

Innovative Approaches to Managing Drug-Resistant Epilepsy in Adults: The Role of Ketogenic Diet Therapy



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July 17, 2025

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Disclosures



Elizabeth Felton, MD, PhD

- Medical Advisory Board: Glut 1 Deficiency Foundation
- Scientific Advisory Board: Epilepsy Foundation of Wisconsin
- Speaking / Consulting Honorariums
 - American Epilepsy Society
 - Nutricia North America
 - Nestle Health Science
 - Medtronic
 - Abbott

Ulrike Reichert, MS (webinar organizer)

Employed by Nutricia North America

Kelly Faltersack MS, RDN, LDN, CD

- Medical Advisory Board: Glut 1 Deficiency Foundation
- Speaking / Consulting Honorariums (Honorariums went to my employer. No personal compensation received.)
 - American Epilepsy Society
 - Metabolic Health Summit
 - Ajinomoto Cambrooke
 - Nutricia North America

Rachel Powers, RD (webinar moderator)

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None pose any conflict of interest for this presentation.

The opinions reflected in this presentation are those of the speaker and independent of Nutricia North America

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Learning Objectives



- Participants in this activity will learn to:
 - Review the clinical evidence supporting the use of ketogenic diet therapy in managing drug-resistant epilepsy in the adult population
 - Learn practical strategies for implementing ketogenic diet therapy in clinical practice, including patient selection, dietary planning, monitoring, and managing potential side effects
 - Understand real-world applications of ketogenic diet therapy in managing drug-resistant epilepsy and identify best practices for optimizing patient care

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Poll Question



- Which population do you work with?
 - Pediatrics
 - Adults
 - Both, but primarily pediatrics
 - Both, but primarily adults

Poll Question

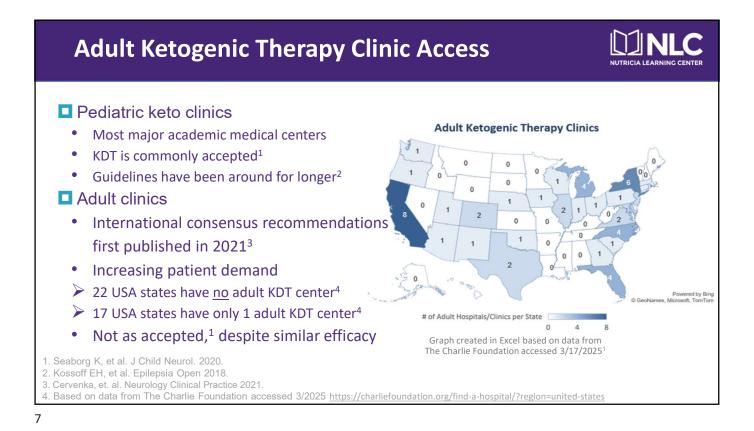


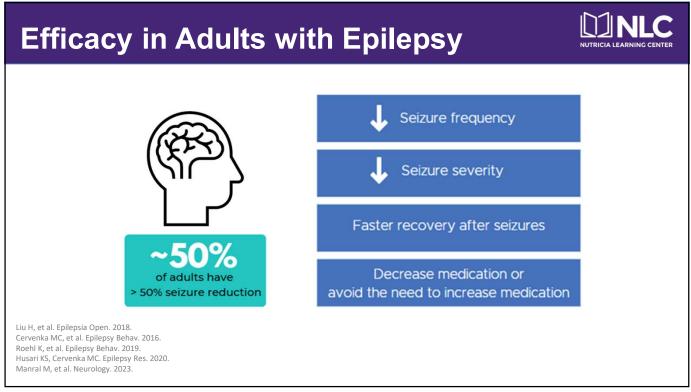
- How many adult patients with epilepsy on ketogenic diet therapy do you currently support?
 - **0**
 - **1-10**
 - **11-20**
 - **21-50**
 - **51-75**
 - More than 75

