to store, process and expel fecal mass residues. These require the generation of giant myoelectrical complexes (GMC) that mix and propel the content. The disparity between mechanical and propulsive activities caused by pathological changes, e.g., diabetes, result in idiopathic/slow-transit constipation, obstructed defecation or diarrhea. Existing diagnostic modalities and techniques of motility disturbances are based on the analysis of GMCs. The diversity of clinical symptomatology and complexities posed by the presence of fecal masses, along with the heterogeneity of experimental findings, makes it difficult to reveal underlying pathophysiological mechanisms. The aim of the study is to investigate numerically the propulsion of the content (bolus) and to assess the dynamics of stress-strain distribution and changes in shape of the colon in diabetic patients. A mathematical model of the gut with an enclosed bolus was constructed. The bolus in motion was subjected to dry and viscous friction. The results of simulations of movement patterns resembled those recorded experimentally and provided quantitative insights into the spatio-temporal patterns of changes in configuration, the distribution of contact forces over the bolus, and also predicted the average velocity of colonic transit. Thus a reciprocal relationship in the contraction of the longitudinal and circular smooth muscle was necessary to guarantee the 'mixing' type of movements. Strong conjoint contractions of both muscle layers were necessary to expel the pellet from the gut. In cases of diabetes, there are significant changes in the electromechanical properties of the tissue that lead to delayed colonic transit.

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INTEGRATION PLATFORM FOR DIABETES RELATED BIOSIGNALS

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In order to easily and efficiently collect, process and evaluate data from clinical studies that focus at correlation between blood glucose level and several other biological signals a new software and database has been developed.

Development has been triggered by recent availability of wearable electronic, sport trackers and smart watches. These devices enables collection of signals like: physical activity (from which energy expenditure can be derived), sleep patterns or heart rate (from which psychophysiological stress can be derived). The use of these devices is unobtrusive and increases patient compliance.

Daily Physical Activity Profiles

Daily BG Profiles based on CGM
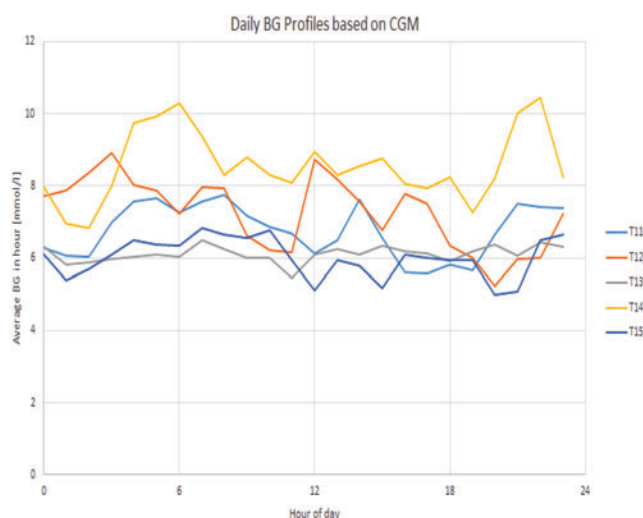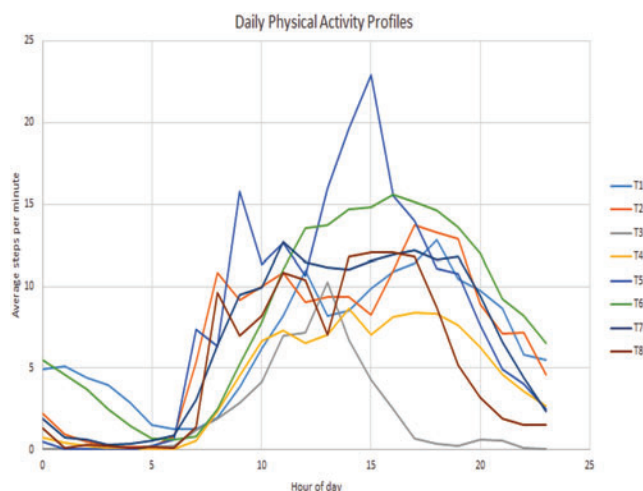
Systems consists of a service running on a server that collects data from various data sources and a database system (Microsoft SQL Server) for efficient and secure data storage. Database is connected to a MS Analysis Services OLAP server that it optimized for fast analysis of large data sets. Frontend is implemented as a web portal through which data files can be manually uploaded and reviewed in form of charts.

