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Complementary and Alternative Medicine in Autism Spectrum Disorder: parents' experience from a middle-income European country

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Introduction: This study quantitatively evaluated the use and perceived efficacy of Complementary and Alternative Medicine (CAM) treatments among individuals with Autism Spectrum Disorder (ASD) in Macedonia, a middle-income country in Southeast Europe.
Methods: A web-based survey was conducted among 103 parents of 103 individuals with ASD, and descriptive statistics and non-parametric tests were used to analyze the data.
Results: For the purpose of this study, special diets and the other CAM treatments were analyzed separately. CAMs were used by 76% of the participants with ASD, while 29% were on a special diet. Over 90% of parents positively rated the efficacy of CAM and special diets. Higher parental education was associated with higher CAM use ($p = 0.042$). The age of the individual with ASD ($p = 0.009$), severity of ASD ($p = 0.037$), and co-occurring neurodevelopmental/neuropsychiatric disorders ($p = 0.029$) also influenced the use of CAMs and/or special diets. Around half of parents were not/were partially informed by their providers about the treatments they recommended.
Conclusion: This study showed a high prevalence of use of CAM (somewhat lower of special diets) coupled with insufficient familiarity with the attributes of these treatments. Found to affect the use of CAM and/or special diets were the level of parental education, the age of the affected individual, severity of ASD, and the presence of co-occurring neurodevelopmental/neuropsychiatric disorders.

KEYWORDS: Autism Spectrum Disorder; Complementary and Alternative Medicine; supplements; diet; Europe; middle-income country

Introduction

Numerous treatment options are available for people with ASD, aiming to improve the core and associated symptoms and deficits. What directs treatment choices are the individual's characteristics (e.g. age, severity of ASD symptoms, cognitive functioning, co-occurring conditions) and parent/family-specific attributes (e.g. income, cultural background, parents' education and perceptions of ASD) (Jonkman *et al.* 2023, Mire *et al.* 2017). In addition to the standard-of-care rehabilitative, educational and pharmacological interventions, individuals with ASD commonly use various CAM treatments.

According to the World Health Organization (WHO) and the US National Center for Complementary and Integrative Health (NCCIH) definitions, complementary and alternative medicine comprises a broad set of health care practices that are not typically part of conventional medical care (NCCIH 2021, WHO 2019). Several practices are included within this treatment approach: (1) nutritional, sometimes referred to as "nutraceuticals" (e.g. supplements, special diets, probiotics, herbs), (2) psychological (e.g. mindfulness), (3) physical (e.g. massage, spinal manipulation) and (4) combinations such as psychological and physical (e.g. yoga, tai chi, acupuncture) or psychological and nutritional (e.g. mindful eating) (NCCIH 2021).

As far as the use of therapy outside of conventional medicine in ASD is concerned, the term "biomedical treatment" is also often encountered in the literature. Namely, numerous biological/physiological irregularities such as: metabolic and nutritional (Jennings and Basiri 2022, Rose *et al.* 2018), immunologic and inflammatory (Hughes *et al.* 2018, Trajkovski *et al.* 2004, 2008), gastrointestinal (Lefter *et al.* 2019, Oh and

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Cheon 2020), etc., are found to be associated with ASD. CAM (biomedical) treatments aim at, and are increasingly proven by high-quality trials to correct some of those irregularities. Although the efficacy and safety of many of the CAM treatments in ASD await more rigorous studies, the body of randomized controlled trials (RCTs) for several CAM treatments has expanded in the recent decade. Positive RCTs indicating improvement of ASD symptoms were concluded for melatonin (Gringras *et al.* 2017), folinic acid (Batebi *et al.* 2021), methyl B12 (Hendren *et al.* 2016), vitamin/mineral supplements (Adams *et al.* 2011), vitamin D (Javadfar *et al.* 2020), omega-3 fatty acids (Doaei *et al.* 2021), N-acetyl cysteine (Lee *et al.* 2021), etc. Yet, mixed or weak findings for the benefits of some CAM supplementation in ASD are also reported in the literature (Hossain *et al.* 2023; Vandana *et al.* 2023).

While exploring publicly available data on CAM practices for ASD, we observed notable inconsistencies among the studies' findings, mainly due to differences in the breadth of treatments included/considered as CAM, current/ever used treatments and in particular, the population and geographical regions involved, etc. Cultural and societies influences on the use of CAM in ASD were observed in several studies. Those conducted in western countries reveal dominant use of supplements and special diets (Lindly *et al.* 2018, Smith *et al.* 2020, Trudeau *et al.* 2019), whereas in the eastern cultures, parents often resort to more traditional methods (e.g. prayer, Chinese medicine, sensory integration, acupuncture, herbals, Ayurveda) (Konuk Sener and Karaca 2020, Narasimhan *et al.* 2020, Wong 2009).