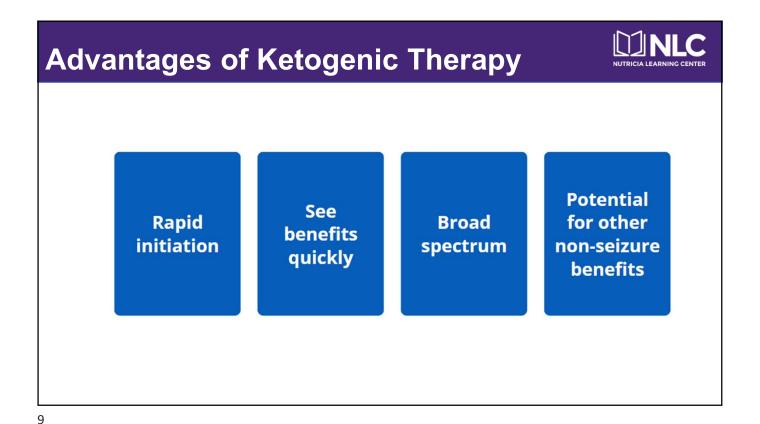
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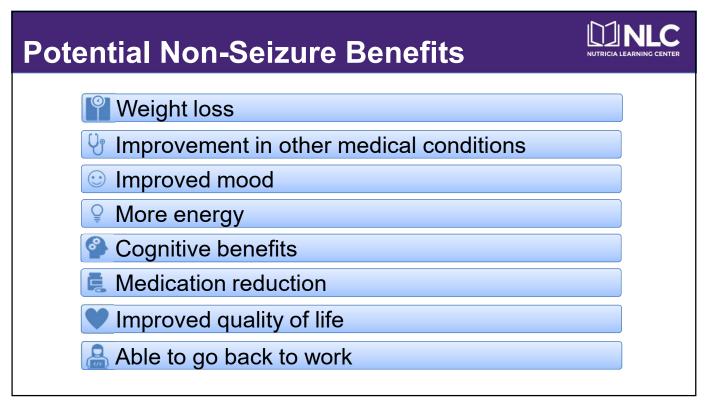


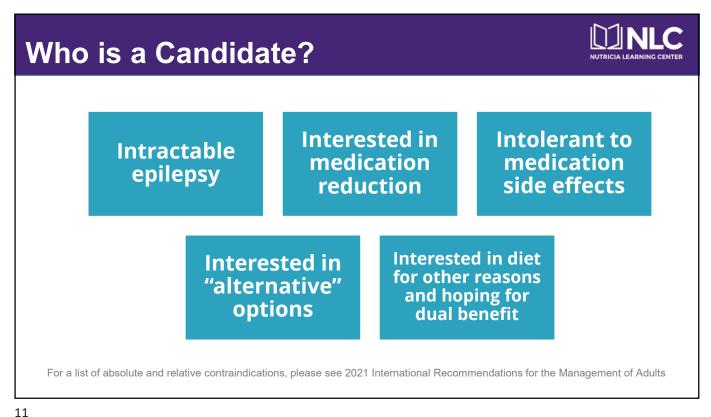
Management of Adults on Ketogenic Diet Therapy