Currently supported biosignals include: blood glucose (Fora), CGM (Medtronics, Dexcom, Abbott), physical activity (Fitbit, Garmin, Adidas), ECG and hearth rate (Corscience, Adidas, Polar, Nonin), body weight and composition (Fitbit, Tanita), BG, carbs, activity and insulin from Diabetesdagboka app etc.

In the test phase over 5 million data points were collected from 22 healthy and diabetic testers over the 1 year period. This data can be complexly queried and results are available in excel format in nearly real time for further processing.

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AUTOMATED GLUCOSE VARIABILITY CALCULATION WITH RAW-DATA FLOW FROM SENSOR-AUGMENTED PUMP USERS

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Aim: To create WEB-program for automated blood glucose variability (GV) calculation from raw-data of CGM for patients and HCP.

Materials and methods: We use data from Endocrinology Research Centre (Moscow) Medtronic Carelink Professional 3.3 database (regular export option in CSV). Algorithms for GV calculation was founded in EasyGV program (Isis Innovation Ltd.) for free academic use. From database we selected 23 T1DM with long-term CGM use on regular basis. For GV calculation only first four month after sensor-augmented pump (SAP) initiation data were used. The first monthly retrospective analysis included 544,066 data-points. We tried to calculate all presented in EasyGV coefficients(SD, CONGA, LI, J-index, LBGI, HBGI, M-value, MAG, GRADE, MODD, MAGE, ADRR) for all patients.

Results: At the moment only several GV coefficients can be automatically calculated via our program: SD;CONGA;LI;J-index;LBGI;HBGI;M-value;MAG.

Almost all of the coefficients are well-correlated with each other (table 2, Spearman Rank Order Correlations).

Conclusions: Further development is needed to create automated calculation of other GV-parameters and make intuitive visual interface for HCP and CGM-users.

	Stddev	**CONGA**	**LI**	**JIndex**	**LBGI**	**HBGI**	**MValue**	**MAG**
Stddev	1.00	**0.71**	**0.71**	**0.86**	0.06	**0.92**	**0.90**	**0.47**
CONGA	**0.71**	1.00	**0.49**	**0.95**	−0.41	**0.88**	**0.69**	**0.38**
LI	**0.71**	**0.49**	1.00	**0.67**	0.01	**0.72**	**0.69**	**0.69**
JIndex	**0.86**	**0.95**	**0.67**	1.00	−0.26	**0.97**	**0.81**	**0.48**
LBGI	0.06	−0.41	0.01	−0.26	1.00	−0.13	0.14	0.01
HBGI	**0.92**	**0.88**	**0.72**	**0.97**	−0.13	1.00	**0.90**	**0.50**
MValue	**0.90**	**0.69**	**0.69**	**0.81**	0.14	**0.90**	1.00	**0.51**
MAG	**0.47**	**0.38**	**0.69**	**0.48**	0.01	**0.50**	**0.51**	1.00

*__bold__ - p < 0.05

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A FAT STORING MACHINE: INCRETINS AND THE STANDARD AMERICAN DIET

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Introduction: The release of insulin ensues from carbohydrate intake, signaling the initiation of fat storing and the suspension of fat burning. This process may be accelerated by the secretion of incretins, which stimulate further insulin production. For example, the consumption of lipids induces the production of acylation stimulating proteins (ASP), triggering insulin secretion and facilitating fat storage. The release of insulin reciprocally stimulates ASP. Additionally, general food ingestion, especially carbohydrate, may result in the release of glucose-dependent insulinotropic polypeptide (GIP), which possesses the same effect but functions only at high blood sugar levels.

Objective: This literature study offers information that promotes further research into developing methods of food pairing to minimize fat storage, risk of diabetes and obesity.

Method: A literature analysis from various diabetes/obesity researches was done to explore past and/or recent efforts pertaining to the understanding of the production of fat in the human body as well as the nutrition of culturally evolved diets that indicates a possible account for the prevalence of obesity in various populations.