Notable CAM use diversities are also noted within the European region. Fjær *et al*. (2020) reported higher use of CAM in countries with greater healthcare expenditure and resources, possibly related to better integration of CAM into the established health care systems. A study carried out by Salomone *et al.* (2015) used a parental survey to examine the rates of CAM usage and correlates in children with ASD from 18 European countries. It showed variable prevalences, types and correlates of CAM use across the continent. However, data on CAM treatments use in autism in Southeast European countries is scarce or nonexistent. As the majority of information on the use of CAMs in ASD originates from western, high-income countries and low- and middle-income countries seem to be underrepresented in autism studies in general, we undertook research to fill the existing paucity of data on the use of CAM treatments in Macedonia, middle-income country (World Bank 2023) in Southeast Europe.

The first objective of the study was to investigate the particulars to the use of CAMs (rates, types, sources of information and treatment recommendation) in our population. In addition to the practices of use of CAMs, our research also aimed at studying the efficacy of CAMs as perceived by parents of children (including adult) with ASD. Although regarded as less objective and biased assessments of treatment efficacy, parental evaluations are crucial, due to parents' continual insight and potential to spot any change into their child's condition (Goin-Kochel *et al*. 2009).

The second objective was to identify possible associations and correlates affecting the use and perceived efficacy of CAMs. Socio-demographic characteristics of parents/families as well as demographic and medical characteristics of their children with ASD were explored for the significance of influence on the use of CAMs. Whether the mentioned characteristics of the children with ASD affect the perceived efficacy of CAMs was also explored.

Out of the four main categories of CAM treatment approaches (NCCIH 2021), our research focused mainly (but not exclusively) on the nutritional ones, as prevailing and most available to our population. Since literature data often showed disparate prevalence of special diets and other CAMs in ASD and factors affecting each of them (Lindly *et al.* 2018, Owen-Smith *et al.* 2015, Trudeau *et al.* 2019), this study explored the use and efficacy of special diets separately from other CAM treatments. Thus, the results are provided for CAMs (mainly nutraceuticals, supplements and the alike) and for special diets separately/independently. Consequently, when referring to the results of our study hereafter, the term CAM will exclude the special diets.

Materials and methods

Participants

Eligible to participate in our research were parents of individuals diagnosed with ASD, Macedonian residents. As for this study, the term child/children is used not to denote age but parent–child relationship. The age of the ASD individuals was not limited to children.

Parents stated their opinions on CAMs and special diets used by their children with ASD by anonymously filling a questionnaire in a web-based survey. One-hundred-three ($n = 103$) of the respondents and their children with ASD ($n = 103$) were included in the final sample, after eliminating two respondents due to insufficient and unclear responses. The ASD diagnosis of the child was parent-reported, and no diagnosis verification documents were required due to the anonymous character of the survey. Taking into account the child's level of functionality, independence and behavior, the severity of ASD was also parent-rated, as the most suitable and prevailing fashion in similar web-based studies (Adams *et al.* 2021, Saral *et al.* 2023).

For the statistical analysis, the ASD sample was divided into three age groups: below 8 years, 8–14 years and 15 years and above, with the middle age group

being most frequent (39%). The majority of parents were between the ages of 40 and 49 (48%) and 30 and 39 (41%) years. Socio-demographic characteristics of parents/families and demographic and medical characteristics of children with ASD are presented in Table 1.

Design and procedures

For our projected quantitative research, we chose to use a parental survey, considering it to be appropriate to investigate treatments which parents are familiar with, and of which no trustworthy and official records of use are available. Parents having children with ASD were approached and recruited by distributing the web-link to the survey questionnaire to parental support groups on social media, associations of parents of children/individuals with autism or developmental disabilities, and through personal contacts of the authors.

The survey was based on an online available questionnaire composed of 42 questions. It was prepared by the researchers following a comprehensive literature search and a consecutive selection of topics of interest. The questionnaire's opening section informed potential participants about the survey's purpose, anonymous nature, and data collection. Ethical approval was not required since no unique identifiable patient data was collected, but still, the utmost protection of confidentiality was ensured. The web-link to the questionnaire was active for 6 months, from December 2021 through May 2022. Parents completed the questionnaire that, apart from demographic data, inquired about the *use* of CAM treatments and special diets by their children as well as parents' perceived *efficacy* of those treatments. For the *use* of CAM treatments, parents answered whether their child: "Doesn't use CAM treatments", "Uses only one CAM treatment" or "Uses more than one CAM treatment", whereas for the use of special diets, the offered answers were "is not on a special diet" and "is on a special diet". The *efficacy* of CAM treatments and special diets used, was rated as follows: "Not effective", "Partially effective" or "Effective".