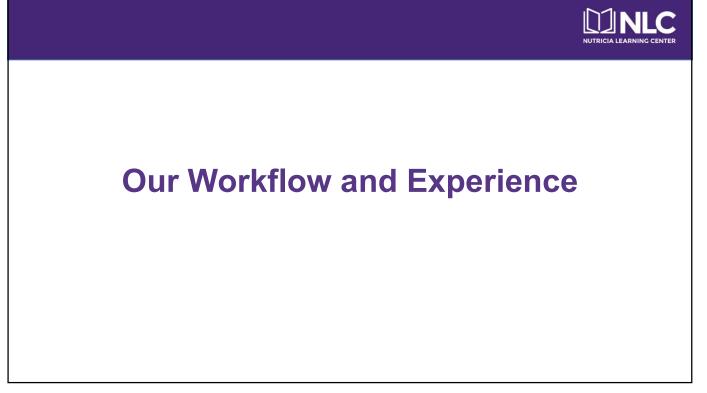


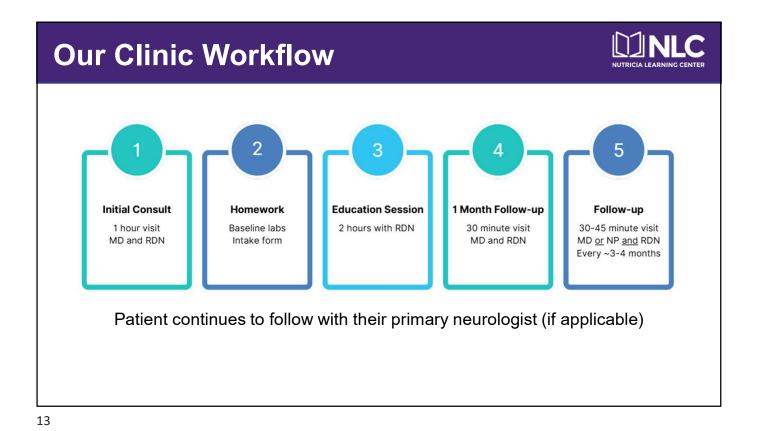












Visit 1: Initial Consultation Take a general epilepsy history Screening questions focused on adults O Coexisting medical conditions* Medications* O Alcohol use **Initial Consult** O Contraception use 1 hour visit O Plans for pregnancy MD and RDN O History of eating disorder O Pre-existing food restrictions (allergies, gluten-free, vegetarian, vegan, low-FODMAP, organic, artificial sweetener avoidance, etc.) Discuss risks vs benefits of ketogenic diet therapy*

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Coexisting Medical Conditions Medical Condition Pre-ketogenic diet therapy After starting ketogenic diet therapy Type 2 Diabetes Baseline HgBA1C and review Monitor blood sugar of medications Improvement in glycemic control is Make sure managing provider common is on board May require medication adjustment Hypertension If uncontrolled, need to address Improvement in BP is common prior to starting ketogenic diet May require medication adjustment therapy Obesity Establish weight goals Weight loss is common and can be Make it clear that weight loss is motivating! Assess for losing weight too quickly not primary focus Hypercholesterolemia If very elevated at baseline, Lipids often increase initially, then proceed with caution trend towards baseline by 1 year If elevated triglycerides – assess for low carnitine

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Coexisting Medications



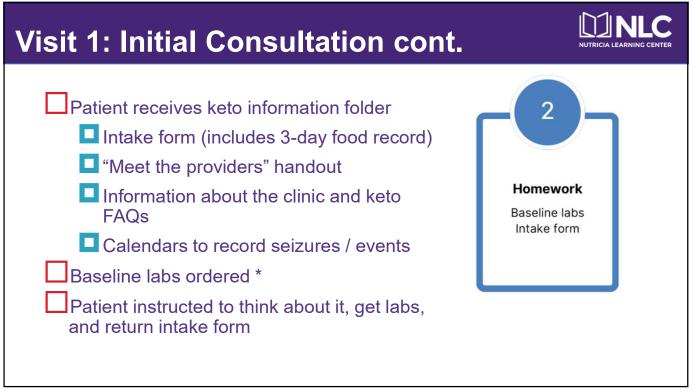
- Adults may be on medications that require additional monitoring
- Examples (focus on non-epilepsy medications):

Medication	Concern	Recommendations
Certain blood pressure medications, such as diuretics	Electrolyte disturbance (potassium, magnesium)	Check electrolytes 1 month after starting ketogenic diet therapy
Oral hypoglycemic, insulin, metformin	Hypoglycemia	Obtain blood glucose/ketone meter and monitor blood sugar, so med adjustments can be made
Olanzapine and other drugs that can increase lipids	Elevated lipids	Check lipid panel more often
Thyroid medication	Changes in thyroid levels	PCP monitors thyroid levels and adjusts med dose if needed
Liquid or sublingual medications	Hidden carbohydrates	Convert to pill when possible Check carbohydrate content

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Side Effects – Our Experience Most Common Occasional Less Common Constipation Other GI side effects Renal stones (e.g. bloating, diarrhea) Weight loss **Acidosis** Dizziness / lightheadedness Hyperlipidemia¹ Weight gain Hair thinning Nutrient deficiency (e.g. vitamin D, carnitine) or loss Change in Hypoglycemia menstrual patterns Keto rash (rare)

