SPECIAL REPORT

What are the minimum requirements for ketogenic diet services in resource-limited regions? Recommendations from the International League Against Epilepsy Task Force for Dietary Therapy

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Summary

Despite the increasing use of dietary therapies for children and adults with refractory epilepsy, the availability of these treatments in developing countries with limited resources remains suboptimal. One possible contributory factor may be the costs. There is often reported a significant perceived need for a large ketogenic diet team, supplements, laboratory studies, and follow-up visits to provide this treatment. The 2009 *Epilepsia* Consensus Statement described ideal requirements for a ketogenic diet center, but in some situations this is not feasible. As a result, the International League Against Epilepsy (ILAE) Task Force on Dietary Therapy was asked to convene and provide practical, cost-effective recommendations for new ketogenic diet centers in resource-limited regions of the world.

KEY WORDS: **Ketogenic, Resources, Global, Diet, Minimum, Epilepsy.**

The use of ketogenic dietary therapy for treatment of epilepsy is more widespread than ever in history: from its origins in 1921 at the Mayo Clinic in Rochester, Minnesota, to today where the ketogenic diet (KD) is available in >50 countries.[1] The Fourth Biannual Ketogenic Dietary Therapy Global Symposium was recently held in Liverpool, United Kingdom, with over 400 attendees from around the world sharing their clinical and research experience. There is growing interest in applications beyond epilepsy, including brain cancer, Alzheimer disease, and autism. Clinical interest worldwide is approaching an all-time high.

In 2009, an expert consensus statement was published in *Epilepsia* to guide the management of patients receiving dietary therapy.[2] These recommendations were largely based on published research, but in addressing topics with mostly anecdotal evidence, a group opinion was obtained and at times voted on. Although several aspects of dietary therapy care were felt to be based on strong evidence, some had less clear scientific underpinnings and were deemed more flexible.[3] This Consensus Statement is primarily referred to today by new ketogenic diet centers as a guide for providing the standard of care to patients.

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Key Points

- The 2009 *Epilepsia* Consensus Statement described ideal requirements for a ketogenic diet center, but in some resource-limited situations these are not feasible. Therefore the ILAE approved this consensus statement to review the minimum standards for ketogenic diet programs in resource-limited regions.
- A physician (preferably a neurologist) familiar with ketogenic diets is mandatory for a new ketogenic diet team with limited resources; a dietitian is mandatory for the classic ketogenic diet, but optional for the alternative diets.
- The minimum laboratory studies at baseline are serum sodium, potassium, bicarbonate, chloride, blood urea nitrogen (BUN), creatinine, and glucose. Fasting lipid profile and urinalysis are to be included with follow-up labs.
- All patients should receive a multivitamin, calcium, and, if infants, have access to ketogenic diet formulas. Other supplements described in this article are recommended or optional.
- Admission to a hospital to start dietary therapies is recommended for infants or patients with comorbidities. For lower-risk patients, outpatient diet initiation can be an option, but all patients need to have an ability to contact their ketogenic diet team in an emergency.

Despite the widespread use of ketogenic dietary therapies, there still exist large regions of the world that do not offer these treatments (Fig. 1). Many of these regions are in the Caribbean, Central America, Africa, Eastern Europe, and Southeast Asia. Although there are a myriad of reasons for the lack of dietary therapy in these parts of the world, they likely include the financial costs of a large ketogenic diet team (including a dietitian and trained neurologists), labs and supplements for patients, and perhaps even the higher fat foods (e.g., dairy and meats) themselves.[4] The detailed information as provided in the 2009 Consensus Statement may appear daunting to a potential new ketogenic diet center in a country with limited financial resources.

