Nutrition Guideline Development Process
Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)
The mission of GMDI is to provide standards of excellence and leadership in nutrition therapy for genetic metabolic disorders through clinical practice, education, advocacy, and research.
Project Organization

HRSA

Southeast Regional Genetics Network (SERN)

National Advisory Board

SERN Project Staff
Adrya Stembridge, Yetsa Osara,
Katie Coakley
Project Staff and Funding

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Core Group

Genetic Metabolic Dietitians International (GMDI)
Content Expertise

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Workgroups

Chair: Dianne Frazier
Amino Acidopathies
MSUD

Chair: Amy Cunningham
Shideh Mofidi
PKU

Chair: Keiko Ueda
Elaina Jurecki
Organic Acidopathies
PROP

Chair: Sandy Van Calcar
Mary Sowa
Fatty Acid Oxidation Disorders

Chair: Rani Singh
Urea Cycle Disorders (future)

Consultants
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Dianne Frazier

Adrya Stembridge
IT and Portal

Librarian
Nutrition Guideline Development Process

Evidence /Consensus Analysis
- Systematic Review of published literature and “gray literature”

Delphi Process – Round 1
- Survey of expert practitioners– MDs and RDs HRSA Genetics Regions

Workgroup Evidence Summary and Preliminary Recommendations
- Recommendations for nutrition management based on literature review
- Identification of variations in practice based on Delphi survey

Nominal Group Technique
- Face-to-Face meeting of expert panel
- Discuss areas of practice variation, vote, discuss recommendations, vote again

Delphi Process - Round 2
- Survey of recommendations and variations in practice identified by Nominal Group Technique panel

Writing Nutrition Guidelines - Workgroups
- Recommendations for nutrition management
- Documentation of areas of consensus and non-consensus

Review Process
- External Review and Field Testing
VLCAD Guidelines Workgroup

- People Involved
  - Core Group: 10
  - Quality Criteria Analysts: 10
  - Workgroup Evidence Analysts: 16
  - Delphi Survey Respondents: 17
  - Nominal Group Experts: 9
VLCAD by the Numbers

• Research Questions 6
• Literature search articles: 951
• Formal literature included: 93
• Gray literature included: 26
• Formal literature excluded: 858
  – Animal or in-vitro study
  – Not published in English language
  – Unrelated to VLCAD treatment or outcomes
  – Genetic studies not related to phenotype
  – General overview article intended to educate those not familiar with VLCAD
  – Published prior to 1990
Guideline Template

- Background
  - Definition
  - Incidence
  - Pre-symptomatic detection
  - Genetics
  - Confirmatory testing
- Biochemical Basis
  - Rationale for treatment
  - Biochemical pathway
- Nutrition Assessment
  - Signs and Symptoms
  - Laboratory Findings
- Nutrition Problem Identification
  - Common Diagnoses using NCP language
- Nutrition Management
  - Healthy
  - Illness
  - Supplements
  - Exercise
  - Pregnancy
- Education
  - Patient Goals
  - Patient Resource
  - Provider Resources
- Monitoring and Evaluation
  - Biomarkers to follow
  - Health benefits
  - Harms (side effects, risks)
- Barriers to Implementation
- References
Expected Products

• Guidelines
  – Evidence and consensus based recommendations for nutrition management

• Toolkit
  – Case study-based practical approach with resources

• FAQ Sheet/Guideline Summary
  – For parents

• Publication
  – Peer-reviewed journal
### PROPIONIC ACIDEMIA (PROP/PA) FREQUENTLY ASKED QUESTIONS

**SERN/GMDI Nutrition Management Guidelines**  
**First Edition 2018**

### NUTRIENT INTAKE

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
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<tbody>
<tr>
<td>How much protein can I consume?</td>
<td>The amount depends on individual tolerance, age, weight, and growth (children) or health maintenance (adults). Your dietitian will use your lab results and your clinical status to adjust your protein goals. (Rec 1.1)</td>
</tr>
<tr>
<td>Do I need a PROP formula?</td>
<td>PROP formula is needed if your food protein tolerance is less than the amount of protein recommended for your age. (Rec 1.2)</td>
</tr>
<tr>
<td>How do I know if I am getting the right number of calories?</td>
<td>The correct number of calories is based on age, weight, activity level and growth (children) or health maintenance (adults). Your dietitian will recommend the right amount of calories for you. Most individuals with PROP need extra calories when ill. (Rec 1.5, 2.1)</td>
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### SUPPLEMENTS

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<tr>
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<tbody>
<tr>
<td>Do I need isoleucine or valine supplements?</td>
<td>If your blood levels of isoleucine or valine are too low, your dietitian may increase food (intact) protein and PROP medical formula protein to bring isoleucine or valine blood levels up rather than giving amino acid supplements. (Rec 1.1, 1.3)</td>
</tr>
<tr>
<td>Do I need carnitine?</td>
<td>Most individuals with PROP need to take a carnitine supplement to keep their blood carnitine level within the normal range. (Rec 3.1)</td>
</tr>
<tr>
<td>Should I take prebiotics?</td>
<td>More research is needed. Discuss with your physician and dietitian if prebiotics (non-digestible substances in foods, usually fiber) are right for you to support bowel health. (Rec 3.6)</td>
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### BLOOD MONITORING

