Metabolic Diet App Suite for inborn errors of amino acid metabolism

Gloria Ho\textsuperscript{a}, Keiko Ueda\textsuperscript{a}, Roderick F.A. Houben\textsuperscript{c}, Jeff Joa\textsuperscript{c}, Alette Giezen\textsuperscript{a}, Barbara Cheng\textsuperscript{a}, Clara D.M. van Karnebeek\textsuperscript{a,b,⁎}

\textsuperscript{a} Division of Biochemical Diseases, BC Children’s Hospital, University of British Columbia, Vancouver, Canada
\textsuperscript{b} Department of Pediatrics, Centre for Molecular Medicine & Therapeutics, Child and Family Research Institute, University of British Columbia, Vancouver, Canada
\textsuperscript{c} Health2Media, Vancouver, Canada

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A B S T R A C T

Background: An increasing number of rare inborn errors of metabolism (IEMs) are amenable to targeted metabolic nutrition therapy. Daily adherence is important to attain metabolic control and prevent organ damage. This is challenging however, given the lack of information on disorder-specific nutrient content of foods, the limited availability and cost of specialty products as well as difficulties in reliable calculation and tracking of dietary intake and targets.

Objectives: To develop apps for all inborn errors of amino acid metabolism for which the mainstay of treatment is a medical diet, and obtain patient and family feedback throughout the process to incorporate this into subsequent versions.

Methods & results: The Metabolic Diet App Suite was created with input from health care professionals as a free, user-friendly, online tool for both mobile devices and desktop computers (http://www.metabolicdietapp.org) for 15 different IEMs. General information is provided for each IEM with links to useful online resources. Nutrient information is based on the MetabolicPro™, a North American food database compiled by the Genetic Metabolic Dietitians International (GMDI) Technology committee. After user registration, a personalized dashboard and management plan including specific nutrient goals are created. Each Diet App has a user-friendly interface and the functions include: nutrient intake counts, adding your own foods and homemade recipes and, managing a daily food diary. Patient and family feedback was overall positive and specific suggestions were used to further improve the App Suite.

Discussion: The Metabolic Diet App Suite aids individuals affected by IEMs to track and plan their meals. Future research should evaluate its impact on patient adherence, metabolic control, quality of life and health-related outcomes. The Suite will be updated and expanded to Apps for other categories of IEMs. Finally, this Suite is a support tool only, and does not replace medical/metabolic nutrition professional advice.

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1. Introduction

Inborn errors of metabolism (IEMs) although individually rare, form the largest group of monogenic disorders amenable to therapies targeting pathophysiology, often a lifelong dietary restriction combined with supplements and medications [1]. Examples include urea cycle defects, which require a protein restricted diet, arginine supplementation and emergency protocols with extra calories and fluids, to prevent hyperammonemia and accumulation of other toxic metabolites [2]. Expanded newborn screening (NBS) programs, increased awareness among clinicians, systematic evaluation of symptomatic patients (e.g. intellectual disability) and advances in diagnostic technologies (e.g. genome-wide sequencing) combined with discoveries of novel diseases and treatment approaches result in increased patient numbers. Consequently, physicians and dietitians are increasingly involved to counsel individuals affected by an IEM [3,4].

Strict adherence to disorder specific metabolic nutrition therapy (MNT) and medications can reduce the morbidity and improve patient outcomes [5]. Early and precise treatment can prevent complications such as severe neurological and other organ damage. In the best scenario, patients can develop at par with their peers [5,6]. Adherence to metabolic diets often interferes with social and cultural traditions, posing a burden for the patient and (extended) family alike [7]. Palatability issues as well as social, economic, educational, and motivational factors all challenge compliancy, and therefore impact metabolic control [8,9].

Phenylketonuria (PKU; OMIM# 261600) is the most common treatable IEM with an incidence of 1 in 10,000 births [10] and a Phenylalanine (Phe) restricted diet is the mainstay of treatment. Walter et al.
(2002) found that blood Phe concentrations exceeded treatment ranges in 30% of children younger than 10 years of age and in 80% of adolescents (aged 15–19 years old) [11]. Poor metabolic control poses the risk of organ damage and negatively impacts health and overall functioning in patients with IEMs [11].