Due to the concern that centers interested in offering dietary treatments may elect not to do so because of perceived inadequate resources, the International League Against Epilepsy (ILAE) Task Force on Dietary Therapy held a 1-day meeting in Liverpool United Kingdom immediately preceding the recent Ketogenic Dietary Therapy Global Symposium. Many of the members of this Task Force had personal experiences training and providing services to countries with limited resources that are trying to develop ketogenic diet centers (including treating children in Honduras, El Salvador, Uganda, Jamaica, Georgia, and rural parts of China and India).[5] The goal was to create a succinct document outlining the core requirements for a ketogenic diet service. The Task Force reviewed articles and then covered specific topics from the Consensus Statement; however, there was a specific focus on cost-savings and determining what was an absolute necessity (vs. ideal aspects of a service), while trying to maintain patient safety and diet efficacy. In several situations there was clear agreement, whereas for other topics a vote was held. This document was not meant to supersede the Consensus Statement, and each individual center is cautioned to use their own judgment based on their population, expertise, and resources. The ILAE and Child Neurology Society continue to endorse the Consensus Statement as standard of care for regions with optimal resources.

This document is a summary of the discussion during the Task Force meeting, the goal of which is to provide new centers with limited resources a guide to the most important resources that should be made available in a ketogenic diet

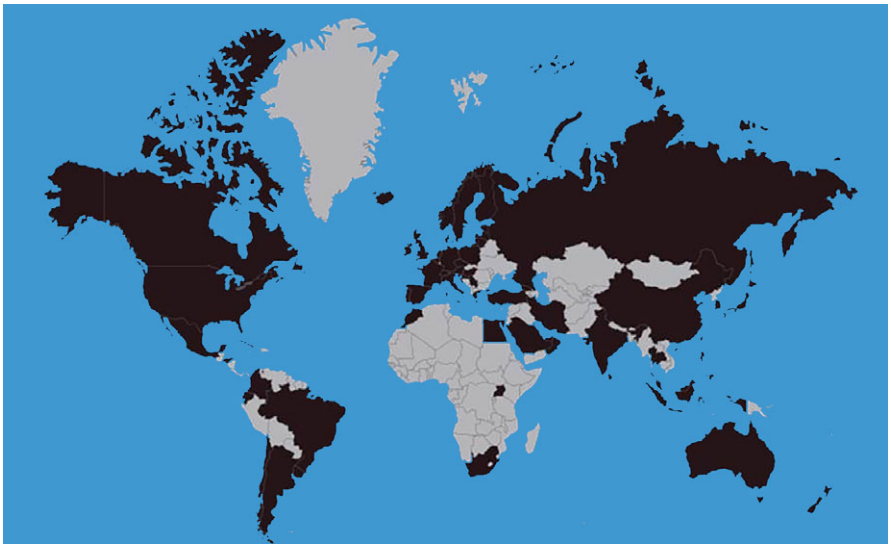

Figure 1.
Countries that offer the ketogenic diet (colored in black), to the knowledge of the co-authors.
Epilepsia © ILAE

center. The Task Force believed strongly that any new center should have the ability to obtain advice from and refer more problematic patients to a more experienced center when necessary. Additional laboratory studies, team members, supplements, and diet components are at the discretion of each ketogenic diet center.

Who are the Critical Members of a Ketogenic Diet Service?

In many ways, the two core members of a ketogenic diet service are a dietitian and a neurologist. Some centers may have only one of these members (typically a dietitian). A recent study of North American ketogenic diet centers from 2014 revealed that some have large teams that also include social workers, pharmacists, and nurses.[6] Given this disparity in resources, we asked what is truly required.

The Task Force was unanimous that it is mandatory that a physician who is knowledgeable about the ketogenic diet be directly involved in the patient's care as part of the team and serve as the leader. This provider should be able to identify and refer patients who are appropriate for diet therapy, know when to start and stop treatment, decide when it is safe to taper anticonvulsant drugs, and recognize and manage side effects. The physician should also be aware of metabolic conditions that are contraindicated with ketogenic diet therapies, particularly in areas of the world with high rates of consanguinity and therefore genetic and metabolic diseases. Screening for these disorders should be undertaken before the ketogenic diet in started. In general, this person is the primary "supervisor" of the dietary therapy center. The group strongly recommended that this physician be a neurologist (pediatric or adult) with training in epilepsy and diet treatments. If a neurologist is not available, a primary care physician such as a pediatrician, internist, or family medicine physician would be sufficient (assuming they have some basic epilepsy training and familiarity with ketogenic diets). If a physician is not available, a well-trained nurse or nurse practitioner may serve in this capacity with a physician as backup remotely if needed. An example was given of the current situation in Uganda, where nurses often act as physicians (with remote backup) and handle medications.

