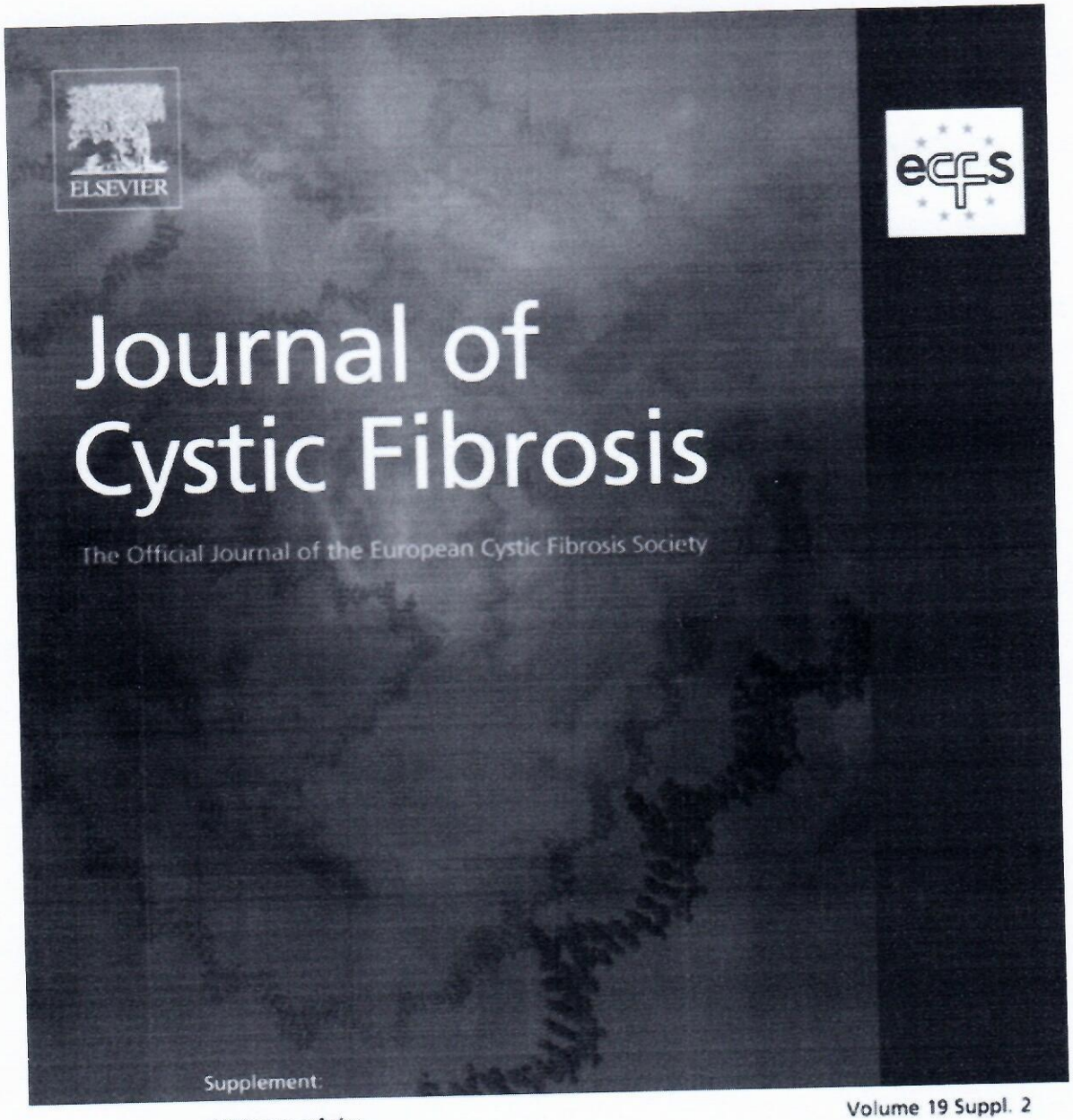


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diagnosis and key outcomes in 2010–2012 (cohort 1, C1), 2013–2015 (C2) and 2016–2018 (C3).

