

# SURVEY ON DIETETIC EXPERTISE AND CLINICAL APPLICATION OF THE KETOGENIC DIET IN ITALY: WHAT PROFESSIONAL RESOURCES ARE AVAILABLE FOR INHERITED METABOLIC DISORDERS?

M. GUGLIEMMETTI<sup>1,2</sup>, R. NURTI<sup>2,3</sup>, C. LESSA<sup>2,4</sup>, A. CIPRIANI<sup>5</sup>,  
E. TROIANO<sup>6</sup>, R. DE AMICIS<sup>2,7,8</sup>

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<sup>1</sup>Ketogenic Metabolic Therapy Laboratory, Department of Public Health, Forensic and Experimental Medicine, University of Pavia, Pavia, Italy

<sup>2</sup>Member of the Italian Scientific Association for Food, Nutrition and Dietetics (ASAND) Working Group on Ketogenic Dietary Therapies

<sup>3</sup>Pediatric Clinical Nutrition Service, UOC Intensive Care Unit and Neonatal Pathology Neonatal Care, Department of Women's and Children's Health, Padova University Hospital, Padova, Italy

<sup>4</sup>ASST Nord Milano, Corporate Dietary Service, Sesto San Giovanni (MI), Italy

<sup>5</sup>Dietetic Unit, Meyer Children University Hospital IRCCS, Florence, Italy

<sup>6</sup>Socio-Educational Services Department, Municipality Rome III; Scientific Association for Food, Nutrition, and Dietetics (ASAND)

<sup>7</sup>Obesity Unit and Laboratory of Nutrition and Obesity Research, Department of Endocrine and Metabolic Diseases, IRCCS Istituto Auxologico Italiano, Milan, Italy

<sup>8</sup>International Center for the Assessment of Nutritional Status and the Development of Dietary Intervention Strategies (ICANS-DIS), Department of Food, Environmental and Nutritional Sciences (DeFENS), University of Milan, Milan, Italy

## CORRESPONDING AUTHOR

Monica Guglielmetti, RD, MSc, Ph.D; e-mail: monica.guglielmetti@unipv.it

**ABSTRACT – Objective:** The aim of this study was to evaluate Italian dietitians' expertise and clinical use of ketogenic dietary therapies (KDTs), with a specific emphasis on their use in inherited metabolic disorders (IMDs).

**Subjects and Methods:** A 30-item multiple-choice questionnaire was distributed to Italian dietitians and physicians (including neurologists, pediatricians and endocrinologists) affiliated with the Italian Scientific Association for Food, Nutrition and Dietetics (ASAND) and/or the Italian Society for the Study of Inherited Metabolic Diseases and Neonatal Screening (SIMMESN) and/or the Italian League Against Epilepsy (ILAE). Participants were recruited from various clinical settings, including hospitals, private practices, and academic institutions. The survey explored professional experience, therapeutic clinical application of KDTs, follow-up strategies, and perceived barriers to implementation in IMDs. Descriptive statistics were used for data analysis.

**Results:** A total of 175 responses were collected. The findings demonstrated substantial variability in expertise on KDTs and usage across different healthcare settings. Only 34.3% of respondents reported the presence of a dedicated ketogenic therapy team ("ketoteam"), whereas 33.7% indicated no available service within their institution. Most dietitians (66%) had fewer than five years of experience with KDTs, and 74.3% devoted less than 25% of their professional time to the management of KDTs. The most commonly employed protocol was the classic KD (39.4%), with minimal adoption of the Medium-chain triglyceride ketogenic diet (MCT-KD). Reported barriers included insufficient staffing (42.7%) and inadequate clinical infrastructure (31.7%).

**Conclusions:** This survey reveals notable variability in expertise on KDTs and clinical practice among Italian dietitians. KDTs are most frequently applied for obesity and weight management rather than for metabolic or neurological disorders. These findings underscore the need for targeted educational programs, enhanced multidisciplinary collaboration, and clearer delineation of the expertise required for use of KDTs in IMDs, taking into account the diversity of protocols and their underlying clinical rationales.

**KEYWORDS:** Ketogenic diet therapy, Metabolism, Inborn errors, Dietitians.

**ABBREVIATIONS:** IMD – Inherited metabolic disorder, IRCCS – Istituto di Ricovero e Cura a Carattere Scientifico, KD – Ketogenic diet, KDTs –Ketogenic dietary therapies, MAD – Modified Atkins diet, MCT – Medium-chain triglyceride, MCT-KD – Medium-chain triglyceride ketogenic diet, VLE KD – Very low-energy ketogenic diet.

## INTRODUCTION

The ketogenic diet (KD) is a high-fat, low-carbohydrate, moderate-protein dietary regimen designed to induce a metabolic state known as ketosis, wherein the body shifts its primary energy source from glucose to fats<sup>1</sup>. This metabolic transition results in the production of ketone bodies –  $\beta$ -hydroxybutyrate, acetoacetate and acetone – which serve as alternative energy substrates for peripheral tissues and the central nervous system<sup>2</sup>.

Specific ketogenic protocols are routinely applied in inherited metabolic disorders (IMDs). The classic KD is defined by a fixed ratio of fats to combined proteins and carbohydrates (typically 4:1 or 3:1), thereby maximizing the state of ketosis. Classic KD is particularly effective in managing glucose transporter type 1 (GLUT1) deficiency syndrome and pyruvate dehydrogenase deficiency, conditions characterized by impaired glucose transport or metabolism<sup>3</sup>.

The medium-chain triglyceride (MCT)-KD utilizes MCTs, which are rapidly converted into ketone bodies. This allows for a higher carbohydrate intake while maintaining ketosis and is often preferred in patients with mitochondrial disorders due to its facilitation of efficient energy production and reduced oxidative stress<sup>4</sup>.

The modified Atkins diet (MAD) represents a less restrictive variant of KD, permitting more liberal protein consumption and flexible carbohydrate distribution. It is occasionally adopted for patients requiring greater metabolic flexibility or those unable to adhere to the rigidity of classic KD<sup>5</sup>.

Finally, the low glycemic index treatment emphasizes the intake of carbohydrates with a glycemic index below 50, stabilizing blood glucose levels while inducing low-to-mild ketosis. Although less stringent, low glycemic index treatment generally produces a less pronounced ketogenic effect than other protocols<sup>6</sup>.