Statistical data analysis

Descriptive statistics (mean, standard deviation, and median) was used to characterize the sample and the use of CAMs and special diets. Taking into account the categorical data and the non-normal distribution (Kolmogorov–Smirnov test, $p < 0.001$), several non-parametric tests were employed for the inferential statistical analysis, to test the association or correlation of parents' and child's characteristics to the use and efficacy of used CAMs and special diets: Fisher's exact test, the Mann–Whitney U test, the Kruskal–Wallis H test as well as the Spearman rank correlation test (as applicable). The Fisher's exact test was preferred for the analyses involving nominal data in the dependent variable. For analyses with ordinal data in the dependent variable, the Mann–Whitney U test was used (in cases of 2-groups independent variable, e.g. gender) or the Kruskal–Wallis H test (analyses with more-than-2-groups independent variable, e.g. age, severity of ASD). The Spearman rank correlation testing was conducted only if both variables were ordinal (not conducted if data were nominal in at least one of the two variables). A difference or correlation was considered statistically significant if $p < 0.05$. The statistical analysis was conducted using the IBM SPSS Ver. 28.0.1.1(15) program.

Table 1. Socio-demographic characteristics of parents and families and demographic and medical characteristics of the children with ASD.

Parents and families ($n = 103$)	*n*	%	Children with ASD ($n = 103$)	*n*	%
Gender of the parent			Gender		
Male	9	8.7	Male	85	82.5
Female	94	91.3	Female	18	17.5
Age of the parent (years)			Age (years) ($\bar{X}$=11.6, $s = 6.22$; $M = 10$)		
Below 30	3	2.9	Below 8	32	31.1
30 to 39	42	40.8	8 to 14	40	38.8
40 to 49	49	47.6	15 and above	31	30.1
50 and above	9	8.7	Severity of ASD		
Educational level of the parent			Mild	38	36.9
Less than high school	5	4.9	Moderate	49	47.6
High school	33	32.0	Severe	16	15.5
University degree	65	63.1	Other neurodevelopmental or neuropsychiatric disorders*		
Employment of the parent					
Unemployed	20	19.4	None	23	23.5
Occasionally employed (or other)	11	10.7	Has one	51	52.0
Regularly employed	72	69.9	Has more than one	24	24.5
Financial condition of the family			Other medical conditions**		
Poor	17	16.5	No	64	64.0
Medium	50	48.5	Yes	36	36.0
Good	36	35.0	* ($n = 98$) ** ($n = 100$)		
Area of living of the family					
Rural	12	11.7			
Suburban	13	12.6			
Urban	78	75.7			

Results

As stated above, when reporting of CAMs for the results of this study, special diets are not included as they are presented and analyzed separately.

Use and perceived efficacy of CAMs and special diets

In our sample, 75.7% of parents reported that their child with ASD currently uses at least one CAM treatment. Of those who do not use CAM, 76.0% stated that CAMs were never suggested as a treatment option by their healthcare provider. A fairly smaller number of parents (29.1%) reported the use of special diets by their children. To 78.1% of those who do not use special diets, change in diet was never proposed as a treatment option by their healthcare provider.

Although 35.9% of children who use CAMs got the recommendation from a neuropsychiatrist/psychiatrist, they were the source of recommendation for special diets to only 13.3% of children who use them. A fairly significant portion of parents use CAMs (28.2%) and special diets (26.7%) for their children, following information from other parents or the Internet. Family doctors or pediatricians were much less involved, being the source for CAM recommendations to 16.7% and for special diets to only 10.0% of cases, while nutritionists were consulted even less (3.9% and 6.7%, respectively).

Parents were asked whether they received information about the efficacy and safety of the treatment from the professional or other source of CAM recommendation. Only a small percent of parents were not informed about what kind of therapy it is and what is expected to improve with its use (7% and 6%, respectively). However, the absence of provided information is present in a quarter of parents when it comes to the possibility of interactions with concomitant therapies (25%), the risks of adverse reactions (23%), and about when and where to turn for advice if a problem occurs after the start of therapy (21%) (Figure 1). Likewise, a smaller proportion of parents were not informed about what the recommended change in diet represents and what is expected to improve with its use (11% and 12%, respectively), but a lack of provided information about the risks of adverse effects and about when and where to ask for advice if a problem occurs after the start of therapy, was reported by as much as 36% and 33% (Figure 2).

An analysis of the used CAMs revealed that more than half use products containing omega 3 (or combinations of omega 3/6/9) fatty acids, followed by therapies with vitamins and minerals. Among those who are on a special diet, the dairy-free and the gluten-free diet prevail, followed by the diet without white sugar (sucrose) (Table 2).

Of the parents of children who take CAMs and gave an overall opinion on the efficacy, the largest percentage consider CAM treatments to be partially effective (63.6%) or effective (29.9%), while only 6.5% consider it ineffective. Similarly, only 7.4% of parents whose children are on a special diet consider diet changes to be ineffective, while 48.2% find them to be partially effective and 44.4%, effective.

Parents were also inquired about the perceived benefits and disadvantages of those particular CAMs and special diets that the children use in improving any of the ASD symptoms and deficits. However, a fairly large portion of parents, not being clear on the source of perceived benefits/adverse effects, precluded the possibility to statistically analyze the responses.