**Results:** Among 6354 infants, there were 2299 in C1, 2172 in C2 and 1883 in C3. Reported age at diagnosis was earlier than AFE. Across time periods, AFE decreased. Weight for age (WFA) and height for age (HFA) Z-scores at age 1 were close to 0 and not different between the cohorts. HFA Z-score at age 5 was better in C2 than C1. *Pseudomonas aeruginosa* (PA) infection rates decreased over time. Results are summarized in the table.

| Patient Characteristics | C1 2010–2012 | C2 2013–2015 | C3 2016–2018 | P-value (test) |
|---|---|---|---|---|
| Age at diagnosis, median (range) | 15 (0–3149) | 14 (0–1630) | 14 (0–945) | 0.439 (Kruskal-Wallis) |
| Age at first event, median (range) | 40 (0–365) | 38 (0–365) | 33 (0–33) | <0.001 (Kruskal-Wallis) |
| WHO WFA Z-score, age 1 mean (SD) | 0.05 (0.95) | 0.08 (0.96) | 0.015 (0.98) | 0.15 (ANOVA) |
| WHO HFA Z-score, age 1 mean (SD) | −0.59 (1.1) | −0.58 (1.1) | −0.66 (1.1) | 0.10 (ANOVA) |
| CDC WFA Z-score, age 5 mean (SD) | −0.04 (0.94) | −0.04 (1.0) | NA | 0.06 (ANOVA) |
| CDC HFA Z-score, age 5 mean (SD | −0.19 (1.0) | −0.06 (0.99) | NA | 0.003 (ANOVA) |
| PA, age 0–1 (%) | 25 | 23 | 18 | <0.001 (Chi-square) |
| PA, age 1–2 (%) | 37 | 37 | 21 | <0.001 (Chi-square) |
| PA, age 3–6 (%) | 37 | 23 | NA | <0.001 (Chi-square) |

[Patient Outcomes]

**Conclusion:** Over the first 9 years of universal NBS in the US, median AFE and PA infection rates decreased and HFA at age 5 increased. While causality cannot be inferred, these data suggest that earlier AFE may be associated with improved CF outcomes.

## P015

### Twelve years of newborn screening - the East London Experience

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**Objectives:** The Royal London Children's Hospital is a regional CF centre following the national newborn screen pathway (IRT & CFTR) since 2007, with automatic notification of positive results. We describe our experience from inception to present day.

**Methods:** Day 5 positive "CF suspected" bloodspot results are notified to the CNS - a raised 1st IRT+ genes or if no genes a 2nd raised IRT. All notified positive cases (not in neonatal care) receive a CNS home visit & sweat test. Confirmed cases receive genetic counselling & MDT review (including home visits) 1–2 weekly according to need. We reviewed hospital records of all babies referred since the onset of screening.

**Results:** 143 babies were referred between July 2007–Jan 2020. Of these, 15 babies (9%) were diagnosed clinically before screening results known (MI 9, family history CF 6). 80 (58%) had CF confirmed by sweat test +/− mutational analysis. 4 babies were not within region so were referred to other CF centres. Sweat tests were arranged & successful in 47/80 (58%) of screen positive babies.9/47 (19%) were designated as CFSPID. 6 screen positive babies died of non-CF causes without completion of investigations. 2 children with CFSPID have since been diagnosed as CF with clinical features. All parents gave written consent to the national CF registry. We have a local database to monitor our population with CFSPID. 63 babies who had CF excluded had the following ethnic distribution - White British 24%, White Other 6%, Mixed 11%, Asian 16%, Black 25%, Chinese 1%,17% had no ethnic code recorded at screening. This was compared to 80 babies diagnosed with CF or CFSPID who were 71% White British, 10% White Other; 5% Mixed, 14% Asian. Our service consistently meets national standards but following a positive CF screening result 40% of babies had CF excluded compared to 16% nationally.