In addition, it was agreed that a registered dietitian was mandatory only specifically for the classic ketogenic and medium chain triglyceride (MCT) diets, in which calculations of ratios of foods are required. In some countries, the ketogenic diet physician is also trained as a dietitian, and would be acceptable therefore as the sole provider on the ketogenic diet team. Dietitians are especially important for the close follow-up of patients to ensure adequate nutrition and diet compliance. Dietitians were believed to be advisable, but not mandatory, for the modified Atkins diet (MAD) and low glycemic index treatment (LGIT) as well. There was recognition of published evidence to support the notion that these diets are sometimes initiated without dietitian supervision.[4,7] The Consensus Statement does not specifically address this point regarding the MAD and LGIT, so these recent articles were used as preliminary evidence that management by a physician alone was at least possible. Should the MAD or LGIT be started without a dietitian, phone or email contact with a dietitian (or physician expert in these therapies) in case of a problem was also strongly advised. In addition, the physician managing the MAD or LGIT should be very familiar with the nutritional aspects of these dietary treatments. Other potential team members such as pharmacists, social workers, nurses, and psychologists are optional. The Consensus Statement did not address the need for these additional providers, with only one recent study discussing North American practice regarding the ketogenic diet team.[6]

What is the Age Range for Which a New Center should be Comfortable and Offer Therapy? Should the Center have the Ability to Take Care of Adults on Dietary Therapy?

The Task Force believed most ketogenic diet centers should be comfortable with treating children ages 2–15 years who have no major comorbidities. If a child has multiple medical comorbidities, there should be a hospital or clinic available nearby for emergency situations. Although many experienced centers will start the ketogenic diet for infants, and certainly children 1-2 years of age, a new center with limited resources may wish to consider referring those patients to a more experienced team. Patients older than 15 years of age should not be started on dietary therapy unless there is an option for transition to a team that is comfortable with treating adults with dietary therapy (to avoid abrupt discontinuation and/or complications).[8] The use of dietary therapy for adults is very promising, but at this time a ketogenic center focusing on children need not agree to initiate the diet in adults.[9] Adult centers should have a physician who is familiar with issues related to adults with epilepsy (e.g., driving, pregnancy, etc.), preferably an adult neurologist.

Should Members of a Center be Formally Trained?

The Task Force strongly recommended that members of a new ketogenic diet center be formally trained in person regarding how to implement dietary therapies. Several anecdotal experiences were shared of centers that started the diet without training and subsequently had severe, adverse patient experiences. This training should include the following: (1) at least one training visit to an established ketogenic diet center, (2) attending a training

conference at a university or hospital, or (3) having a ketogenic diet team travel to their center to help educate them in how to use this treatment. Training should include the core ketogenic diet team members and others who may be interested (including parents or traditional healers in some regions). Given that training may not always be feasible or affordable for all centers, other optional methods of training may be included on-line with social media (videos), DVDs, video conference calls, etc. These methods were discussed as future ways to potentially expand ketogenic diet usage. The duration of ketogenic diet training was left optional, but is often 1–5 days according to Task Force members with personal experience in providing ketogenic diet education. It was strongly recommended that new ketogenic diet centers keep current on treatments and recommendations in the ketogenic diet field and in close contact with their training center for years afterwards, especially for help with difficult cases. This issue of how to train new ketogenic diet centers is a novel one with no published information to our knowledge.

Which Diets should be Offered? Should All Four Dietary Therapies be Offered?

The Task Force believed it was mandatory that a ketogenic diet center be at least familiar with the basics of all four dietary therapies (KD, MCT, MAD, and LGIT). However, the individual ketogenic diet center should determine which diets they wish to offer based on their resources and comfort levels. For example, a center with very limited resources, inability to hospitalize, and no dietitian may choose to only offer the LGIT or MAD. This may also be true for adult dietary therapy centers.