Result: It is evident, from various incretins studies, that diets with high combinations of carbohydrates and fats will induce accelerated fat storing and may predispose individuals to obesity. Such diets are unfortunately commonplace in many modern cultures, particularly Western; the combination of dense carbohydrates and fats are seemingly embedded in the standard American diet/foods.

Conclusion: A further research in the effect of food/macronutrients pairing is needed to promote healthier food pairing to reduce fat storing and high blood sugar effects.
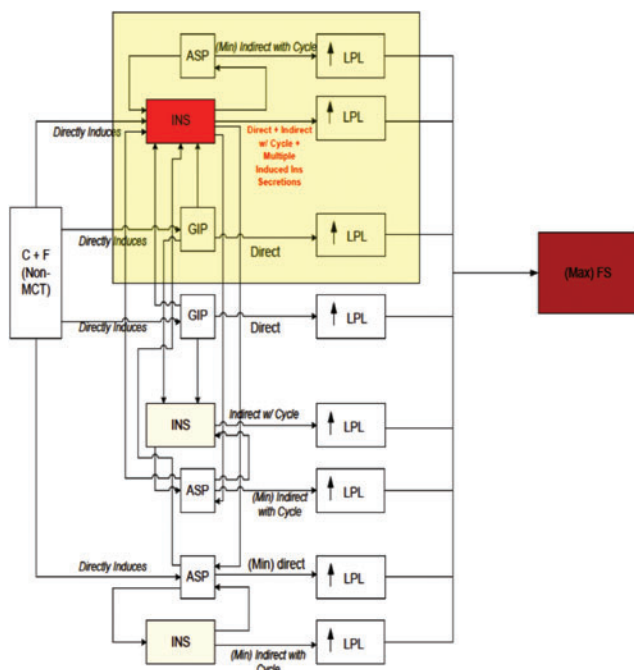
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OSTEOCALCIN AMELIORATES INSULIN RESISTANCE IN MONOSODIUM GLUTAMATE-INDUCED OBESE MICE

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Osteocalcin is a protein synthesized by osteoblasts and its role has been shown to be beyond bone metabolism. Recent studies has demonstrated that uncarboxylated osteocalcin (uOCN) acts as an hormone, with positive effects on insulin secretion and fat metabolism. Considering that insulin resistant subjects has reduced circulating uOCN levels, the aim of the present study was to investigate if uOCN has beneficial effects on glucose metabolism in vivo. For this, hypothalamic obesity was induced with monosodium glutamate; then, lean control, non-treated obese and uOCN-treated obese mice were subjected to insulin tolerance test to determine insulin sensitivity based on plasma glucose disappearance rate. As expected, obese mice showed reduced insulin sensitivity when compared to control (reduction of 70%, $p < 0.05$) when compared to control mice. Interestingly, treatment with uOCN for 4 weeks ameliorated insulin resistance in obese mice when compared with non-treated obese (increase of 66%, $p < 0.05$). In conclusion, our data point out that uOCN has beneficial effect on insulin resistance in vivo and could be an excellent candidate for insulin resistance treatment.

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METFORMIN RESTORES TUBULAR, BUT NOT GLOMERULAR, INJURY IN TYPE 2 DIABETIC RATS

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Recent studies have demonstrated antioxidant and anti-inflammatory properties of metformin, that could result in some positive effects on kidney function in diabetes. Indeed, metformin has been shown to ameliorate injury in tubular cell and podocyte culture. However, in our previous study metformin didn't improve routine renal function markers in insulinopenic diabetic rats.

To examine whether metformin possesses tubuloprotective properties in vivo we evaluated not only glomerular dysfunction marker (albuminuria), but also novel markers of proximal tubular injury (KIM-1, NGAL) in rats with non-genetic type 2 diabetic nephropathy.

In 3 weeks after unilateral nephrectomy 27 male Wistar rats were randomly divided into diabetic group (fed high-fat diet for 5 weeks and then successively received nicotinamide (230 mg/kg) and streptozotocin (65 mg/kg) intraperitoneally) and non-diabetic group (ND) fed with normal diet and received citrate

buffer without streptozotocin. 10 weeks later, diabetic animals were divided to receive either metformin (M group) 300 mg/kg/day or placebo (P group) for another 10 weeks.