Associations and correlates of the use and overall efficacy of CAMs and special diets

Influence of socio-demographic characteristics of parents and families on the use of CAMs and special diets

Parental level of education. The analysis showed no statistically significant difference in the use of *CAM treatments* among children of parents with various levels of education ($H(2) = 4.462$, $p = 0.107$). However, a significant weak positive correlation between these variables does exist ($r = 0.201$, $p = 0.042$). The use of *special diets* did not differ significantly ($p = 0.060$) between children of parents with different educational levels (Table 3).

Parental employment status, financial condition of the family and living location. The influence of parental employment was shown to be insignificant concerning the use of CAM ($H(2) = 2.402$, $p = 0.301$) and special diets ($p = 0.454$) in their children. The same was detected for the financial condition of the family ($H(2) = 3.655$, $p = 0.161$ for CAM and $p = 0.916$ for special diets) and location of living ($H(2) = 1.020$, $p = 0.601$ for CAM and $p = 0.757$ for special diets) (Table 3).

Influence of demographic and medical characteristics of children with ASD on their use of CAM and special diets

Gender. Neither the use of CAM ($U = 607.5$, $p = 0.140$) nor of special diets ($p = 1.000$) was significantly affected by gender (Table 3).

Age. The ASD sample was divided in three age groups: below 8 years, 8–14 years and 15 years and above. The use of *CAM treatments* significantly differed among the age groups ($H(2) = 9.495$, $p = 0.009$), the youngest receiving most CAM and significantly separating from the other two older age groups ($p = 0.004$ and $p = 0.017$). A significant weak negative correlation was

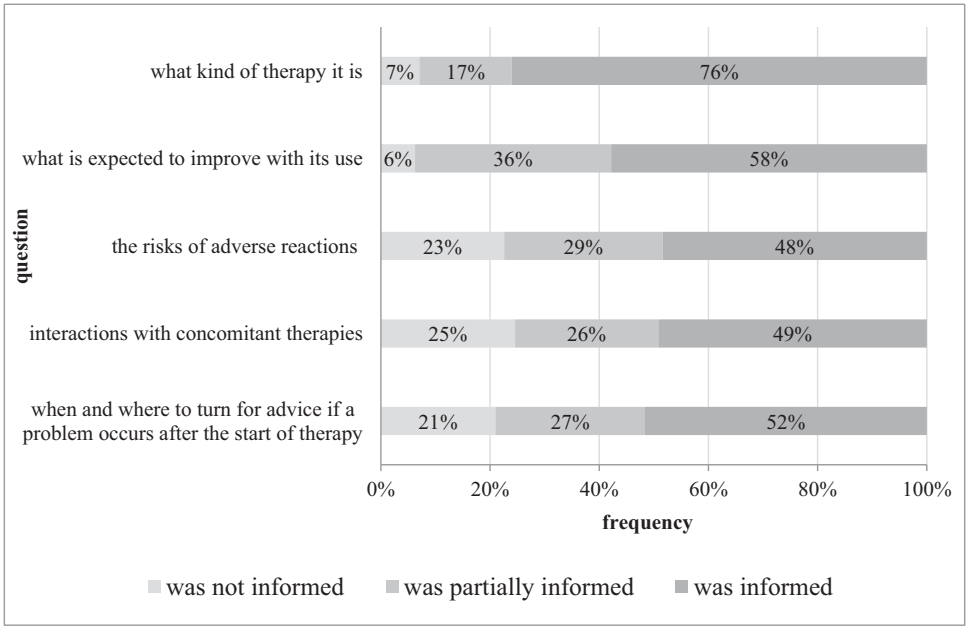

Figure 1. Parents' received information and familiarity with the attributes of the recommended CAM treatments.

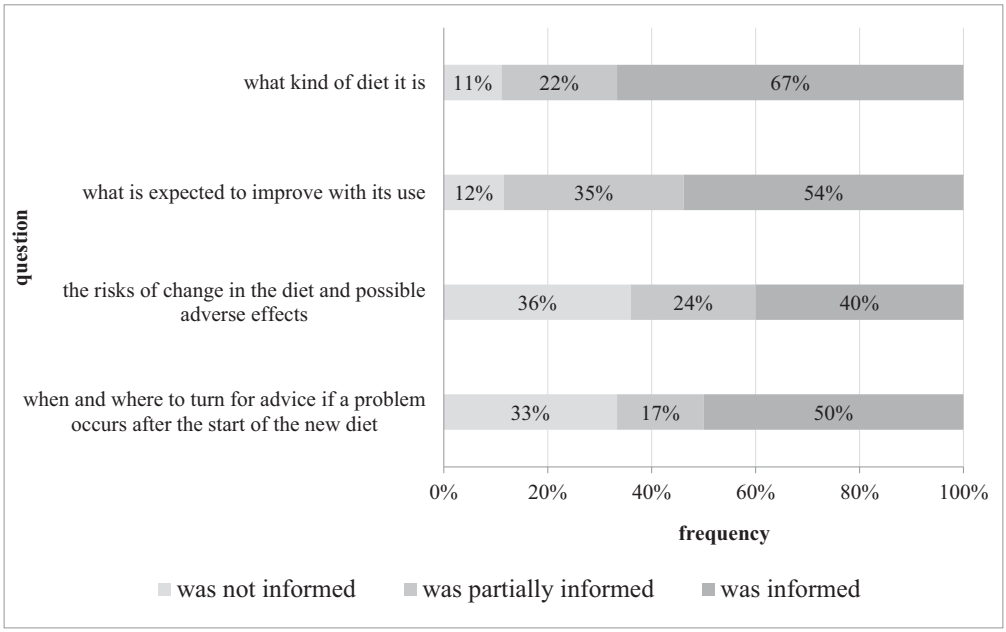

Figure 2. Parents' received information and familiarity with the attributes of the recommended special diet.