Despite its growing popularity and diverse applications, the term ketogenic diet is often used ambiguously to describe a broad spectrum of dietary protocols with distinct therapeutic purposes, leading to confusion in both clinical and non-clinical contexts<sup>2</sup>. Ketogenic regimens are employed for various indications, including weight loss<sup>7</sup>, neurological disorders<sup>8</sup> and metabolic diseases<sup>1</sup>. While ketogenic diets for obesity typically emphasize caloric restriction and fat oxidation, ketogenic dietary therapies (KDTs) for conditions, such as epilepsy and certain IMDs, are specifically formulated to sustain nutritional ketosis through precise macronutrient manipulation<sup>2</sup>. IMDs comprise a group of rare genetic disorders characterized by defects in metabolic pathways that impair the body's ability to process carbohydrates, fats, or proteins efficiently<sup>9</sup>. In these conditions, KDTs serve as an alternative energy source by elevating circulating ketones, which bypass metabolic blockades and supply energy to tissues – particularly the brain, which under normal conditions relies predominantly on glucose<sup>3</sup>.

The implementation of KDTs in IMDs involves several key phases: indication and assessment, wherein candidates are identified based on clinical evaluation and diagnostic markers; initiation and induction, referring to the gradual introduction of dietary modifications to establish ketosis while monitoring tolerance; and follow-up and monitoring, involving parameters such as blood ketone levels ( $\beta$ -hydroxybutyrate), glycemia, and metabolic biomarkers like acetylcarnitine C2<sup>3,10,11</sup>.

Clinical evidence<sup>12</sup> supports the efficacy of KDTs in improving neurological function and metabolic stability in patients with GLUT1 deficiency syndrome, pyruvate dehydrogenase deficiency and various mitochondrial disorders. However, side effects – including nausea, vomiting, and gastrointestinal discomfort – may occur, particularly in vulnerable populations<sup>13</sup>.

KDTs have also shown promise in improving exercise tolerance, reducing muscle pain and damage, and potentially restoring physiological function in patients with glycogen storage disease types III, V, and VII, underscoring nutrition as a key therapeutic strategy<sup>14-16</sup>.

To minimize risks and optimize therapeutic outcomes, the implementation of KDTs for IMDs requires a multidisciplinary approach involving dietitians, metabolic specialists, and physicians. Specific expertise in both KDTs and dietary management of IMDs is highly desirable<sup>17</sup>.

This survey aims to provide an overview of Italian dietitians' expertise with KDTs and their current clinical application, emphasizing the potential role of KDTs in the nutritional management of IMDs.

## SUBJECTS AND METHODS

An online survey was developed by the strategic Working Group on Ketogenic Dietary Therapies of the Italian Scientific Association for Food, Nutrition and Dietetics (ASAND) ([Supplementary Material](#)) to collect relevant data. The survey was disseminated to a range of Italian healthcare professionals, including dietitians and physicians – specifically neurologists, pediatricians, and endocrinologists – *via* the mailing lists and social media channels of ASAND, the Italian League Against Epilepsy (ILAE) and the Italian Society for the Study of Inherited Metabolic Diseases and Neonatal Screening (SIMMESN). This distribution strategy aimed to provide a broad overview of the number of dietitians engaged in the clinical application of KDTs in IMDs. To maximize outreach, recipients were encouraged to share the survey with their professional networks.

The analysis focused specifically on responses from dietitians, as the clinical management of IMDs often involves complex, multidisciplinary care requiring coordination across multiple hospital departments and specialized knowledge of KDTs.

Data collection took place between September 2024 and March 2025. The questionnaire included 30 items. The first six questions gathered general information, such as how participants received the survey, their professional role, the type of employing institution and the availability and composition of ketogenic therapy services (e.g., dedicated “ketoteams”) within their workplace.

The remaining 24 questions of the survey were organized into four thematic domains related to various aspects of KDTs:

- **Training (Questions 7-9):** This section examined whether respondents had received specific training in KDTs, the type of training undertaken (e.g., residential courses, distance learning, internships), and whether the courses were national or international. Participants who reported no formal training on KDTs were directed to Question 28.
- **Clinical Management and Application (Questions 10-27):** This extensive section addressed topics including years of experience with KDTs; indications for use of KDTs (e.g., obesity, drug-resistant epilepsy, GLUT1 deficiency syndrome, other IMDs); patient demographics (adult or pediatric); routes of administration of KDTs (oral vs. enteral) and rationale for exclusive enteral use; number of patients managed with KDTs annually; use of dietary supplements; proportion of professional time dedicated to patients under KDTs; types of protocols for KDTs implemented [e.g., classic KD, MAD, very low-energy KD (VLC ED)]; types of foods used (e.g., common foods, foods for special medical purposes); ketone monitoring practices; tools used for diet planning (e.g., specialized software, Excel); and nutritional follow-up procedures, including personnel involved and assessment methods (e.g., anthropometric measurements, dietary intake analysis, biochemical testing). Several items in this section permitted open-ended responses, including average duration of KDTs (Q16), specific supplements used (Q18), and ketone monitoring frequency (Q23).
- **Barriers to Prescription of KDTs (Question 28):** This item investigated obstacles to implementation of KDTs, such as the absence of dedicated facilities or insufficiently trained staff.
- **Further Interest and Feedback (Questions 29-31):** The final section assessed respondents' interest in further education on KDTs, gathered open-ended suggestions, and requested consent to be recontacted for future initiatives.

Multiple answers were allowed for several questions (e.g., Q6, Q8, Q11, Q14, Q21, Q22, Q27, Q28). Therefore, the total percentages for each question may exceed 100%.

### Statistical Analysis

Responses were analyzed using descriptive statistics. Results are reported as absolute numbers (n) and percentages (%). As this was a multiple-choice survey, participants were permitted to select more than one response per item; therefore, the total percentages for each question may exceed 100%.

## RESULTS

A total of 175 professionals responded to the survey. Of these, 113 participants received the survey *via* ASAND, 6 through SIMMESN contacts, and 56 through social media or other channels.

### Respondent Characteristics and Professional Settings

Among the respondents, 49.7% were hospital-based dietitians, 28% were freelance dietitians, and 8.6% were university-affiliated dietitians. A minority of respondents (8.6%) included dietologists, metabolic pediatricians, endocrinologists, neurologists, and other professionals with expertise in nutrition.

With regard to professional settings, 46.9% reported working in public hospitals or IRCCS (Istituti di Ricovero e Cura a Carattere Scientifico – Scientific Institute for Research, Hospitalization and Healthcare), 20% in private outpatient settings, and 18.9% in university hospitals. A smaller proportion worked in universities, private clinics, rehabilitation centers, or other healthcare structures.

### Availability of Ketogenic Therapy Services and Ketoteam Composition

Regarding the presence of a dedicated service for KDTs, 34.3% of respondents reported the availability of a structured service with a dedicated team (“ketoteam”). In 25.7% of cases, a service for KDTs was provided without a designated team, while 33.7% reported that no such service was available in their workplace (Figure 1A).