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Baseline Labs



All patients	Select patients
Complete metabolic panel, Magnesium, Phosphorus	Selenium
Complete blood count	Zinc
Lipid Panel	Copper
Vitamin D	Vitamin B12, RBC Folate, MMA, Homocysteine
Carnitine (free and total)	Urine organic acids, serum amino acids*
Urinalysis	24 Hour Urine
Urine pregnancy (in people of childbearing potential)	Hemoglobin A1C, Fasting insulin
Antiseizure medication (ASM) levels	Beta-hydroxybutyrate (BHB)
	Celiac screening: tTG-IgA, IgA

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Practical Tips



- Do not make 2 changes at once.
- Wait one month after a medication change before starting keto
- Wait 3 months after starting ketogenic therapy to make medication changes (unless there is an emergent need to make a change)
 - Set expectations up front!

Visit 2: Dietitian Education Session

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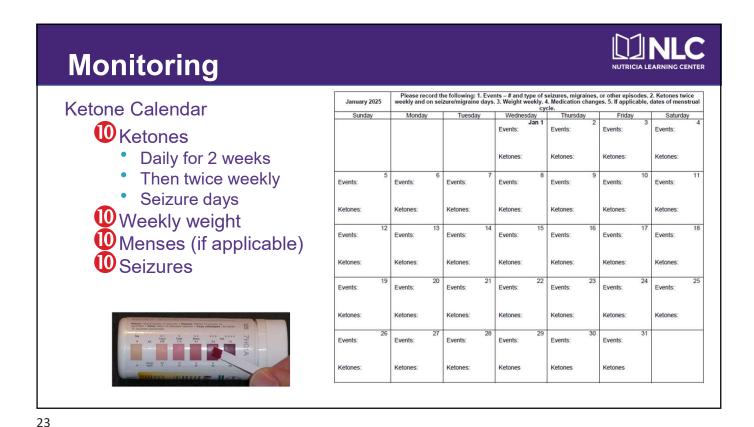
- Individualized
- Anyone involved in food prep attends
- Video visit
- "Keto starter kit"
- Supplements
 - Multivitamin with mineral (or prenatal multivitamin)
 - Calcium + D
 - *Vitamin D (as needed if deficiency is present)
 - *Levocarnitine (if carnitine deficiency is present)
 - *Potassium Citrate (if hypocitraturia on 24 hour urine)



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Diet Versions The Modified Atkins Diet Low Glycemic Index (LGIT) (Pfeifer and Thiele 2005) (MAD) 240-60 grams total carbohydrate (Kossoff 2003) Foods with glycemic index (GI) <50 20 grams net carbohydrate Meals and snacks balanced with ★ Net = Total – Fiber protein and fat ★ Sugar alcohols are not subtracted* Low Glycemic Index **Modified Atkins Diet** Kossoff EH, et al. Neurology. 2003. Pfeifer, HH and Thiele EA. Neurology. 2005

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Follow-Up Visits Check vitals, including weight (important to do without shoes/coat) Review seizure/ketone calendars Monitor labs* 5 Discuss side effects, barriers, impressions of efficacy and other benefits 1 Month Follow-up Follow-up Ongoing education and 30-45 minute visit 30 minute visit troubleshooting MD and RDN MD or NP and RDN Every ~3-4 months Most important: provide encouragement!

1 Month Labs for Select Situations **Medications** Labs Carbamazepine Eslicarbazepine BMP + BHB Oxcarbazepine Diuretics Chlorothiazide, Hydrocholorothiazide, BMP, Mag, BHB Chlorthalidone, Furosemide, Bumetanide, Torsemide Potassium citrate **BMP Situations** Classic Ketogenic Tube Feeding BMP + BHB Outpatient Initiation

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Lab Monitoring		NUTRICIA LEARNING CENT
Frequency	All patients	Select patients
3-4 monthsThen every 6 months	Complete metabolic panel, Magnesium, Phosphorus	Selenium
Annual for long-term patients who are stableMay check subset of interim labs	Complete Blood Count	Zinc
	Lipid Panel	Vitamin B12, RBC Folate, MMA, Homocysteine
Other considerations	Vitamin D	24 Hour Urine
ASM levels in patients with significant weight loss	Carnitine (free and total)	Hemoglobin A1C, Fasting insulin
PCP monitor thyroid labs if	ВНВ	Specific micronutrients
taking thyroid meds	Urinalysis	
	ASM levels	Other labs possible

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Antiseizure Medication (ASM) Levels



- o Dose is often weight based in children, but not in adults
- Helpful to have baseline levels prior to KDT and follow-up levels after initiating
- ASM KDT interactions are not straightforward and depend on many factors
- Possible mechanisms of interactions
 - Dehydration
 - · Modified serum protein binding

Armeno and Kossoff. Epileptic Disorders. 2023.