Table 2. Types of CAM treatments and special diets - frequency among users.

CAM treatment	%	Special diet	%
Omega-3 or omega-3/6/9	53.8	Dairy-free	70.0
Vitamins	43.6	Gluten-free	66.7
Minerals	21.8	No white sugar	33.3
Probiotics	17.9	No additives or preservatives	10.0
Combined products	12.8	Organic food	6.7
Zeolite	5.1	Fructose-free	3.3
Canabidiol (CBD)	5.1	No cured meet	3.3
Homeopathy	3.8	Yeast free	3.3
Carnosine	3.8	Soy-free	3.3
Royal jelly	2.6	Raw food	3.3
Grapefruit seed oil	2.6		
Heavy metal detox	2.6		

observed ($r = -0.239$, $p = 0.015$). The age was also strongly associated with the use of *special diets* ($p = 0.009$), with the youngest age group using special diets most, and again, significantly separating from the other two, older age groups ($p = 0.005$ and $p = 0.036$) (Table 3).

Severity of ASD. We divided the sample in three groups according to parent-rated ASD severity: very mild/mild, moderate and severe/very severe ASD. The difference among these groups in the use of *CAM treatments* was not significant ($H(2) = 0.813$, $p = 0.666$), although biggest between the severely affected (receiving most CAM treatments) and the other two groups.

Table 3. Influence of the characteristics of parents, families and children with ASD on the use of CAMs and special diets.

	Use of CAM treatments		Use of special diets	
	Difference (*p*)	Correlation (*p*)	Difference (*p*)	Correlation (*p*)
Parents and families				
Parental level of education	.107 [(a)]	**.042** [(c)] ($r = 0.201$)	.060 [(d)]	/
Parental employment status	.301 [(a)]	/	.454 [(d)]	/
Financial condition of the family	.161 [(a)]	.105 [(c)] ($r = -0.161$)	.916 [(d)]	/
Living location	.601 [(a)]	/	.757 [(d)]	/
	Use of CAM treatments		**Use of special diets**	
	Difference (*p*)	Correlation (*p*)	Difference (*p*)	Correlation (*p*)
Child with ASD				
Gender	.140 [(b)]	/	1.000 [(d)]	/
Age	**.009**[(a)]	**.015** [(c)] ($r = -0.239$)	**.009** [(d)]	/
Severity of ASD	.666[(a)]	.429 [(c)] ($r = 0.079$)	**.037** [(d)]	/
Other neurodevelopmental or neuropsychiatric disorders	.093[(a)]	**.029** [(c)] ($r = 0.221$)	.451 [(d)]	/

[(a)] Kruskal–Wallis H test, [(b)] Mann–Whitney U test, [(c)] Spearman correlation test, [(d)] Fisher's exact test.
"/" – correlation test not conducted (not applicable due to nominal data in at least one of two variables).
Results of significance are **bolded**.

The severity of ASD symptoms and deficits, however, was significantly associated with the use of *special diets* ($p = 0.037$). The severe/very severe group uses special diets significantly more than the other two groups ($p = 0.038$ and $p = 0.022$) (Table 3).

Other developmental or neuropsychiatric disorders. With regard to this variable, the sample of ASD individuals was divided in three groups: no other developmental or neuropsychiatric disorders, one, and more than one developmental or neuropsychiatric disorder. No significant difference was generally observed between the groups as to the use of *CAM treatments* ($H(2) = 4.757$, $p = 0.093$). Nonetheless, the consumption of CAM was significantly higher in individuals with more than one coexisting developmental or neuropsychiatric disorder compared to no other such disorder ($p = 0.029$). This, together with the weak, but significant positive correlation ($r = 0.221$, $p = 0.029$) could point to a certain association between these two variables. Conversely, the use of *special diets* was shown to be unassociated with the coexistence of other developmental or neuropsychiatric disorders ($p = 0.451$) (Table 3).

Influence of demographic and medical characteristics of children with ASD on the parental perceived overall efficacy of CAM and special diets

Neither the perceived efficacy of used CAMs nor that of special diets was significantly associated with any of the four tested variables: gender ($U = 447$, $p = 0.784$ and $U = 47.5$, $p = 0.650$), age ($H(2) = 0.404$, $p = 0.817$ and $H(2) = 2.505$, $p = 0.286$), severity of ASD ($H(2) = 1.801$, $p = 0.406$ and $H(2) = 0.354$, $p = 0.838$) and other developmental or neuropsychiatric disorders ($H(2) = 0.885$, $p = 0.643$ and $H(2) = 0.473$, $p = 0.789$) (Table 4).