Among respondents who reported the presence of a “ketoteam” ( $n = 60$ ), the majority (95.0%, 57/60) indicated that a dietitian was part of the team. A dietologist was present in 63.3% of teams (38/60), and a medical specialist – typically a neurologist or endocrinologist – was included in 53.3% (32/60). Nine respondents (15%) reported the involvement of other nutrition-trained professionals, while 5 (8.3%) indicated the presence of a pediatrician. Single cases also reported the involvement of other professionals, such as an internist or nurse (Figure 1B).

### Experience and Clinical Practice with KDTs

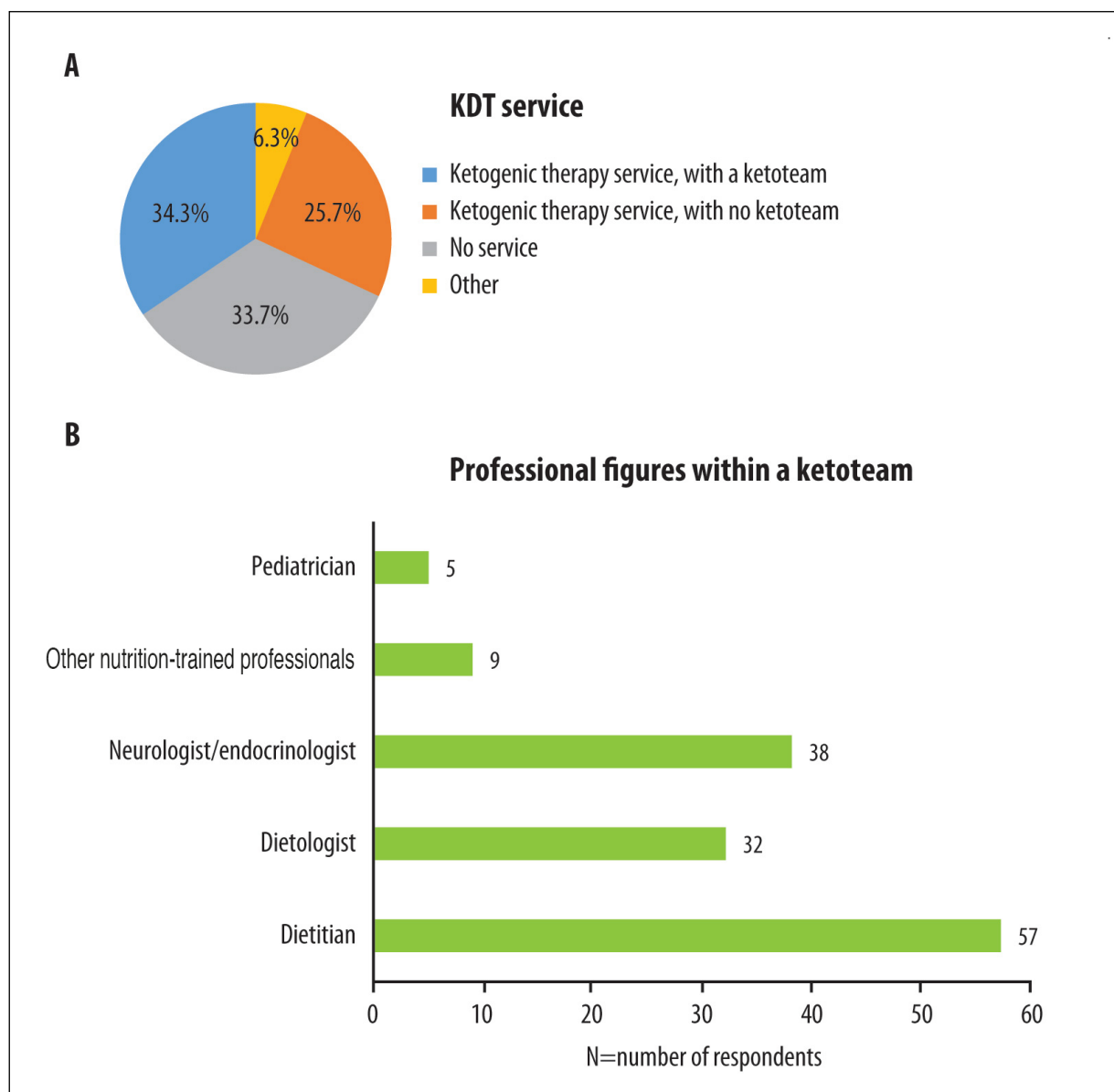
A subgroup of 109 respondents provided detailed information regarding their experience and clinical practice with KDTs unless otherwise specified. Among these professionals, 22.9% reported having <1 year of experience with KDTs, 43.1% had 1-5 years, 14.7% indicated 5-10 years, and 19.3% reported >10 years of clinical experience in this field.

When asked about the number of patients treated with KDTs during the previous year, 37.6% (41/109) had managed <5 patients. In comparison, 26.6% (29 respondents) had treated 5-10 patients, 16.5% (18 respondents) reported managing 10-20 patients, and 19.3% (21 respondents) had followed >20 patients over the same time frame.

Regarding patient demographics, the majority of respondents (56.9%, 62/109) reported working primarily with adult patients, while 28.4% (31 respondents) managed both adults and children receiving KDTs. As for the proportion of work time dedicated to KDTs, 74.3% (81 respondents) indicated that they devoted <25% of their professional time to this field. In contrast, 20.2% (22 respondents) allocated 25-50% of their time to KDTs, and only a small minority reported dedicating >50% of their working time to patients undergoing ketogenic therapy.

### Clinical Application of KDTs

In terms of clinical indications for KDTs, 50.5% of the 109 respondents reported its use in the management of IMDs. Among these, GLUT1 deficiency syndrome was the most frequently cited condition, reported by 28.4% (31 respondents). Glycogen storage diseases type III or V were noted by 8.3% (9 respondents), pyruvate dehydrogenase deficiency by 3.7% (4 respondents), mitochondrial diseases by 3.7% (4 respondents), and other unspecified metabolic disorders by 4.6% (5 respondents).



**Figure 1. A, Service for KDTs and B, Professional figures within a ketoteam.**

KDTs were also used for non-metabolic conditions. Obesity was the most frequently mentioned, with 65.1% (71 respondents) indicating its use in this context. Weight loss was reported in 44.0% of cases (48 respondents), headache in 31.2% (34 respondents), drug-resistant epilepsy in 33.0% (36 respondents), insulin resistance and diabetes in 5.5% (6 respondents), and polycystic ovary syndrome (PCOS) in 3.7% (4 respondents), as illustrated in Figure 2.

With regard to administration routes, 59.6% (65 respondents) used KDTs *via* oral solid food, while 37.6% (41 respondents) administered it through enteral nutrition. The choice for enteral administration was primarily attributed to the ease of management and the lack of training or availability of specialists for implementing oral KDTs.

