

# Practical Aspects for Meeting Distinctive Nutritional Requirements through Modification of the Diet alone

## Intractable Epilepsy and the Ketogenic Diet

**Eric H. Kossoff, MD**

Professor, Neurology & Pediatrics  
Johns Hopkins Hospital  
Baltimore, Maryland USA

August 13, 2019



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# Disclosures

- Consultant: Atkins Nutritionals, Nutricia, NeuroPace
- Royalties: Demos, UpToDate, Oxford
- Data Safety Monitoring Boards: NIH, Greenwich, BioPharm

# Why do we need options besides drugs?

The New England Journal of Medicine

## EARLY IDENTIFICATION OF REFRACTORY EPILEPSY

PATRICK KWAN, M.D., AND MARTIN J. BRODIE, M.D.

- 2000 : 47% with 1<sup>st</sup> drug, 14% with 2<sup>nd</sup>, 1% with 3<sup>rd</sup>

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Research

JAMA Neurology | Original Investigation

## Treatment Outcomes in Patients With Newly Diagnosed Epilepsy Treated With Established and New Antiepileptic Drugs A 30-Year Longitudinal Cohort Study

Zhibin Chen, PhD; Martin J. Brodie, MD; Danny Liew, MD, PhD; Patrick Kwan, MD, PhD

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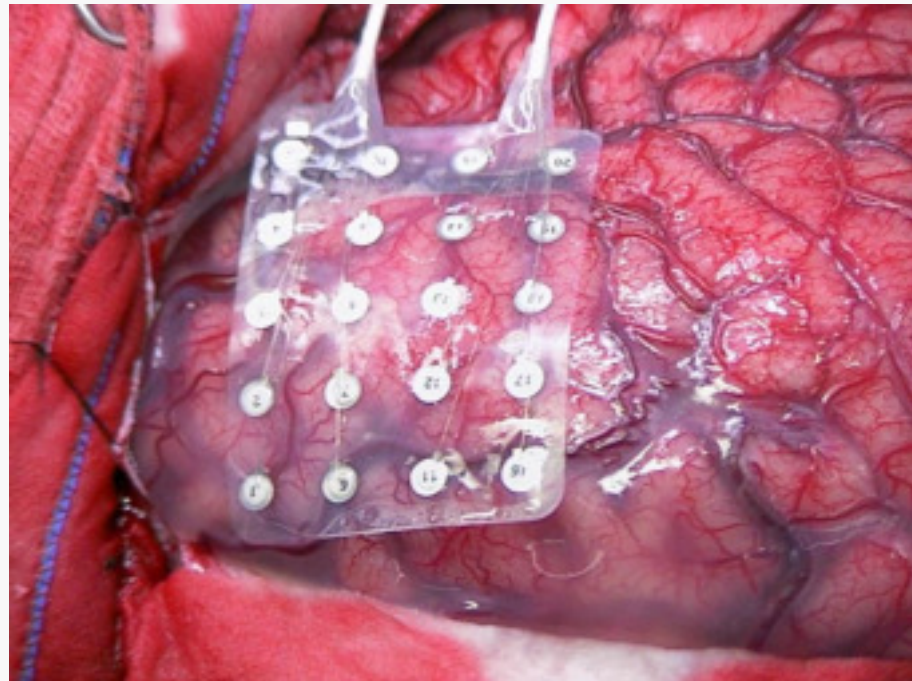
## Treatment Outcomes in Patients With Newly Diagnosed Epilepsy Treated With Established and New Antiepileptic Drugs A 30-Year Longitudinal Cohort Study

Zhibin Chen, PhD; Martin J. Brodie, MD; Danny Liew, MD, PhD; Patrick Kwan, MD, PhD

- 2018 : 50% with 1<sup>st</sup> drug, 12% with 2<sup>nd</sup>, 1% with 3<sup>rd</sup>