Discussion

The selection of treatment for their ASD children faces parents with an immense responsibility, given the abundant extant options on the one hand, and the fact that none of these treatments fully addresses nor corrects the core and associated symptoms of ASD, on the other. To add to that, the advisory input from professionals seems insufficient, as parents often report having difficult relationships with professionals (Mackintosh *et al.* 2012).

Furthermore, as discussed below, studies that particularly survey the selection and use of CAMs as treatment options for ASD come to similar conclusions. They find that some of the health care providers admit being unaccustomed to either discussing or giving opinions about CAMs to families as well as being unfamiliar with the advantages and disadvantages of CAM treatments for ASD. When trying to discuss CAM as a therapeutic option for their child with ASD, parents are often dissatisfied with the interaction, but still attempt self-initiation without consulting physicians about the efficacy and safety of certain therapies (Levy *et al.* 2016; Marathe and Sengupta 2020). However, parents commonly choose and widely accept CAMs as viewed as more effective and safer option compared to pharmacological treatments (Lindly *et al.* 2018).

Table 4. Influence of the characteristics of children with ASD on the parental perception of overall efficacy of CAMs and special diets.

	Efficacy of CAM treatments		Efficacy of special diets	
	Difference (*p*)	Correlation (*p*)	Difference (*p*)	Correlation (*p*)
Child with ASD				
Gender	.784 [b]	/	.650 [b]	/
Age	.817[a]	.719 [c] $r = 0.042$	.286[a]	.115 [c] $r = 0.310$
Severity of ASD	.406[a]	.201 [c] $r = -0.147$	.838[a]	.869 [c] $r = -0.033$
Other neurodevelopmental or neuropsychiatric disorders	.643[a]	.567 [c] $r = 0.069$	.789[a]	.532 [c] $r = 0.128$;

[a] Kruskal–Wallis H test, [b] Mann–Whitney U test, [c] Spearman correlation test.
"/" – correlation test not conducted (not applicable due to nominal data in at least one of two variables).

Use and perceived efficacy of CAMs and special diets

The prevalence of CAM and special diets ***use*** in the ASD population as reported by parents/caregivers is varying. In the review of 20 studies with a total of 9,540 participants, it ranged from 28% to 95% (Höfer *et al.* 2017). Moreover, disparities extend further to particular treatments' choices and preferences, as well as beliefs on their efficacy and safety. The main reasons behind these inconsistencies lie in the differences in methodological study approaches, as well as terminology/classification of CAMs. Therefore, as illustrated below, any attempted comparisons should be weighed cautiously.

Among the participants in our study, the prevalence of CAM (comprised mainly of supplements) and special diets use were 75.73% and 29.13%, respectively. Comparable prevalences of CAM use were reported in other parental surveys: a study from the USA – 75.2% (Adams *et al.* 2021) and from Canada – 79.5% (Trudeau *et al.* 2019). Interestingly though, a prevalence of only 30.7% (46.4% in pediatric-age participants) was recently reported in a Dutch survey for the CAM use in general, and only 4.7% for vitamin/supplement treatments (Jonkman *et al.* 2022). Similarly, 47% of children participating in the study by Salomone *et al.* (2015) conducted on the territory of Europe used CAM and the percentage was even smaller (40%) within the region of South Europe. The rates of using diets and supplements in particular, were much lower in this study – 24% in the overall European sample and 20% in the South European sample, where our sample is located. On the other hand, in a recent study from Serbia, a country also in that region, the reported rates of vitamin/supplement (65.3%) and special diets use (54.2%) were much closer to that from our study (Arsić *et al.* 2021).

It seems that neuropsychiatrists/psychiatrists are somewhat reluctant to consider and endorse CAM or special diet as treatment options to individuals with ASD in our sample. Thus, 35.9% of CAM users and only 13.3% of those on a special diet got the recommendation from a neuropsychiatrist/psychiatrist, whereas family doctors or pediatricians were even less frequently the source of CAM treatment recommendation (in 16.7% and 10.0% of cases, respectively). An indicatively large portion of parents in our sample use CAMs (28.2%) and special diets (26.7%) for their children after being recommended by other parents or the Internet. In the studies by Trudeau *et al.* (2019) and Guner *et al.* (2021), the primary source of information on the CAM treatment came from health-care professionals (65.2% and 54.8%), possibly indicating a more substantial involvement of physicians in the process of treatment selection compared to our sample, while media were the source in 16.5% and 47.9%, respectively. Wong and Smith (2006) stated that 56% of parents are interested in discussing CAM treatment options for their child with ASD with the physician. However, around 1/3 of parents refrain from disclosing the use of some or all CAMs to their child's physician, mainly due to the perceived physician lack of knowledge on CAM, fear of disapproval and judgment, and the restricted available time they have during visits (Konuk Sener and Karaca 2020, Trudeau *et al.* 2019, Wong and Smith 2006). As Marathe and Sengupta (2020) conclude, "physicians often do not ask about CAM use, and families do not bring it up themselves".