The majority of respondents (91.7%, 100/109) reported using dietary supplements alongside KDTs, most commonly vitamins. Regarding the type of protocols prescribed for KDTs, the classic KD was the most frequently reported (39.4%, 43 respondents), followed by the VLC ED in 35.8% (39 respondents) and the MCT-KD in 10.1% (11 respondents).

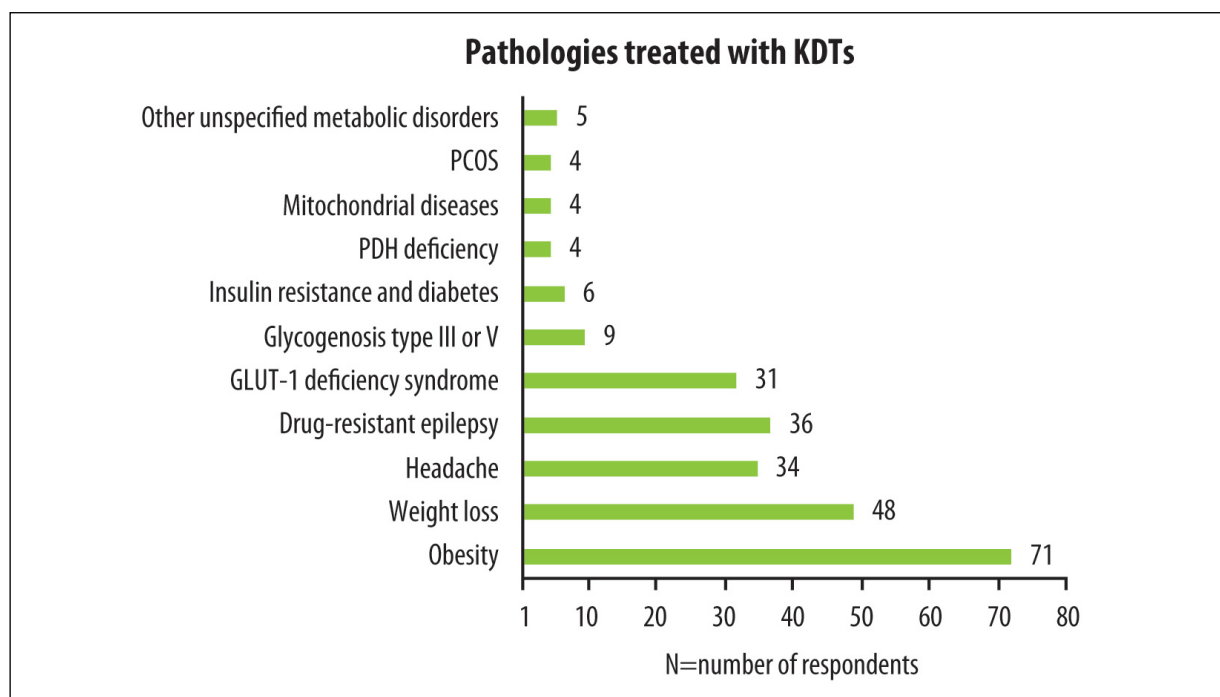


Figure 2. Pathologies treated with KDTs.

### Diet Elaboration, Monitoring, and Follow-up

Among the tools used for designing KDTs, Excel was reported as the most common method used by 40.4% of respondents (44/109). Additionally, 30.3% (33/109) of participants reported using general diet-creation software, while 10.1% (11/109) used software specifically developed for KDTs. Of the respondents who did not use any specific software (65/109), a substantial proportion – 35.4% (23/65) – reported prescribing VLE KDs. In terms of dietary components, 74.3% of respondents (81/109) indicated that common food items formed the primary basis of their KDTs. Foods for special medical purposes were incorporated by 52.3% (57/109), while non-foods for special medical purposes, food supplements, were used by 33.0% (36/109), and protein substitutes were reported in 15.6% of cases (17/109).

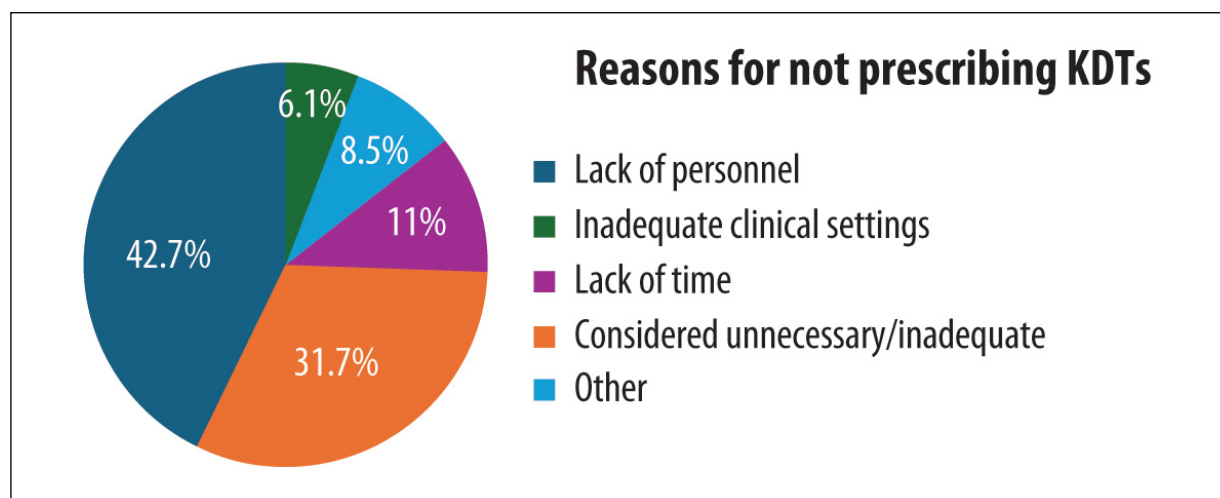
Monitoring of ketone levels was conducted using urine tests in 43.1% of cases (41/109), while 36.7% (40/109) of respondents recommended blood testing. Notably, 33.9% (37/109) indicated that they did not recommend any ketone testing. Within this latter group, approximately half (18/37) frequently prescribed VLE KD, suggesting a possible association between the protocol type and omission of ketone monitoring.

Follow-up care was reported to be conducted jointly by both a specialized physician and a dietitian in 52.3% of cases (57/109), while 39.4% (43/109) indicated that follow-up was managed exclusively by dietitians. Regarding the format of follow-up visits, 55.0% (60/109) were conducted in person, whereas 43.1% (47/109) involved a mixed model combining tele-assistance and in-person visits.

Respondents reported a range of follow-up procedures, most commonly anthropometric assessment (91.7%, 100/109), dietary intake analysis (81.7%, 89/109), objective evaluation of nutritional status (79.8%, 87/109), and biohumoral tests (71.6%, 78/109). Additional procedures included body composition analysis (61.5%, 67/109) and instrumental examinations (34.9%, 38/109).