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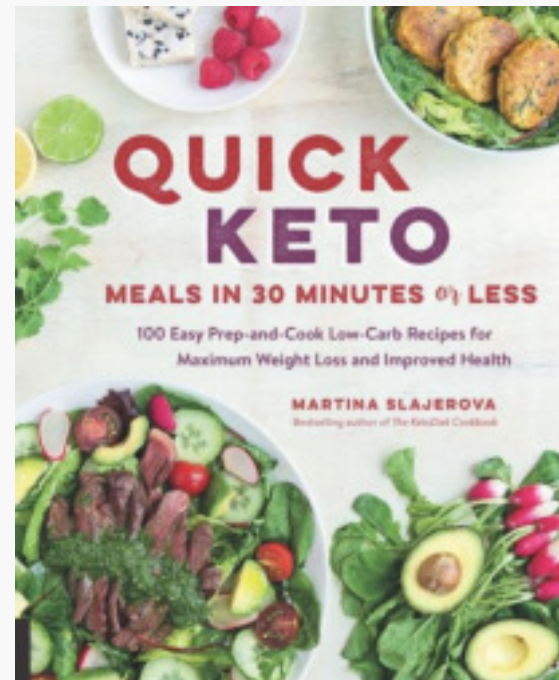
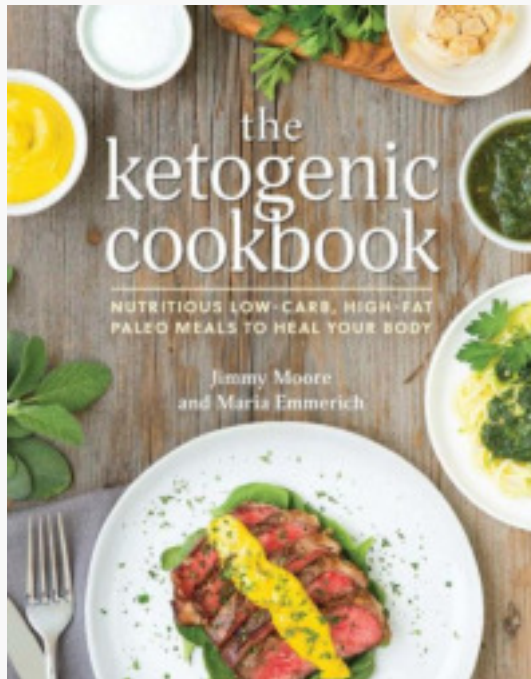
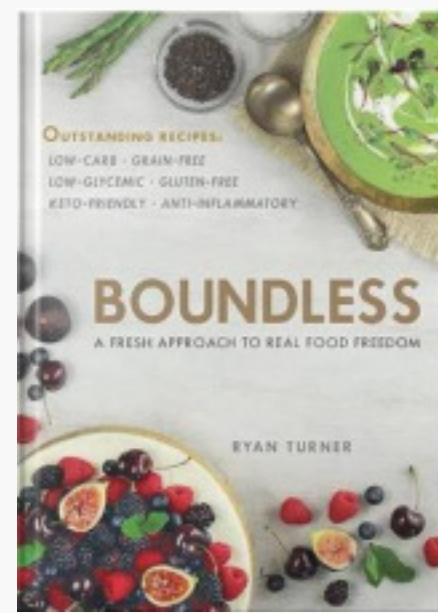
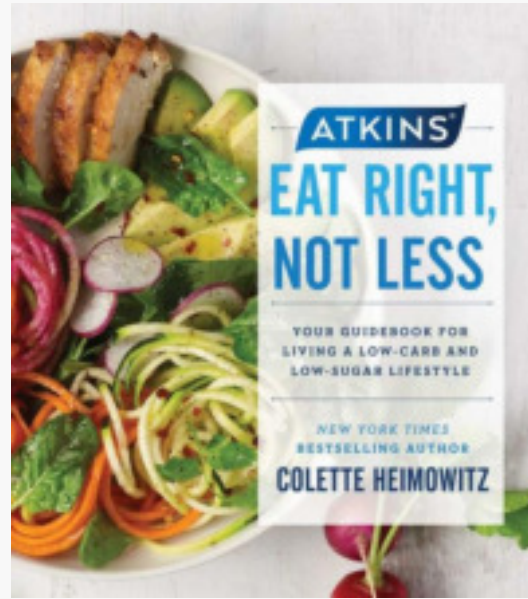
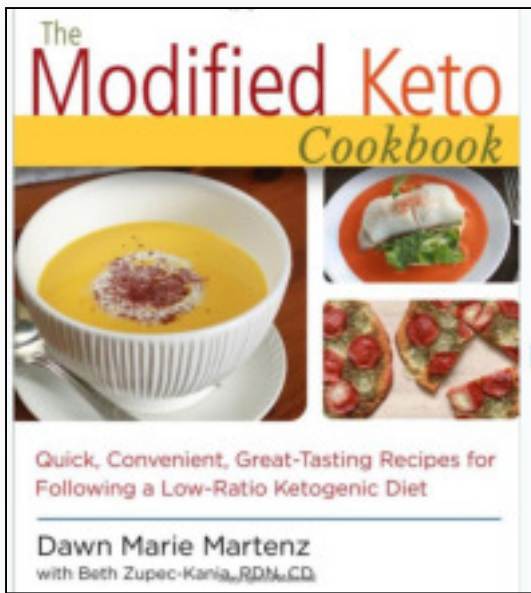
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**DIET**