Possibly as a consequence of the deficient parent/family – health care provider communication and share of information, poor familiarity with the attributes of the recommended CAM treatments and special diets was observed among the parents in our sample. While a smaller percent of parents were not informed about what kind of therapy it is and what is expected to improve with its use (below 10%), the absence of provided information is more pronounced when it comes to the possibility of interactions with concomitant therapies and the risks of adverse reactions (around one quarter of users each). The corresponding rates were somewhat higher for the special diets. To improve the familiarity and understanding of these treatments by the parents, they need proper and safe information from knowledgeable practitioners. Those working with

families of children with ASD should improve their own understanding of CAM, as parents currently perceive little interest in and poor knowledge of CAM by physicians (Angell *et al.* 2023; Vandana *et al.* 2023).

An analysis of the used CAMs revealed that products containing omega-3 (or combinations of omega-3/6/9) fatty acids and vitamins are used most (54% and 44% of CAM users), with other CAM treatments used less (minerals, probiotics, cannabidiol, etc.). These rates are similar to those observed in a study from a neighboring country – 35.6% and 65.3% (Arsić *et al.* 2021) and from Canada – 42.5% and 77.8% (Trudeau *et al.* 2019), but are much higher than those from a Dutch sample – 4.7% (Jonkman *et al.* 2022), pointing potentially to regional/national views and preferences.

Among those who are on a special diet, the dairy-free (70.0%) and the gluten-free (66.7%) prevail. Compared to our results, the recent Canadian study reported 23.5% lactose-free, 17.6% casein-free and 30.9% gluten-free diet users among those on a special diet (Trudeau *et al.* 2019). The considerably higher rates of dairy-free and gluten-free diet in our sample could (at least in part) be explained by the identified predominance of immunological disturbances (including food intolerances, allergies, etc.) among the other health conditions in our sample. This finding corroborates two previous studies conducted using samples from the same population, reporting statistically significant higher plasma concentration of food-specific antibodies in children with ASD compared to their typically developing siblings (Trajkovski *et al.* 2008) as well as the prevalence of immunologically based disorders/conditions compared to neurotypical controls (Koceski and Trajkovski 2022).

Unlike studies conducted to determine the prevalence of CAM/special diets use in ASD, not many studies deal with the parents' opinions on the ***efficacy*** of these practices. A very large percent of CAM and special diets users in our survey (approximately 93% each) rated them as partially effective/effective. Comparably high percent of Turkish parents found CAMs and special diets beneficial: probiotics (100%), omega-3 fatty acids (81%), multivitamins (63%), restriction of processed foods and sweets (100%) (Konuk Sener and Karaca 2020). Nutraceuticals were also regarded as having a positive effect in a large US parental survey ($n = 1286$) by over three quarters of participants (Adams *et al.* 2021) whereas special diets – by half of users, in another US parental survey ($n = 479$) (Goin-Kochel *et al.* 2009). No noticeable effect in both studies was seen in about 23–24%, compared to our study (around 7%). In the Owen-Smith *et al.* (2015) study, the perceived efficacy of CAM therapies ranged from 20% to 79%, with melatonin and probiotics rated as helpful by 79% and 65% of the parents, and the special diets by 72%. The remarkably high perceived effectiveness and low ineffectiveness of CAM and special diets among current users in our study may indicate that these treatments are used only by those who are positive to sufficiently benefit from them. It also might point to adherence to those treatments/diets as a consequence of positive effects coupled with no or negligible/insignificant adverse effects.

Ambiguous responses on the efficacy of specific CAM treatments and special diets were seen in the survey responses, which is somewhat expected and justifiable. Concomitant utilization of several different treatments (behavioral, pharmacological, CAM, etc.) is typical for ASD and it hampers the evaluation of a single treatment. The findings from an online parental survey (Goin-Kochel *et al.* 2007) reported that, on average, children with ASD simultaneously use between four and six different treatments. Nonetheless, a simple overview of the responses revealed that the effects of used CAMs and special diets in most cases fall within the ranges of the expected and described in published literature, though even paradoxical, opposite effects were also reported (e.g. reduced/increased hyperactivity and reduced/more frequent repetitive behaviors from omega-3 products, etc.).

Associations and correlates of the use and overall efficacy of CAMs and special diets

Influence of socio-demographic characteristics of parents and families on the use of CAMs and special diets

Our study showed that out of the four socio-demographic parental/family factors tested (level of education, employment status, financial condition and living location), only the parental level of education emerged as influential on the use of CAM treatments. It is reasonable to believe that the higher level of education of the parents contributes to greater familiarity with the therapeutic alternatives for ASD and openness to the non-conventional therapeutic modalities. In several other studies, the higher level of education was also found to be predictive of higher CAM use (Guner *et al.* 2021, Jonkman *et al.* 2022).