### Barriers to Prescription and Availability of Training for KDTs

Only a subgroup of 82 respondents answered the question concerning barriers to prescribing KDTs. The most frequently cited reason was a lack of personnel, reported by 42.7% (35/82). Inadequate clinical settings were identified by 31.7% (26/82), while 6.1% (6/82) mentioned time constraints. Additionally, 8.5% (7/82) reported that KDTs were considered unnecessary or inappropriate either by patients or physicians (Figure 3).



**Figure 3.** Reasons for not prescribing KDTs.

Regarding training availability, based on 170 responses to this item, 60.6% (103/170) reported that structured training courses on KDTs were available. Among those who provided further details (n=119, with multiple responses allowed), 31.9% (38/119) reported having completed on-site courses, 36.1% (43/119) indicated participation in telematic courses, and 43.7% (52/119) had access to a mixed training model combining on-site and remote formats. Additionally, 18.5% (22/119) mentioned hands-on internships. Of those specifying the language of instruction (n=115), most reported that courses were conducted in Italian (70.4%, 81/115), while 27.0% (31/115) reported availability in both Italian and other languages.

## DISCUSSION

The findings from this survey reveal substantial heterogeneity in both the expertise and clinical application of KDTs among Italian dietitians, particularly in the management of IMDs.

Over the past three decades, the KD has gained recognition as a promising therapeutic intervention for a range of inborn errors of metabolism<sup>3,12,18</sup>. Its most well-established application is in GLUT1 deficiency syndrome, where KDTs have been associated with marked improvements in epileptic seizures and movement disorders. Nevertheless, some symptoms may remain refractory to dietary intervention<sup>19</sup>. Positive outcomes have also been reported in subsets of patients with mitochondrial diseases<sup>20,21</sup>, with evidence of seizure reduction and enhanced cognitive function, as well as in pyruvate dehydrogenase complex deficiency<sup>22</sup>, where benefits include improvements in lactic acidosis, psychomotor development and neurological symptoms.

KDTs have demonstrated therapeutic potential in muscular glycogen storage diseases as well. In patients with Glycogen storage disease (GSD) type V, improved patient-reported outcomes have been documented<sup>23</sup>. In GSD III, reductions in cytokines (CK) levels, along with improvements in cardiomyopathy and hepatopathy, have been reported<sup>24-26</sup>. Furthermore, specific studies have validated the role of KDTs in the management of other rare metabolic conditions. For example, resolution of neurological symptoms and normalization of electroencephalogram activity have been observed in congenital hyperinsulinism due to a glucokinase mutation<sup>19</sup>. Similar findings have been documented in animal models of succinic semialdehyde dehydrogenase deficiency, where KD led to the normalization of ataxia and electroencephalogram (EEG) patterns<sup>27,28</sup>.

Despite these encouraging outcomes, the implementation of KDTs requires careful clinical oversight due to the potential for adverse effects. Various dietary protocols, including the classic KD, MAD and MCT-KD, have been employed in clinical case series and reports. Commonly reported side effects in patients with IMDs include gastrointestinal disturbances such as nausea, vomiting, and constipation, as well as metabolic complications including hyperlipidemia, hyperuricemia, and hypercalciuria<sup>18</sup>. These effects are often observed during the initial months of treatment and underscore the need for long-term patient follow-up. Notably, tolerability profiles differ by condition. For instance, patients with mitochondrial diseases may be at increased risk for hypoglycemia and metabolic acidosis<sup>20,29</sup>, while individuals with GSD V often tolerate the diet well, with few or no adverse effects reported<sup>23</sup>.

These findings underscore the importance of proactive monitoring and individualized management to safeguard metabolic stability and ensure long-term adherence to KDTs. The role of dietitians and multidisciplinary care teams is therefore critical in optimizing both safety and therapeutic outcomes for patients with IMDs undergoing ketogenic therapy<sup>30,31</sup>.

It would be valuable for future research to compare these findings – such as the percentage of structured “ketoteams”, dietitians’ years of experience, and time allocated to KDTs – with data from other countries or prior Italian studies. Such comparisons would help determine whether the observed challenges are unique to the Italian context or reflect broader international trends.

In this survey, the majority of participating dietitians reported using the VLE KD predominantly for obesity and weight loss. These clinical applications follow protocols and practices that differ markedly from those used in the management of epilepsy or IMDs, where therapeutic KDTs require more stringent macronutrient manipulation and closer monitoring. This finding suggests that the number of dietitians with specific expertise in therapeutic ketogenic protocols may be limited, effectively narrowing the workforce available to manage patients with IMDs who require such specialized interventions. In this context, it is important to clarify some of the differences between VLE KD and KDTs used for neurological and neurometabolic disorders, including IMDs. The term ketogenic diet refers to all those regimens that determine the production and maintenance of circulating ketone bodies but sometimes it is applied even to diets that do not induce ketosis at all<sup>2</sup>. Moreover, the use of the term implies that “ketosis” is a key part of the diet’s therapeutic mechanism. While this is true for conditions such as epilepsy<sup>32</sup> and GLUT1 deficiency syndrome (GLUT1-DS)<sup>33</sup> or other IMDs, where ketone bodies serve as an alternative energy source for the brain, the role of ketosis in treating obesity, when achieved, remains unclear and is limited to a debated effect on appetite suppression<sup>34</sup>. Another distinction is related to calories and macronutrient prescription. Energy prescription in classic ketogenic diet (CKD), MCT-KD, and MAD protocols is tailored to individual needs. Consequently, these are typically eucaloric dietary regimens, with caloric intakes ranging from 500 kcal/day (for infants) to 2,500 kcal/day or more (for normal-weight adults)<sup>2</sup>. In contrast, VLE KDs, aiming at weight loss, allow for *ad libitum* calorie intake, although they often lead to a spontaneous reduction in energy consumption through various mechanisms<sup>35,36</sup>. By definition, very low-calorie ketogenic diets are strictly hypocaloric, reaching a maximum of 700-1,000 kcal/day<sup>37</sup>. Moreover, in KDTs, protein intake is ‘controlled’, although adequate to reach the recommended intakes, in order to avoid a reduction in ketosis, while fats are encouraged. On the other side, VLE KDs still ‘control’ protein intake but at the same time, also reduce fat intake, relying more on endogenous fats from adipose tissue instead of the exogenous ones<sup>2,35</sup>.

The availability of dedicated ketogenic therapy services remains highly variable across healthcare settings. This inconsistency appears to be compounded by key barriers identified in the survey, most notably the lack of adequately trained personnel and the inadequacy of clinical infrastructure. These two factors were cited as the main reasons for not prescribing KDTs by a substantial proportion of respondents. The situation is further exacerbated by the limited time professionals are able to dedicate to activities related to KDTs. Indeed, 74.3% of respondents reported spending less than 25% of their working hours on management of KDTs, highlighting a systemic limitation in resource allocation.