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Special Situations and Optimizing Ketogenic Diet Therapy for Adults

Poll Question



- When does your center initiate ketogenic diet therapy for status epilepticus?
 - Within 48 hours
 - Within 7 days
 - After a couple weeks
 - □ ~1 month or more
 - Only as a last-ditch effort
 - Have never used keto in the ICU

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Ketogenic Diet for Status Epilepticus



- Ketogenic diet therapy has been successfully used as an emergent, acute therapy in adults with status epilepticus
- Tips:
 - Protocols and orders sets are important to prevent errors
 - W UW Health Clinical Practice Guideline
 - Best Practice Alert
 - No propofol in last 24 hours
 - Pharmacy assistance to minimize carbohydrates in medications

Hypoglycemia is only treated if less than 50 mg/dL

AVOID CARBS IN MEDS TIPS TO MINIMIZE CARBS 2 CHEW TABS Use normal saline, half normal saline or lactated ringers DEXTROSE IV FLUIDS Base solution of infusion should **DEXTROSE INJECTIONS** be changed to 0.9% sodium chloride or straight drug (if able) **OR INFUSIONS**

Cervenka MC et. al. Neurology. 2017. McDonald TJW, et al. Semin Neurol. 2020. Kaul N, et. al. Neurol Clin Pract. 2021. Wickstrom R, et. al. Epilepsia. 2022



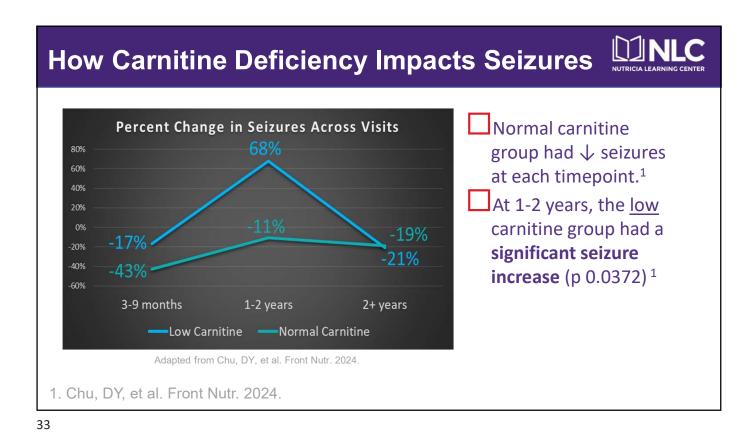
Carnitine

and its effect on seizure control

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Carnitine Oconditionally essential nutrient Plays an essential role in fat metabolism **10** L-Carnitine is required to transport long chain fatty acids into the mitochondria for βoxidation to produce energy (ATP) f f 0KDT may increase the risk of carnitine More than 1 in 3 adults deficiency^{1,2} developed carnitine 10 38% of adults developed carnitine deficiency deficiency on MAD on MAD³ Most (55%) within 3-9 months³ Can occur at any time³ Carnitine Deficiency Free carnitine < 25 µmol/L 1. Neal EG, et al. Epilepsy Res. 2012. 2. Kossoff EH, et al. Epilepsia Open. 2018. 3. Chu, DY, et al. Front Nutr. 2024.