Influence of demographic and medical characteristics of children with ASD on their use of CAM and special diets

Neither the use of CAM nor of special diets was significantly affected by **gender**. Guner *et al.* (2021), however, found that the male gender was related to higher CAM use.

The use of *CAMs* in our sample significantly differed among the **age** groups with the youngest (below 8 years) using CAMs most. This replicates the findings from the recent Jonkman *et al.* (2022) study as well as those from Lindly *et al.* (2018), who found that with each additional year in the child's age, the probability

of using CAM therapy decreased by about 15%. The higher use of CAMs at a young age could stem from the parental determination to provide the child with all possible therapeutic options as early as possible, with the aim of not missing the young, developmental age of the child when any intervention would be expected to have the strongest effect. This is in agreement with the attitudes of some parents for the use of CAM therapy starting from an early age, in the study by Lindly *et al.* (2018). The use of *special diets* was also strongly associated with the age, with the youngest age group using special diets most. The implementation of dietary changes may be somewhat easier and more feasible in younger children, unlike the adolescents and adults, to whom imposing significant changes/restrictions and deviations from dietary habits could be much more challenging.

Our study showed that *CAM therapy* is used without significant differences between people with different levels of **ASD severity**. CAM products, at least the majority of them, are relatively easily available, they are dispensed without prescription, and have a reputation for not being harmful, which probably results in massive use throughout the sample regardless of ASD severity. Parents easily decide to start CAM treatments, assessing that the potential benefits will outweigh the risks. As a confirmation of this, the extensive study of Adams *et al.* (2021) showed that parents rate nutraceuticals as mildly to moderately useful, with minimal unwanted effects. Nonetheless, the severity of ASD symptoms and deficits was significantly associated with the use of *special diets*. The most severely affected use special diets most. Dietary changes are considered difficult to implement in an autistic individual. However, parents of the severely affected individuals probably turn even to that option, since other treatments for the severely affected (apart from pharmacological) are very limited, practically inexistent in our region.

A positive correlation detected between the co-occurring **other neurodevelopmental or neuropsychiatric disorders** and CAM use could point to a certain association between these two variables. The use of special diets, however, was shown to be unassociated with this variable. In the Jonkman *et al.* (2022) study, CAM use was found to be associated with the existence of other diagnoses in addition to the ASD.

Influence of demographic and medical characteristics of children with ASD on the parental perceived overall efficacy of CAM and special diets

Only a couple of relevant studies examined the factors affecting the overall efficacy of CAMs and diets. In our study, neither the perceived efficacy of used CAMs nor that of special diets was significantly associated with any of the four tested variables: gender, age, severity of ASD and presence of other developmental or neuropsychiatric disorders. Similar results were reported by Adams *et al.* (2019) in a randomized controlled study: age, gender and developmental history (early-onset or regressive autism) were not found to be significantly related to the efficacy of a comprehensive nutritional and dietary intervention. A subsequent study with a new version of the supplement confirmed that the overall benefit was not significantly affected by gender, age, autism severity, developmental history, intellectual disability, or seizures, use of psychiatric or seizure medications (Adams *et al.* 2022). The non-detection of a statistically significant influence of the tested four factors on the effectiveness of therapy could be a result of uncertainty on the part of the parents when evaluating the effectiveness, due to simultaneous use of other therapies. Additionally, it could mean that the effectiveness of the therapy is truly not associated with the tested variables, i.e. individuals of different age, gender, severity of ASD and other co-occurring developmental or neuropsychiatric disorders could equally benefit from treatments. A possibility remains that other factors, which are not included in this research, could be more influential.

Strengths and limitations of the study

The study was quantitative, enabling objective assessment of the goals set. The sample was not large, but justifiable considering the population from which it was drawn and the examples from similar researches. Our study is distinct from other similar ones, for it explores the use and efficacy of special diets separately from those for other CAM treatments. Furthermore, it covers a region and a middle-income country, both infrequently presented in autism treatment research.

Implications and conclusion

Practices of CAM and special diets use in ASD are variable in general. We researched those in a Southeast European middle-income country, anticipating them to be specific and to differ to some extent from findings from high-income countries. Our findings showed high CAM but lesser special diets use. Parents are insufficiently informed by the providers about the treatments they recommended and often use such treatments on their own. Health care providers that care for ASD individuals need to be aware that the majority of them do take CAMs (whether the provider is informed or not) and that a substantial portion of parents are insufficiently acknowledged with the essential information on those treatments.

Higher parental educational level is significantly associated with higher consumption of CAMs. The younger age and the more severe form of ASD significantly determine the use of special diets, while the younger age and the presence of other

neurodevelopmental or neuropsychiatric disorders significantly influence the use of biomedical treatments.

Overall, the study provided a much-needed overview of the use of CAMs and special diets in ASD, characteristic of an underrepresented region and middle-income country.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Disclosure statement

The authors have no relevant financial or non-financial interests to disclose. First author is employed by the pharmaceutical company Alkaloid AD-Skopje, that was not related in any way to this research or the manuscript.

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