Altogether, these findings underscore the urgent need to enhance dedicated services for KDTs – both in terms of institutional settings and the availability of trained personnel – to ensure adequate care for patients requiring nutritional therapy for IMDs. Addressing these barriers is essential for the development of structured “ketoteams”, the diffusion of best practices, and the long-term sustainability of programs on KDTs within multidisciplinary care frameworks.

Furthermore, the survey revealed that professional experience with KDTs is still in a developmental stage, with approximately 66% of dietitians reporting fewer than five years of experience in this area. While 60.6% of respondents indicated the availability of training courses on KDTs – delivered through various formats, including residential, remote, and hybrid models – the observed variability in the clinical application and monitoring of KDTs suggests that the current training landscape may not guarantee uniform or standardized practice across professionals.

This inconsistency, when combined with the limited clinical experience reported by many respondents, likely contributes to the heterogeneity observed in the implementation of KDTs. These findings underscore the urgent need for standardized frameworks for clinical practice, including well-defined ketogenic protocols tailored specifically for IMDs. Standardized training curricula, endorsed by expert consensus, could help reduce practice variation and enhance the quality of patient care.

The data also indicate a marked preference for traditional ketogenic modalities, particularly the classic KD, while the use of MCT-KD and the MAD appears limited. Although the survey identified which type of KDTs was most frequently used (Question 20), it did not explore the reasons behind this preference.

However, a detailed interpretation can be provided based on clinical rationale, as the choice of protocol is highly dependent on the specific metabolic condition being treated. For instance, in GLUT1 deficiency syndrome, the classical ketogenic diet remains the first-line treatment due to the critical need for stable and sustained ketosis. Conversely, in mitochondrial diseases, the use of ketogenic diets is approached with caution due to the inherent risks of hypoglycemia and lactic acidosis. In conditions such as muscle glycogen storage diseases, the classical ketogenic diet may not be strictly necessary; indeed, the modified Atkins diet (MAD) is frequently a suitable and effective alternative in these cases. Historically, the therapeutic use of ketogenic diets has evolved significantly: the classical diet was introduced in the 1920s, followed by the development of the Medium-Chain Triglyceride (MCT) ketogenic diet in the 1970s, and later, the MAD. Each of these protocols can have a different impact on the stability of nutritional ketosis, and the selection of the most appropriate diet should be individualized<sup>30,31</sup>. In addition to these clinical rationales, several plausible factors may account for the underuse of MCT-KD and MAD, including limited familiarity due to insufficient training, the higher cost or reduced availability of MCT-based products, which might not be covered by the national healthcare system for all IMDs, and a perception of increased complexity in the dietary planning and follow-up required. These aspects merit further investigation in future studies.

It is important to note that VLE KDs, while frequently reported in this survey, are not appropriate for the management of IMDs, as the underlying rationale, nutritional goals, and patient monitoring strategies differ significantly from those of KDTs used in clinical metabolic care.

At present, the main protocols for KDTs applied in the management of IMDs include classic KD, MCT-KD, and MAD.

Moreover, it remains unclear whether a stable state of ketosis and specific blood ketone levels is required for each IMD<sup>3,12</sup>. The state of ketosis can be an extremely important marker for developing KD plans, as it depends on the daily grams of carbohydrates and the proportion relative to other nutrients like fat and protein. This also impacts the management and dietary complexity of the patient. Therefore, the types of protocols applied for individual IMDs need to be studied in greater depth to achieve maximum efficacy with minimal impact on quality of life and overall nutritional risk, considering the potential side effects reported in IMDs and the issue of poor long-term adherence. Given the intrinsic metabolic fragility of these patients, the application of KD therapy can expose them to greater risks, making careful specialist evaluation and rigorous clinical monitoring essential. The fundamental difference compared to the VLE KD for obesity lies precisely in the therapy's duration and purpose. For inherited metabolic disorders, the diet is a chronic, often lifelong, treatment that acts as a true metabolic therapy through diverse mechanisms of action. One is to bypass a genetic defect of metabolism and provide the nervous system and the body with an alternative fuel (ketones) from fat if other nutrients cannot be used efficiently, while for other IMDs, KDTs could have an indirect effect based on mitochondrial biogenesis, neurotransmitter metabolism, and antioxidant effect.

## Limitations

It is important to acknowledge several limitations in this study. Firstly, there may be a selection bias, as dietitians with a particular interest or involvement in KDTs might have been more inclined to participate. Secondly, the data are self-reported and thus reliant on participants' recall and perception, which could introduce some inaccuracies.

Another limitation of this study is the relatively small sample size, which may affect the generalizability of the findings. Although efforts were made to reach a broad audience through the Italian Scientific Association for Food, Nutrition and Dietetics (ASAND) and the Italian Society for the Study of Inherited Metabolic Diseases and Neonatal Screening (SIMMESN) and the Italian League Against Epilepsy (ILAE), it is possible that some professionals across the country were not reached. This may have occurred if they were not affiliated with either scientific society or were not informed by their colleagues, thereby limiting the representativeness of the sample.

Additionally, as a quantitative tool, the survey may not have fully captured the complexity and nuances of clinical practice and decision-making involved in the implementation of KDTs. The structured format may have constrained the expression of context-specific challenges or innovative adaptations in real-world settings.

Despite these limitations, the findings of this study highlight the necessity of expanding targeted educational programs and fostering multidisciplinary collaboration. Differentiating the expertise of dietitians who apply KDTs for IMDs is essential, particularly given the diverse protocols and underlying pathophysiological rationales involved. Future efforts should focus on optimizing the availability of ser-

vices, ensuring the presence of dedicated “ketoteams”, and promoting ongoing professional development to support the adoption of evidence-based protocols for KDTs tailored to IMDs.

Standardizing clinical care pathways, including the integration of telemedicine tools for follow-up and patient monitoring, could help overcome current limitations in accessibility and continuity of care. In parallel, qualitative studies are needed to explore more deeply the perceived barriers, training needs, and contextual constraints experienced by dietitians working with KDTs in the management of IMDs. Furthermore, investigating the clinical impact of implementing standardized multidisciplinary teams would provide valuable insights into patient outcomes and service efficiency. Such research could contribute to the design of tailored interventions aimed at improving the quality of care in this highly specialized and evolving field.

## CONCLUSIONS

This survey highlights considerable variability in the expertise and clinical application of KDTs among Italian dietitians, particularly in the context of metabolic and neurological disorders. To address this heterogeneity and improve the quality of care, the standardization of protocols and the implementation of specific training for healthcare professionals – integrated within a multidisciplinary team – are essential to ensure structured, consistent, and effective therapeutic approaches. These findings underscore the need to expand targeted educational initiatives, promote interdisciplinary collaboration, and clearly define the specialized skills required for dietitians applying KDTs for IMDs, considering the diverse protocols and underlying clinical rationales involved.