Tracking daily dietary intake of disorder specific amino acids is difficult since this information is not readily displayed on food labels. Patients and their caregivers are at risk of under- or over-estimating amino acid content of foods, and threatening metabolic control. To enhance availability of nutrient information and to simplify the task of diet tracking and meal planning, we developed a digital tool for patients and their caregivers. With mobile digital health technology (DHT) integrated in our daily lives, we expect that this Metabolic Diet App Suite will fill a useful gap and facilitate varied meal planning and treatment adherence for this growing group of rare disease patients.

2. Methods

2.1. Ethics board approval

The University of British Columbia regional ethics board approved the current survey study (H14-00,818.)

2.2. Parameters

For inclusion in this App Suite, we selected inborn errors of amino acid metabolism for which a dietary therapy is deemed ‘standard of care’. In total, 15 different IEM disorder specific apps were created plus one general protein restriction diet app. The target user groups of this tool were defined as IEM patients and their caregivers as well as their health care professionals. This tool does not replace management and follow up visits with their physician and/or registered dietitian. It cannot be used as a replacement for complete diet assessments done using comprehensive tools such as GMDI’s Metabolic Pro™ nutrient analysis program.

2.3. Access

This App Suite can be accessed free of charge online via http://www.metabolicdietetapp.org (or the shortened URL http://mdapp.org). The App Suite can be viewed and used in the latest versions of all browsers (with a recommendation for Chrome, Firefox and Safari). Users are required to create a login to access and personalize the diet app on their desktop computers. Subsequently, based on the IEM chosen in the sign-up process, the user has access to his/her own digital database with food items on both their desktop computers and handheld devices (smartphones, tablets etc). All information entered into the App Suite is de-identified and encrypted via secure sockets layer (SSL) technology.

2.4. Data source

The nutrient values of foods were sourced from the Genetic Metabolic Dietitians International (GMDI) MetabolicPro™ food database accessed in 2014. MetabolicPro™ is a diet analysis program widely used by North American metabolic dietitians. The database contains nutrient information on over 100,000 food products. It is based on the U.S. Department of Agriculture’s National Nutrient Databank for Standard Reference food composition database, with additional nutrient information on medical formulas and specialty low protein foods.

2.5. Survey methods

In phase 1, an online feedback survey (see supplementary materials for details) was developed for parents after testing the Diet App for pyridoxine-dependent epilepsy (due to ALDH7A1 deficiency; OMIM# 266100). The feedback obtained was integrated to generate the second version of the PDE App and a first version of the PKU App. An additional feedback function was added to these Apps, which encouraged users to submit comments and questions to the developers (RH, JJ), allowing development of the model for cloning all 15 Diet Apps in the suite.

2.6. Design

Metabolic dietitians (KU, BC, AG), a metabolic diseases specialist physician (CVK), a nutrition sciences undergraduate student (GH), and two developers (RH, JJ) collaborated on the design and content of the tool.

Phase 1: Initially, we had compiled information from the USDA nutrient file version 26 [12]. In addition, nutrient values for low protein food items distributed to IEM patients in our province by the British Columbia Metabolic Nutrition Program (BCMNP) were manually added to the database. Once the database was complete, Health2Media translated it into the first version of the Diet App for Pyridoxine Dependent Epilepsy (PDE due to ALDH7A1 deficiency) for mobile devices and subsequently for desktops. Physicians, registered dietitians and researchers at our tertiary care centre (BC Children’s Hospital, Vancouver, Canada) tested the Diet App and parents of PDE patients were given access to pilot test the PDE diet app. Feedback was used to develop the next versions of the PDE Diet App.

Phase 2: After receiving feedback from the parents and health care providers, it was clear that the raw USDA foods database was not detailed enough for families on specialized metabolic diets counting daily amino acid dietary intakes, nor did it contain the many special foods and formulas required by these diets. We acquired a food composition database from GMDI used for their Metabolic Pro diet analysis program, which included food composition data for specialty low-protein foods and metabolic formulas in addition to the USDA food database selections. Once the GMDI database was implemented, the updated PDE Diet App and the new PKU Diet App were tested by physicians, metabolic dietitians and researchers, prior to being sent out to patients for beta-testing. An additional feedback function was added to the Apps, which allowed users to submit comments and questions to the developers, who subsequently used this to further improve the tools.