HbA1c in diabetic groups was considerably higher compare to ND (4.6 ± 0.12%). Even though metformin didn't attenuate routine kidney dysfunction markers such as creatinine, creatinine clearance and albuminuria (61 ± 2.9 μmol/l ; 2.6 ± 0.18 ml/min/kg; 25.9 ± 4.6 mg/24 h, respectively) compared to P group (65 ± 3.6; 2.3 ± 0.21; 38.8 ± 2.5, P ≥ 0.05 each), urinary levels of KIM-1 (589 ± 93.3 ng/ml) and NGAL (1544.9 ± 100.6 pg/ml) were significantly lower than that in diabetic rats without treatment (1097 ± 91.1; 1918.6 ± 118.1, respectively), P ≥ 0.05 each.

Thus, metformin has shown tuboloprotective properties without any effects on glomerular dysfunction in type 2 diabetic rats.

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GLUCOSE TRANSPORT BY SLC26 CHLORIDE TRANSPORTERS IN KIDNEY AND INTESTINE: ROLE IN THE PATHOGENESIS OF HYPERTENSION AND WORSENING OF HYPERGLYCEMIA IN DIABETES MELLITUS

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Several members of the solute carrier family SLC26 are expressed in the kidney and intestinal and in conjunction with the Na+/H+ exchanger play important roles in salt absorption and blood pressure regulation. The chloride/bicarbonate exchanger SLC26A3 (DRA) and SLC26A6 (PAT-1) are expressed on the apical membrane of villi in small and large intestines whereas SLC26A4 (pendrin) and SLC26A6 (PAT-1) are expressed on apical membrane of kidney collecting duct and proximal tubule, respectively. Our data show that in a mouse model of type 1 diabetes mellitus, the expression of Pendrin in the kidney collecting duct and the expression of PAT-1 in the kidney proximal tubule and small intestine are increased significantly vs. normal mice or diabetic mice treated with insulin. We tested the hypothesis that SLC26 family members can transport glucose and contribute to hyperglycemia. Cultured kidney COS7 cells were transiently transfected with the full length cDNA encoding SLC26A3 (DRA), SLC26A4 (Pendrin), and SLC26A6 (PAT1) and compared to the glucose transporter Glut2 or fructose transporter Glut5. ^{14}C glucose or fructose uptake was measured at 10 min. The results demonstrated that amongst the SLC26 isoforms, PAT1 has the highest affinity to transport glucose and

Pendrin has the highest affinity to transport fructose. We propose that the upregulation of PAT1 in proximal tubule and small intestine in patients with type 1 diabetes not only contributes to enhanced salt absorption and eventually hypertension but also increases glucose absorption in the intestine and kidney and contributes to the worsening of hyperglycemia.

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EVIDENCE-BASED PATIENTS' HEALTH OUTCOMES: A FOCUS ON PERSONS WITH DIABETES IN WESTERN JAMAICA

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Objective: To determine the perception of health care workers' [HCW] communication by persons with diabetes, and to what extent it influenced their health outcomes (adherence to prescribed medication, appropriate eating habits, regular physical activities, self blood glucose monitoring and daily foot examination).

Method: A cross sectional method was employed using a quantitative approach; as well as the Trans-theoretical [TTM] and Health Belief [HBM] Models, to ascertain the effect of perception on health behaviour. The study population consisted of patients attending medical clinics, who have been entered in the chronic disease register, having been diagnosed with diabetes. Using the University of Florida IFAS PEOD6 document a sample size of 212 persons was calculated [Formula: n = N/1 + N (e)^2, where n = sample, N = population size, e = level of precision, 0.05, CI = 95%]. Convenience sampling was used to recruit the persons, based on the clinic attendance rate. Sociodemographics, medical history, rating of provider communication, evaluation of specific health care workers and information sharing, as well as assessment of the patients' knowledge of self-care and self-management skills were ascertained via an interviewer administered questionnaire. Biochemical data (RBG, BP and HbA1c) were included via docket search.

Result: There was no statistical association between HCWs' communication and patients' health outcomes.

Conclusion: Respondents were satisfied with HCWs' communication and there was a general understanding of information exchange. However, factors such as support, finance and frustration were reported as affecting their capacity to be compliant, and may be considered of more value and therefore superseded proposed treatments.