Which Laboratory Studies are Mandatory?

One topic that required considerable discussion from the Task Force was the minimal requirements for laboratory studies. Recognizing the large list from the Consensus Statement, and recent concerns regarding selenium and vitamin D deficiency as well as bone density changes with continued diet therapy use, the Task Force attempted to narrow the list of mandatory studies that were truly essential to follow.[2] This information is listed in Table 1.

The value of following urinary ketones was a topic of some discussion separately as well. There is a growing recognition that ketosis may not be a direct mechanism of action of the ketogenic diet.[10] This is especially true for the LGIT and possibly MAD, where ketones may be low or undetectable. The group voted 10-2 that while recognizing the insufficient data supporting their relevance, the ability to at least periodically check urine ketones should be mandatory in a center, especially if a family is considering stopping the diet because of lack of efficacy (as low ketones may be a marker of noncompliance and insufficient hepatic fat metabolism). This is similar to the Consensus Statement, which does suggest periodic checking of urine ketones.

Table 1. Baseline and follow-up information, and diagnostic and laboratory studies for children and adults receiving the ketogenic diet

	Baseline (pre-KD)	Follow-up (at clinic visits)
Mandatory	Basic counseling, weight and height, history of food allergies and intolerances, food availability/preferences Labs: sodium, potassium, bicarbonate (CO_2), chloride, BUN, creatinine, glucose Metabolic testing to identify etiology, especially when suspected high risk based on presentation and family history	Weight and height Labs: sodium, potassium, bicarbonate (CO_2), chloride, BUN, creatinine, glucose, lipid profile, urinalysis Urine ketone testing (no consensus – 10 Task Force members voted "mandatory", and 2 voted "advised"); mandatory if patient is not doing well on the diet and considering stopping. Recommendations are also highly dependent on which diet patient is on, e.g., for LGIT no ketone testing may be required
Advised	Calorie count (e.g., three-day food record) Labs: hematocrit, white blood cell count, platelets (recommended especially in countries where nutritional anemia rates are high), calcium, vitamin D level (especially on first-generation anticonvulsants), fasting lipid profile (strongly recommended if history of personal or familial hyperlipidemia, cardiovascular risk factors), liver function tests (mandatory if on hepatically metabolized anticonvulsants)	Labs: liver function tests (if patients is receiving hepatically metabolized anticonvulsants; some discussion about whether this should be mandatory instead), vitamin D level, complete blood count, calcium, free carnitine (strongly recommended if receiving anticonvulsants such as valproate that deplete carnitine)
Optional, but not required	Free carnitine, selenium, magnesium, phosphorus, urinalysis, anticonvulsant levels	Selenium, magnesium, phosphorus, anticonvulsant levels, renal ultrasound, urine calcium and creatinine ratios (especially if not on citrates), DEXA scans

CO_2 = bicarbonate; BUN = blood urea nitrogen; LGIT = low glycemic index treatment; DEXA = dual-energy X-ray absorptiometry

Follow-up was also generally recommended in a manner similar to the Consensus Statement, with patients being evaluated every 3–6 months (3 months is recommended if the patient is resides close to the center). In-person visits are advised, but telemedicine or phone visits are theoretically possible if distances to the ketogenic center are extreme.[7] This concept is relatively new with an email-administered MAD study published in 2012 (3 years after the Consensus Statement). [7] Infants should be seen more frequently, especially if complications occur. It is important to recognize that ketogenic diet management by physicians should be similar to anticonvulsant medication management; both treatments may cause side effects. The entire ketogenic diet team should be involved in ensuring that labs are obtained and follow-up appointments are kept.

What is the Required Basic Supplementation for Dietary Therapies?