Phase 3: The Diet Apps for thirteen other IEM’s were created based on the final versions for PDE and PKU. The functional design of each App is similar, but as its content is IEM-specific it displays only nutrients that are relevant to the selected IEM. Each Diet App has its own specific logo and color pattern, making it easily recognizable for users.

3. Results

3.1. General

The available functions were designed to aid users in the task of food counting and thereby improve dietary adherence. The diet app was devised to be user friendly with the use of lay language and distinctive icons. In total, diet apps were developed for 15 different IEMs: pyridoxine dependent epilepsy (MIM:266100), phenylketonuria (MIM 261600), maple syrup urine disease (MIM248600), methylmalonic acidemia (MIM 251000), glutaric acidemia type 1 (MIM 231670), homocystinuria (MIM 236200), propionic Acidemia (MIM 606054), isovaleric Acidemia (MIM 243500), argininemia (OMIM 207800), argininosuccinic aciduria (OMIM 207900), carabamoyl phosphate synthetase 1 (MIM 608307), tyrosinemia (MIM 276700), ornithine transcarbamoylase deficiency (MIM 311250), α-acetylgutamate Synthetase Deficiency (OMIM#237310), & argininosuccinate Synthetase Deficiency/citrininemia 1 (OMIM 215700) [13]. An introduction with basic information about the IEM along with links to internationally recognized digital resources including the Genetics Home Reference [14] and Gene Reviews are included [15]. We added an additional app, which may be useful for other IEMs requiring a protein-free diet.
The App Suite is available on two platforms (same login): The mobile version can be accessed on electronic devices, such as smart phones (e.g. android and Iphone) and tablets (e.g. Ipad). The desktop version can be accessed on both desktop and laptop computers. The mobile version was designed for ‘on the go’ use, whereas the desktop version has more functionality, such as creation of own recipes and the option to export diet logbooks in PDF documents which users can share with their health care providers for monitoring and management purposes.

3.2. Account

3.2.1. Create an account

In order to access the Diet App users are asked to create a unique username and password that is linked to their email address (Fig. 1a). Users specify their preferred IEM diet app with relevant nutrient information specific to their IEM medical nutrition therapy. There is an option for users to enter their weight.

3.2.2. Reset password and retrieve username

Should a user forget their password or username, a message can be sent to the registered email address to retrieve these.

3.2.3. Edit profile

As diet prescriptions are dynamic and change as the patient grows, a function to modify the user profile is available on both mobile and desktop versions.

3.3. App features

3.3.1. IEM specific nutrient content of foods

For each IEM the Diet App displays macro-nutrient content of foods: energy (kcal), carbohydrates (grams), fats (grams) and protein (grams). In addition, amino acid content specific and relevant to the users’ selected IEM is provided. Some nutrients are visibly tracked whereas those that are usually not tracked by the lay user but are of interest to the health care provider are blinded. For example, for Maple Syrup Urine Disease (MSUD; OMIM# 248600) food content information on the amino acid Leucine (Leu) is provided [18]. Nutrients monitored by metabolic clinic professionals for medical management and follow up but not routinely counted by patients or caregivers in their daily meal planning are ‘blinded’. Such blinded nutrient content does appear in exported summary diet logs but is accessible via the digital database. For example in the MSUD Diet App, while Leu and protein are visibly tracked, the ‘blinded’ nutrients include the other branch chain amino acids valine and isoleucine [19]. For PDE, examples of clinically relevant but blinded nutrients in the PDE Diet App include Arginine (Arg), Vitamin B6 and Tryptophan (Trp) [16,17].

3.3.2. IEM specific nutrient tracking

The vast list of food products in (MetabolicPro™) for which amino acid content is available includes regular foods as well as specialty low protein food products. The Metabolic Diet App will count the nutrients relevant to the specified treatable IEM. A pie chart visually tracks how much of the user’s IEM specific target nutrient has been consumed and if the user has reached or exceeded the daily goals. The desktop version, displays pie charts for both daily protein and the IEM specific amino acid intake.