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Practical Tips for Carnitine Supplementation



- Best absorbed and tolerated in divided doses with food
- © Can cause GI side effects
- Start with 1 tab per day and work up to goal dose to improve tolerability
- Must be kept in blister packaging or tabs dissolve
 - May not fit in pill box



Photo by Marek Studzinski on Unsplash

Serving	L-Carnitine (mg)
3.5 oz	190
3 oz.	81
3 oz.	80
3 oz.	24
3 oz.	20
8 oz (1 cup)	8
3 oz.	5
3 oz.	3
2 oz.	2
1 medium	2
½ cup (6 spears)	0.2
	3.5 oz 3 oz. 3 oz. 3 oz. 3 oz. 8 oz (1 cup) 3 oz. 3 oz. 2 oz. 1 medium

Carnitine Food Sources

Table adapted from the references below https://ods.od.nih.gov/factsheets/Carnitine-HealthProfessional/ https://lpi.oregonstate.edu/mic/dietary-factors/L-carnitine Kulczyński B, et. al. Antioxidants. 2019.

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Medium Chain Triglycerides (MCT)

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Medium Chain Triglycerides (MCTs)



- Rapidly absorbed and converted to ketones
- Boosts ketosis
- Does not require carnitine
- Studies have shown an anti-seizure effect from C10 MCT
- Ochoose MCT oil with both C8 (Caprylic Acid or Octanoic acid) and C10 (Capric Acid or Decanoic acid) oil.
- Can be expensive
- Of GI side effects may be hard to tolerate
 - Useful tool to manage constipation

Shah ND, Limketkai BN. Practical Gastroenterology. 2017. Chang P, et al. Brain. 2016. Schoeler NE, et al. Brain Commun. 2021.

Practical Tips for MCT



- Better tolerated if increased slowly and given in divided doses
- Can be mixed into food or drinks
- Do not use for heat cooking
- Should not be sole source of fat
 - · Essential fatty acids must be included
- MCT oil pills? Not recommended
 - · Pill burden is too high
 - 5 MCT capsules = 1 tsp.
 - 15 capsules = 1 tsp. per meal
- Wait to introduce MCT

Example MCT Oil Titration

Day	MCT Amount
1	1 tsp. (5 mL) 3 x daily
4	2 tsp. (10 mL) 3 x daily
7	1 Tbsp. (15 mL) 3xdaily



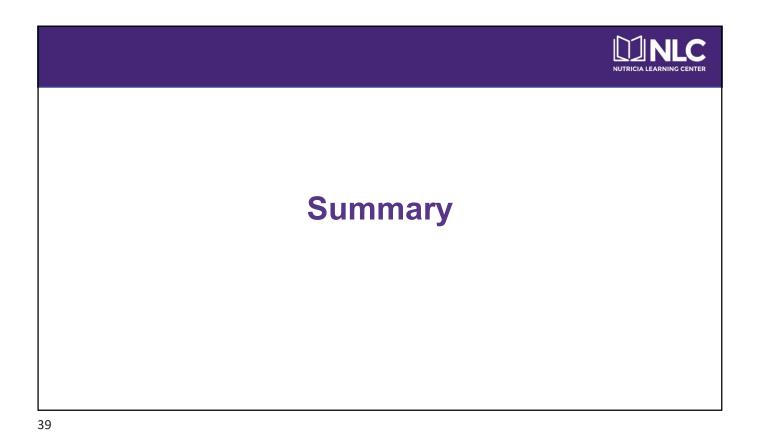
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MCT Oil – Favorite Strategies



- Incorporate with breakfast
- Dose with meals like a medication
- Pair MCT and LCT for evening snack





Ketogenic therapy is safe and effective for adults with epilepsy.

Ketogenic therapy should be presented as an option.

Expanded access is needed for more widespread implementation in adults.

Medical supervision from a specialized team of experts is critical because there are several important considerations and strategies that may impact efficacy.

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Acknowledgements



Thanks to our team!

- Adult neurologist / epileptologist
 - Elizabeth Felton, MD, PhD
- Registered dietitian nutritionists
 - Kelly Faltersack, MS, RDN, LDN, CD
 - Megan Grassl, MS, RDN, CNSC, CD
 - Abiel Wettstein, MS, RDN, CNSC, CD
 - Joanna Otis, MS, RDN, CNSC, CD
 - Allix Ice MS, RDN, CNSC, CD

- Epilepsy nurse practitioner
 - Therese Aschkenase, DNP
 - Epilepsy nurses
 - Neurology social workers
 - Epilepsy pharmacists
 - Lisa Hawk, PharmD
 - Lauren Schleicher, PharmD



Thank you! Questions?

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