### ACKNOWLEDGEMENTS:

We thank Alice Dianin and Giulia Bruni for their support.

### ARTIFICIAL INTELLIGENCE-ASSISTED TECHNOLOGIES:

No artificial intelligence-assisted technologies were used in the production of this article.

### AUTHORS' CONTRIBUTIONS:

Study conception and design: MG, RDA; collection and interpretation of data: MG, RDA, CL, ET; statistical analysis: MG, RDA; manuscript drafting: MG, RDA, CL, ET, RN, CL; manuscript editing: MG, RDA, CL, ET, RN, CL; approval to submit: MG, RDA, CL, ET, RN, CL.

### AVAILABILITY OF DATA AND MATERIAL:

All data generated or analyzed during this study are included in this published article and its [Supplementary Material](#) or from the corresponding author upon reasonable request.

### CONFLICTS OF INTEREST:

The authors declare that they have no conflict of interest to disclose.

### ETHICS APPROVAL:

Ethical approval was not required as this survey was not classified as a clinical study, also according to the most recent national regulatory framework outlined in Decision No. 425/2024. Specifically, the survey did not involve clinical outcomes or patient-specific data but was exclusively conducted among healthcare professionals, aligning with the definition established in the current legislative reference.

### FUNDING:

No funding was received for this study.

### INFORMED CONSENT:

Participants were informed about the study's purpose, their voluntary involvement, and data confidentiality. Informed consent was considered implicit, as participation was entirely voluntary, free from coercion, and responses were de-identified. The study involved no interventions and posed no risk to participants.

### ORCID ID:

Monica Guglielmetti: 0000-0001-6327-9959  
Roberta Nurti: 0009-0002-7871-7856  
Chiara Lessa: 0000-0003-1665-5784  
Ramona De Amicis: 0000-0003-0403-5465  
Ersilia Troiano: 0000-0002-3640-9655

## REFERENCES

1. Ul-Haq I, Saleem S, Iftikhar H, Abdi G. Nutritional ketosis as therapeutic regimen for metabolic disorders: Perspectives and challenges. *J Agric Food Res* 2025; 21: 101981.
2. Tagliabue A, Armeno M, Berk KA, Guglielmetti M, Ferraris C, Olieman J, van der Louw E. Ketogenic diet for epilepsy and obesity: Is it the same? *Nutr Metab Cardiovasc Dis* 2024; 34: 581-589.
3. Scholl-Bürgi S, Höller A, Pichler K, Michel M, Haberlandt E, Karall D. Ketogenic diets in patients with inherited metabolic disorders. *J Inherit Metab Dis* 2015; 38: 765-773.
4. Greco T, Glenn TC, Hovda DA, Prins ML. Ketogenic diet decreases oxidative stress and improves mitochondrial respiratory complex activity. *J Cereb Blood Flow Metab* 2016; 36: 1603-1613.
5. Malinowska D, Żendzian-Piotrowska M. Ketogenic diet: a review of composition diversity, mechanism of action and clinical application. *J Nutr Metab* 2024; 2024: 6666171.
6. Pfeifer HH, Lyczkowski DA, Thiele EA. Low glycemic index treatment: implementation and new insights into efficacy. *Epilepsia* 2008; 49 Suppl 8: 42-45.
7. Bachar A, Birk R. Ketogenic Diet Intervention for Obesity Weight-Loss- A Narrative Review, Challenges, and Open Questions. *Curr Nutr Rep* 2025; 14: 43.
8. Rubio C, López-Landa A, Romo-Parra H, Rubio-Osornio M. Impact of the Ketogenic Diet on Neurological Diseases: A Review. *Life (Basel)* 2025; 15: 71.
9. Ferreira CR, Rahman S, Keller M, Zschocke J; ICIMD Advisory Group. An international classification of inherited metabolic disorders (ICIMD). *J Inherit Metab Dis* 2021; 44: 164-177.
10. Anderson JC, Mattar SG, Greenway FL, Lindquist RJ. Measuring ketone bodies for the monitoring of pathologic and therapeutic ketosis. *Obes Sci Pract* 2021; 7: 646-656.
11. Hung PL, Lin JL, Chen C, Hung KY, Hsieh TY, Hsu MH, Kuo HC, Lin YJ. An examination of serum acylcarnitine and amino acid profiles at different time point of ketogenic diet therapy and their association of ketogenic diet effectiveness. *Nutrients* 2020; 13: 21.
12. Kök Şan C, Muslu M, Gökçay GF. Ketogenic diet interventions in inborn errors of metabolism: a review article. *Clin Exp Health Sci* 2024; 14: 283-295.
13. Newmaster K, Zhu Z, Bolt E, Chang RJ, Day C, Mhanna A, Paudel S, Farooq O, Swaminathan A, Acharya P, Cheungpasitporn W, Gupta S, Samanta D, Mahfooz N, Mainali G, Carney PR, Naik S. A review of the multi-systemic complications of a ketogenic diet in children and infants with epilepsy. *Children (Basel)* 2022; 9: 1372.
14. Reason SL, Godfrey RJ. The potential of a ketogenic diet to minimize effects of the metabolic fault in glycogen storage disease V and VII. *Curr Opin Endocrinol Diabetes Obes* 2020; 27: 283-290.
15. Løkken N, Hansen KK, Storgaard JH, Ørngreen MC, Quinlivan R, Vissing J. Titrating a modified ketogenic diet for patients with McArdle disease: A pilot study. *J Inherit Metab Dis* 2020; 43: 778-786.
16. Francini-Pesenti F, Tresso S, Vitturi N. Modified Atkins ketogenic diet improves heart and skeletal muscle function in glycogen storage disease type III. *Acta Myol* 2019; 38: 17-20.
17. Tumienė B, Del Toro Riera M, Grikinienė J, Samaitienė-Alekniėnė R, Praninskienė R, Monavari AA, Sykut-Cegielska J. Multidisciplinary care of patients with inherited metabolic diseases and epilepsy: current perspectives. *J Multidiscip Healthc* 2022; 15: 553-566.
18. Kök Şan C, Mucahit M, Gökçay FG. Ketogenic Diet Interventions in Inborn Errors of Metabolism: A Review Article. *Clin Exp Health Sci* 2024; 14: 283-295.
19. Klepper J, Akman C, Armeno M, Auvin S, Cervenka M, Cross HJ, De Giorgis V, Della Marina A, Engelstad K, Heussinger N, Kossoff EH, Leen WG, Leiendecker B, Monani UR, Oguni H, Neal E, Pascual JM, Pearson TS, Pons R, Scheffer IE, Veggliotti P, Willemsen M, Zuberi SM, De Vivo DC. GLUT1 deficiency syndrome (GLUT1DS): State of the art in 2020 and recommendations of the international Glut1DS study group. *Epilepsia Open* 2020; 5: 354-365.
20. Zweers H, van Wegberg AMJ, Janssen MCH, Wortmann SB. Ketogenic diet for mitochondrial disease: a systematic review on efficacy and safety. *Orphanet J Rare Dis* 2021; 16: 295.
21. Maiorana A, Caviglia S, Greco B, Alfieri P, Cumbo F, Campana C, Bernabei SM, Cusmai R, Mosca A, Dionisi-Vici C. Ketogenic diet as elective treatment in patients with drug-unresponsive hyperinsulinemic hypoglycemia caused by glucokinase mutations. *Orphanet J Rare Dis* 2021; 16: 424.
22. Sofou K, Dahlin M, Hallböök T, Lindefeldt M, Viggedal G, Darin N. Ketogenic diet in pyruvate dehydrogenase complex deficiency: short- and long-term outcomes. *J Inherit Metab Dis* 2017; 40: 237-245.
23. Løkken N, Nielsen MR, Stemmerik MG, Ellerton C, Revsbech KL, Macrae M, Slipsager A, Krett B, Beha GH, Emanuelsson F, van Hall G, Quinlivan R, Vissing J. Can a modified ketogenic diet be a nutritional strategy for patients with McArdle disease? Results from a randomized, single-blind, placebo-controlled, cross-over study. *Clin Nutr* 2023; 42: 2124-2137.
24. Olgac A, İnci A, Okur İ, Biberoğlu G, Oğuz D, Ezgü FS, Kasapkara ÇS, Aktaş E, Tümer L. Beneficial Effects of Modified Atkins Diet in Glycogen Storage Disease Type IIIa. *Ann Nutr Metab* 2020; 76: 233-241.
25. Francini-Pesenti F, Tresso S, Vitturi N. Modified Atkins ketogenic diet improves heart and skeletal muscle function in glycogen storage disease type III. *Acta Myol* 2019; 38: 17-20.
26. Brambilla A, Mannarino S, Pretese R, Gasperini S, Galimberti C, Parini R. Improvement of Cardiomyopathy After High-Fat Diet in Two Siblings with Glycogen Storage Disease Type III. *JIMD Rep* 2014; 17: 91-95.
27. Nylen K, Velazquez JL, Likhodii SS, Cortez MA, Shen L, Leshchenko Y, Adeli K, Gibson KM, Burnham WM, Snead OC 3rd. A ketogenic diet rescues the murine succinic semialdehyde dehydrogenase deficient phenotype. *Exp Neurol* 2008; 210: 449-457.
28. Nylen K, Likhodii S, Burnham WM. The ketogenic diet: proposed mechanisms of action. *Neurotherapeutics* 2009; 6: 402-405.
29. Wesół-Kucharska D, Greczan M, Kaczor M, Ehmke Vel Emczyńska-Seliga E, Hajdacka M, Czekuć-Kryśkiewicz E, Piekutowska-Abramczuk D, Halat-Wolska P, Ciara E, Jaworski M, Jezela-Stanek A, Rokicki D. Efficacy and safety of ketogenic diet treatment in pediatric patients with mitochondrial disease. *Nutrients* 2024; 16: 812.