3.3.3. Add new foods

To accommodate new foods not included in the Metabolic Pro data and thus missing from the Diet App’s food database, a function ‘add your own foods’ was included. If the user does not enter the IEM specific amino acid content for the new food, the Diet App will calculate its amino acid content based on an average percentage of that amino acid in total protein content. For example, phenylalanine content averages 5% of the protein in food products, and this is used to calculate Phe intake in the PKU Diet App; for lysine this is 4% (Diet App for PDE and glutaric acidemia IMIM 231670) and for leucine this is 6% (MSUD). These average percentages of amino acid content in protein were determined by a review of expert opinion and the literature [17,20]. The user must be aware that the actual amino acid content in protein may vary per food group, for example the lysine content of meat is about 8%, exceeding the average lysine content of 4%.

3.3.4. Review food logs & edit food entries

Users are able to review food logs to determine trends in their diet. Users can edit foods incorrectly entered or not actually consumed.

3.3.5. Favorite foods

This function is unique to the mobile version and is a shortcut to add foods to daily logs. Due to diet restrictions and individual food preferences, people living with diet-treated metabolic disorders often do not consume a large variety of foods. Most commonly selected foods are automatically added to the user’s favorites section. Subsequently, users can quickly access their favorite foods and conveniently add foods to their daily intake log for diet tracking.

3.3.6. Export food logs (desktop only)

On the desktop version, there is an export food log function that allows users to download their diet intake logs into a portable document format (PDF) or excel file, which can be shared with their metabolic health care providers (Fig. 1c). The diet history table exported from the ‘daily logs’ tab contains all the displayed IEM specific nutrients seen by users, as well as other clinically relevant IEM-specific ‘blinded’ nutrients.

3.3.7. Create own recipe (desktop only)

The ‘Your Recipes’ function is available to enter homemade low protein meals and recipes with a combination of food ingredients. For example, ‘basic homemade rice crispy squares’, a single food product, is made from butter, rice crispy cereal and marshmallows. The metabolic diet apps will add up the IEM specific nutrient content of each of the entered ingredients, and calculate the IEM specific nutrients per serving in the entered recipe.

3.3.8. Feedback and logout

In order to improve and update the metabolic diet apps, users are able to provide online feedback and comments to app developers.

At any time, users can logout of the metabolic diet app and all entered data is saved.

3.3.9. Family survey and oral feedback

During phase 1 the survey was sent to 5 families using the PDE Diet Apps; their responses are summarized in Supplemental Table 1. The feedback was positive overall (‘a great help in tracking lysine intake’, ‘user-friendly’, ‘robust’, visually attractive’, and most importantly ‘makes following the diet easier’). The requested changes were incorporated into the next App version, including: expand units of measurement, inclusion of low protein products, decrease abbreviations, and increase efficiency of the search process. To address the latter a 2-step search process was developed, with an initial choice in food category (e.g. ‘vegetables and fruits’) to narrow down the number of products and increase the ease of subsequent search for the specific food product.

Fig. 1. Screenshots to illustrate the Metabolic Diet App Suite: a. Home page with the login/Create your account function. b. Personalized dashboard (PDE Diet App example) with food groups, nutrient information per serving size, and pie charts showing target and actual intake of specific amino acid and total protein. c. Daily logbook and mobile nutrient tracker.
4. Discussion

Families impacted by IEMs have the responsibility of managing multicomponent regimens including medical nutrition therapy, administration of medication, completion of blood work, lifestyle adaptations and attendance of clinic visits with an array of health care professionals.

Complex and time-consuming diet treatment is a burden on families already dealing with the stress of the impact of IEMs on the child’s peer relationships, performance at school and in sports [21].

Online apps have been incorporated into the dietary interventions for many disorders, and shown to improve self-monitoring and adherence; for IEMs this is the first of its kind however [22]. Compared to paper records, digital self-monitoring of diets was found to have positive effects on the behavior of users [23–25]. Furthermore, real-life applications allow for fast and accurate adjustments of dietary requirements, leading to stable metabolic control [26]. Constant tracking and feedback of the diet increases users' accountability [27]. A metabolic diet app for IEMs can empower families to become more active and make the necessary lifestyle adaptation [28,29]. By capitalizing on digital innovations, we hope to alleviate some of the burden of medical nutrition therapy for families.