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<tr>
<td>What are the goals for isoleucine, valine, threonine and methionine blood levels?</td>
<td>For individuals with PROP the goal is to maintain amino acid levels in the blood within the normal range. (Rec 1.1, 1.3, 4.4)</td>
</tr>
<tr>
<td>How often should blood testing be done?</td>
<td>Your physician and dietitian will work with you to establish a lab testing schedule that is best for you based on past lab results. Discuss with your team how often to come to clinic to check your labs as well as your health and nutrition status. (Rec 4.4, 4.5)</td>
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### ILLNESS

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<tbody>
<tr>
<td>What should I do if I become ill?</td>
<td>Call your metabolic physician. Refer to your emergency letter. (Rec 2.7)</td>
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</table>
| How does management change during illness?                               | Sick day instructions from your metabolic physician and dietitian may include:  
  • Reduce or hold protein intake, but for no more than 48 hours  
  • Increase liquids and calories  
  • Stay in contact with your metabolic clinic to report any changes  
  For more severe illnesses, medications such as Carbaglu® or Flagyl® may be recommended. (Rec 2.7, 3.3, 3.4) |

### LIVER TRANSPLANT

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<tr>
<td>How does treatment for PROP change after a liver transplant?</td>
<td>After transplant, an individual with PROP may be able to increase food (intact) protein intake to the recommended amount for someone their age without PROP. Most will likely need to continue taking carnitine and stay in contact with their metabolic clinic. (Rec 7.4, 7.5)</td>
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### PREGNANCY

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<tr>
<td>Have any women with PROP been able to have children?</td>
<td>With close monitoring and medical management women with PROP have had children. (Rec 5.2, 5.3, 5.4, 5.5)</td>
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This document is not meant to substitute for the medical advice provided by your doctor.

1. For the child, teenager, or adult living with PROP and their caregivers.
Mild VLCAD

- Infants have mildly to moderately elevated concentrations of long chain acylcarnitines on newborn screening.
- Diagnostic testing should confirm the diagnosis, although the plasma acylcarnitine profile may be near normal.
- Individuals remain asymptomatic beyond infancy and tolerate various stressors without clinical symptoms typically associated with metabolic decompensation.
- Metabolic labs may be normal when the individual is healthy.
- Individuals may present during adolescence or adulthood with intermittent rhabdomyolysis, muscle pain and/or exercise intolerance, but it is unknown during infancy and childhood if the late myopathic presentation will occur later in life.
Moderate VLCAD

- Infants have mildly to moderately elevated concentrations of long chain acylcarnitines on newborn screening.
- Diagnostic testing, including an abnormal plasma acylcarnitine profile, should confirm the diagnosis.
- Individuals are asymptomatic at diagnosis, but may experience, or are considered at high risk for, episodes of hypoketotic hypoglycemia or rhabdomyolysis with stressors such as illness, fasting or exercise.
- Metabolic labs remain abnormal even when patient is healthy. However, cardiomyopathy or other cardiac presentation is considered unlikely.
Severe VLCAD

- Infants have significantly elevated concentrations of long chain acylcarnitines on newborn screening.
- Diagnostic testing, including an abnormal plasma acylcarnitine profile, should confirm the diagnosis.
- Individuals may be symptomatic at diagnosis or within the first months of life.
- The clinical picture may include hypertrophic or dilated cardiomyopathy, pericardial effusion and arrhythmias, as well as hypotonia, hepatomegaly, intermittent hypoglycemia and rhabdomyolysis.
VLCAD Classifications

- Severe
- Moderate
- Mild

Asymptomatic (Q 1)

Illness /Symptomatic (Q 2)

- Cardiomyopathy
- Rhabdo
- Exercise

Q.5

Q4 Monitoring

Pregnancy Q7

Q3 Supplements
VLCAD Research Questions

1. For healthy individuals with VLCAD, what nutrient intake goals are associated with positive outcomes?
2. For the individual with VLCAD what nutrition interventions are associated with positive outcomes during illness (including cardiomyopathy or rhabdomyolysis), surgery or other stress?
3. For individuals with VLCAD, do other specific nutrient supplementation or other treatment modalities (i.e. L-carnitine, triheptanoin, bezafibrates) improve outcomes?
4. For individuals with VLCAD, monitoring of which parameters is associated with positive outcomes? For individuals with VLCAD, monitoring of which parameters is associated with positive outcomes?
5. For the individual with VLCAD what nutrition interventions are associated with positive outcomes during exercise?
6. For the woman with VLCAD, what nutrition interventions are associated with positive outcomes during menstruation, pregnancy, delivery and the post-partum period?
Ex: Question 1- Topics

- For **healthy** individuals with VLCAD, what nutrient intake goals are associated with positive outcomes.
  - Diet composition based on severity
    - Fat composition
    - Macronutrients
  - Breastfeeding
  - Essential fatty acids
  - Cornstarch/night time snack/night drip feedings