**Conclusion:** East London is ethnically diverse, this data calls into question the appropriateness of the standard screening algorithm/mutation panel in our region.

## P016

### First results from national newborn screening program for cystic fibrosis in the Republic of North Macedonia

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**Objectives:** After a pilot study in 2018, newborn screening (NBS) for cystic fibrosis (CF) was introduced as a national program on all newborn population in R.N. Macedonia in April, 2019. R.N. Macedonia is a multiethnic country with approximately 2 million inhabitants, and total neonatal population of approximately 22,000 births per year. Macedonians of Slavic origin are the majority (about 55%), then ethnic Albanians (about 30%) and others.

**Methods:** Two steps IRT-IRT algorithm were performed, and then a sweat test for confirmation/exclusion of the CF diagnosis when IRT values were both over the cut off (70 ng/ml and 40 ng/ml, respectively). In cases of positive or borderline sweat tests, mutation analysis of *CFTR* gene was performed (snapshot reaction for 11 most common regional *CFTR* mutations or extended gene analysis). If the baby was under 3 kg, a genetic diagnosis was made as first.

**Results:** During the period from April to December 2019, 15.033 newborns were screened for CF. Recall rate was 0.38% (No = 57). Out of 22 screening positive cases, the diagnosis of CF was confirmed in 8. Sweat test results were: 108, 112, 102, 90, 108, 104, 52 and 70 mmol/L). 6 were ethnic Albanians and 2 were ethnic Macedonians. The majority of diagnosed cases (No = 6) at the end of the first month of life, already had symptoms consistent with the diagnosis of CF and 2 were asymptomatic. The patient's genotypes were: F508del/F508del (4), F508del/G542X, G542X/N1303K, N1303K/G126D and 457TAT > G/CFTRdupexon22. In the last case, a new *CFTR* mutation/variant (duplication of exon 22) was found with unknown significance. This case has two positive sweat test results (70 mmol/L), and so far no symptoms of CF disease.

**Conclusion:** The NBS for CF showed a high incidence of the disease in our region (1:1880), especially among Albanian population.

## P017

### Improving the efficiency of cystic fibrosis newborn screening (CF NBS) in the Khanty-Mansi region (Russia) using immunoreactive trypsinogen (IRT) floating cut-off approach

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**Objectives:** Generally used in Russia CF NBS protocol IRT/IRT has some disadvantages, among them high numbers of IRT-1 false positives (FP) and absence of obligatory DNA testing. Thus we tried to improve NBS efficiency at regional level by increasing its specificity within regular NBS protocol.

**Methods:** Descriptive survey covered period 2006–2019 ys and included all relevant data accumulated since NBS inception (IRT values, number of FP, false negatives (FN), positive/negative predictive values (PPV/NPV), confirmed CF cases, specificity (Sp), sensitivity (Se). CF regional incidence and prevalence were evaluated as median (Me) with 1st (Q1) and 3rd quartiles (Q3). Floating cut-off IRT-1 levels were calculated using newly developed proprietary software fIIRT®.

**Results:** Retrospective analysis was conducted for decade-long (2006–2016) CF regional NBS performed as IRT/IRT protocol using fixed cut-off IRT levels (57,8 ng/mL) for 260,602 newborns (~99.0% coverage). Mean FP rate was 1.97%, Se-100%, Sp-98.1%, PPV-0.64%, NPV-100%, CF was confirmed in 29 newborns. Several validating simulations showed that using floating IRT cut-off with most appropriate 99.5 percentile instead of fixed values decreased FP rate while maintaining FN rate low. This approach was applied during 2017–2019 ys in prospective study of NBS efficiency: 65,813

# 43rd European Cystic Fibrosis Conference 2020

Organiser: K.I.T. Group GmbH


and includes topics covering the entire spectrum of cystic fibrosis related issues. Invited experts present the latest findings and updates in cystic fibrosis research and care within plenary sessions, symposia, workshops, special interest groups, and meet the experts sessions.

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**Event Date:** 3 – 6 June 2020
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