30. Kossoff EH, Zupec-Kania BA, Auvin S, Ballaban-Gil KR, Christina Bergqvist AG, Blackford R, Buchhalter JR, Caraballo RH, Cross JH, Dahlin MG, Donner EJ, Guzel O, Jehle RS, Klepper J, Kang HC, Lambrechts DA, Liu YMC, Nathan JK, Nordli DR Jr, Pfeifer HH, Rho JM, Scheffer IE, Sharma S, Stafstrom CE, Thiele EA, Turner Z, Vaccarezza MM, van der Louw EJTM, Veggiotti P, Wheless JW, Wirrell EC; Charlie Foundation; Matthew's Friends; Practice Committee of the Child Neurology Society. Optimal clinical management of children receiving dietary therapies for epilepsy: Updated recommendations of the International Ketogenic Diet Study Group. *Epilepsia Open* 2018; 3: 175-192.
31. De Giorgis V, Tagliabue A, Bisulli F, Brambilla I, Camerini A, Cusmai R, Darra F, Dianin A, Domenica E, Lodi MAM, Matricardi S, Messina T, Operto F, Ragona F, Russo E, Varesio C, Volpi L, Zanaboni MP, Pasca L, Veggiotti P. Ketogenic dietary therapies in epilepsy: recommendations of the Italian League against Epilepsy Dietary Therapy Study Group. *Front Neurol* 2023; 14: 1215618.
32. Rho JM, Boison D. The metabolic basis of epilepsy. *Nat Rev Neurol* 2022; 18: 333-347.
33. Pong AW, Geary BR, Engelstad KM, Natarajan A, Yang H, De Vivo DC. Glucose transporter type I deficiency syndrome: epilepsy phenotypes and outcomes. *Epilepsia* 2012; 53: 1503-1510.
34. Gibson AA, Seimon RV, Lee CM, Ayre J, Franklin J, Markovic TP, Caterson ID, Sainsbury A. Do ketogenic diets really suppress appetite? A systematic review and meta-analysis. *Obes Rev* 2015; 16: 64-76.
35. Kirkpatrick CF, Bolick JP, Kris-Etherton PM, Sikand G, Aspary KE, Soffer DE, Willard KE, Maki KC. Review of current evidence and clinical recommendations on the effects of low-carbohydrate and very-low-carbohydrate (including ketogenic) diets for the management of body weight and other cardiometabolic risk factors: A scientific statement from the National Lipid Association Nutrition and Lifestyle Task Force. *J Clin Lipidol* 2019; 13: 689-711.e1.
36. Gardner CD, Vadiveloo MK, Petersen KS, Anderson CAM, Springfield S, Van Horn L, Khera A, Lamendola C, Mayo SM, Joseph JJ; American Heart Association Council on Lifestyle and Cardiometabolic Health. Popular Dietary Patterns: Alignment With American Heart Association 2021 Dietary Guidance: A Scientific Statement From the American Heart Association. *Circulation* 2023; 147: 1715-1730.
37. Muscogiuri G, El Ghoch M, Colao A, Hassapidou M, Yumuk V, Busetto L; Obesity Management Task Force (OMTF) of the European Association for the Study of Obesity (EASO). European Guidelines for Obesity Management in Adults with a Very Low-Calorie Ketogenic Diet: A Systematic Review and Meta-Analysis. *Obes Facts* 2021; 14: 222-245.