Owing to the restrictive quantity of nutrient-dense foods in the diet, the use of a multivitamin with trace minerals (including selenium) was deemed mandatory by the Task Force; adult tablets can be crushed and a carbohydrate-free preparation is advised.[11,12] If the only multivitamin regionally available has carbohydrates, it should still be given, perhaps with recalculation of diet ratios to account for the alteration in the carbohydrate daily limit. The Task Force did comment that there are some situations where being on a ketogenic diet, with strict dietary intake, may in fact improve the nutritional state of a malnourished child (e.g. in certain areas of Africa), even when a multivitamin is not provided. Calcium was also felt to be mandatory. Some ketogenic diet pre-made formulas do include vitamins and calcium, especially when the diet provides the entirety of a patient's nutrition. Finally, the ability to provide a liquid formulation of the ketogenic diet (either commercial or modularly created) is mandatory for a center that treats infants. These recommendations were identical to the Consensus Statement.

Supplemental vitamin D, not always included in calcium tablets, was strongly recommended. There is growing evidence of vitamin D deficiency in patients receiving anticonvulsants, and several Task Force members commented that supplementing Vitamin D without checking levels may be cost-effective.[13] The routine prescription of extra vitamin D, carnitine, oral citrates (strongly recommended with a prior history of kidney stones), laxatives, trace elements, medium chain triglyceride oil, coconut oil, sodium, and ketogenic diet formulas (for patients unable to intake solid food) was deemed optional, similar to the Consensus Statement recommendations. The ketogenic diet commercially available formulas can be very expensive for patients and are not required universally to be available.

Should a Patient be Admitted or Fasted to Start Dietary Therapy?

There is evidence to support safe outpatient initiation of all dietary therapies, so therefore the ability to admit a patient is optional.[14–16] In a study from 2010, half of centers starting children on the ketogenic diet in United Kingdom did so as on an outpatient basis.[14] Should the ketogenic diet be started as an outpatient, the group suggested that no fasting period be used with the option of using more gradual introduction for safety purposes. For patients at high risk (infants, patients with comorbidities), inpatient hospitalization to start dietary therapy is strongly recommended. If an admission is not possible due to lack of resources or center/family choice, very close follow-up for these patients such as by phone (or email), and local pediatrician access with proximity to the ketogenic diet team is mandatory. It is strongly recommended that anyone starting a ketogenic diet have access to a nearby clinic or hospital in case of emergencies. These recommendations are similar to that of the Consensus Statement, in which 73% of the panel believed an outpatient initiation could be used.[2]

Several members of the Task Force endorsed the concept of discussing basic nutrition with families prior to starting this treatment to help improve later compliance. This discussion can involve reducing sugars and added sweets, reading food labels, and cooking meals for individual children in a family. Should these preliminary interventions fail to be followed by the family, it may be prudent to avoid ketogenic diet implementation. There are no data to support the value of this pre-ketogenic diet discussion, yet most of the attendees used this approach.

How Should Follow-Up Support be Handled?

It was felt mandatory that the ketogenic diet team or a designated covering specialist be available at all times for patient emergencies. The patient should have access to means of rapid communication, and whereas phone contact is strongly recommended, some communities may have other methods of contact (e.g., runners with written messages in Africa) that are sufficient. It is mandatory that a member of the ketogenic diet team (preferably all members) have access to a telephone. Electronic patient records for ketogenic diet patients and email for rapid contact are advised, but may not be possible. The Task Force also felt it was advised that a newly established ketogenic diet team had the capability to request a second opinion from a more experi-

enced team, even if by phone or email, when difficult issues were identified. There is no published evidence to our knowledge on this topic.

Are Written Materials Recommended?

The Task Force believed it was strongly recommended that written materials be available in the patients' and care providers' primary language for counseling and providing ketogenic diet education. The Internet is advised as a resource due to the large amount of recipes, resources, and support available, but not required. Many materials are available at the ILAE Task Force for Dietary Therapy website: http://www.ilae.org/Commission/medther/keto-index.cfm.

Conclusions

This document provides guidance for a new ketogenic diet center in areas with limited resources with regard to the minimal requirements necessary to offer this service for patients with epilepsy. It is not a substitute for the 2009 Consensus Statement, but rather focuses on cost-savings and what is mandatory compared to advised (or optional). Should new information regarding safety with the use of dietary therapy become available, this document will be updated. The ILAE Task Force on Dietary Therapy welcomes comments on this document from new and established ketogenic diet centers alike.

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Disclosure of Conflict of Interest

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