The survey feedback supported the development of an IEM specific online diet app. The two major reported challenges families face with adhering to the diet are food planning and/or preparation and the social aspects around a restricted diet [29,30]. Families indicated that the metabolic diet app made it “way easier to track quickly”, allowing them to redirect their time to other activities. The Metabolic Diet App reduces the risk of human error since calculations of nutrient content and intake are automatized. Data has consistently shown that strict adherence to dietary treatment can reduce the morbidity of the disorder, and in some severe cases, mortality [21]. Sadly the current situation is far from ideal: 50–75% of children and adolescents with chronic conditions requiring self-management are non-adherent to their prescribed treatment [31], and during adulthood there is further deterioration, often due to loss of parental guidance and support [8]. Unfortunately, poor self-management can lead to a vicious cycle. With poor management of the diet, brain dysfunction with reduced attention span and memory occurs, affecting their ability to self-manage their restricted diet [8].

Subsequently, low impulse control and mood swings associated with low adherence to dietary restrictions further hinder ability to comply [8]. With technology integrated into our daily lives, the digital Diet App might ameliorate this cycle, providing a quickly accessible and familiar platform for self-management, supporting affected teens and young parents. 88% of American teens between 13 to 17 years old have access to a mobile phone, while 87% have access to a desktop or laptop [32]. In addition, 92% of teens report going online daily, with a quarter of them using the Internet “almost constantly” [32].

A restricted diet poses challenges to the individuals and family’s social life [29]. Especially the dissatisfaction with the available quality and variety of low-protein foods [8,29] negatively influences adherence. Many families feel limited due to the ambiguity of incomplete, invalidated, amino acid information in foods and feed their child what they know is safe. This uncertainty prevents families from consuming a larger variety of foods. The Metabolic Diet App, allows for real-time accurate analysis and calculations of over 10,000 regular foods and specialty low protein food products. With IEM relevant amino acid content more readily available via the Metabolic Diet Apps, people living with diet treated metabolic disorders and their families may be able to eat a larger variety of foods, reduce food cost, save time and enjoy meals together more easily.

The GMDI database comprises data for North-American food products. The nutrient content of certain products may differ in other geographical locations. Users who travel or live outside of this continent must keep this limitation in mind. Currently, the ‘Your Foods’ function provides a solution, as nutrient information available from labels (e.g. protein, energy, carbohydrates) can be manually entered and used.

The second limitation is the amino acid specific conversion factor utilized to determine the amino acid content in foods for which this data is missing; although this does provide an estimate, the actual amino acid content varies depending on the type of food. Third, the user must be aware of the risk for human error, especially in the step of entering the serving size, which determines the calculated nutrient intake. Patients with co-morbidities and extremely complex diet restrictions may not find the Metabolic Diet App useful as only IEM specific amino acids are displayed. Finally, access to the Internet and/or desktop and handheld devices may limit or prevent use of the Diet App in rural settings or where budget restrictions exist.

The Metabolic Diet App will be regularly updated to concur with MetabolicPro™ revisions. In the future, we plan to tailor diet apps for other IEMs such as fatty acid oxidation disorders and IEM requiring the ketogenic diet. We aim to collaborate with colleagues in other countries and settings to adapt the Diet App Suite to their needs and situation; funding and reliable nutrient databases are prerequisite. Furthermore, we are currently adding a function which excludes fruits and vegetables from the amino acid calculations, as in some dietary IEM regimens these are freely permitted. Finally, formal studies evaluating the effect of the Metabolic Diet Apps on adherence, monitoring and quality of life are necessary.

In conclusion, we designed this digital tool to help individuals affected by one of more than 15 rare IEM. This type of personalized medicine should increase accuracy of diet tracking and information transfer between patients and health care providers, and thus advance adherence to medical nutrition therapy and metabolic control. Future directions include collection of feedback from health care professionals, patients, and their caregivers with integration into the App Suite for further improvement, as well as formal evaluation of the App Suite users’ profiles and behaviors, and the impact of App use on dietary adherence; somatic growth, metabolic growth, quality of life and other relevant effect measures.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jyngmne.2015.12.007.

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