## Sometimes a 90% Fat Diet Is Good For You

By **MEREDITH MELNICK** @meredithm November 13, 2010 17

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This weekend, the *New York Times Magazine* has an [article](#) written by Fred Vogelstein, a contributing editor to *Wired* and father to a young boy with epilepsy. Sam's condition is severe: at one point, the boy was having up to 130 seizures a day and was not responsive to medication. To treat him, the family has put Sam on a special diet: a typical breakfast consists of eggs mixed



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## Epilepsy's Big Fat Miracle

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ILLUSTRATION BY THE NEW YORK TIMES. FOOD STYLE: SHOT KUBERT

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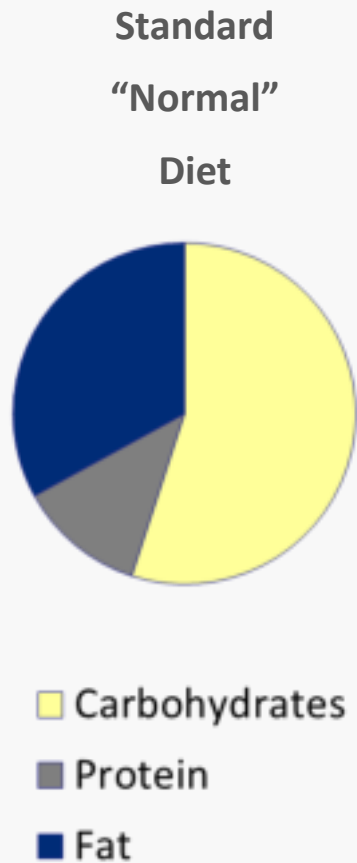
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# Ketogenic Diet for Epilepsy: The Basics

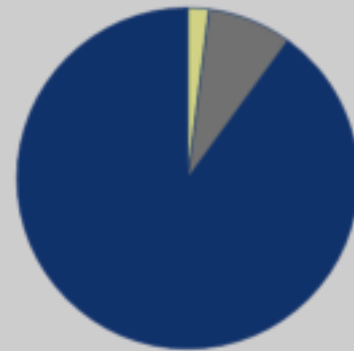
- Traditionally started in the hospital over 2-3 days, after a 24 hour fast
  - Families educated daily
- Ratio (fat (g): carbs and protein (g))
  - 4:1 : more strict
  - 3:1 : infants and adolescents
- Calories and fluids measured
- Solid foods and/or formula



# Four Ketogenic Diets



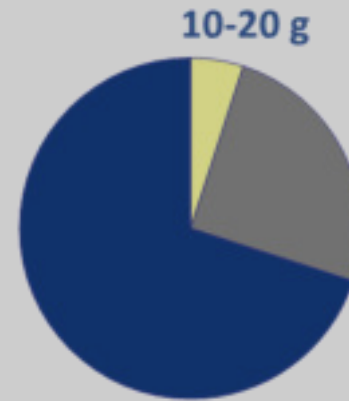
**Ketogenic Diet**



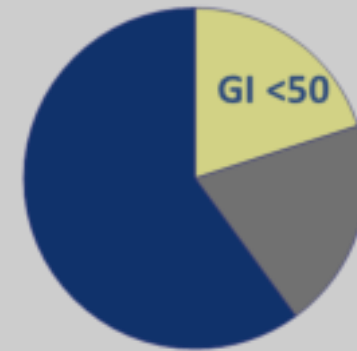
**Medium Chain Triglyceride Diet**



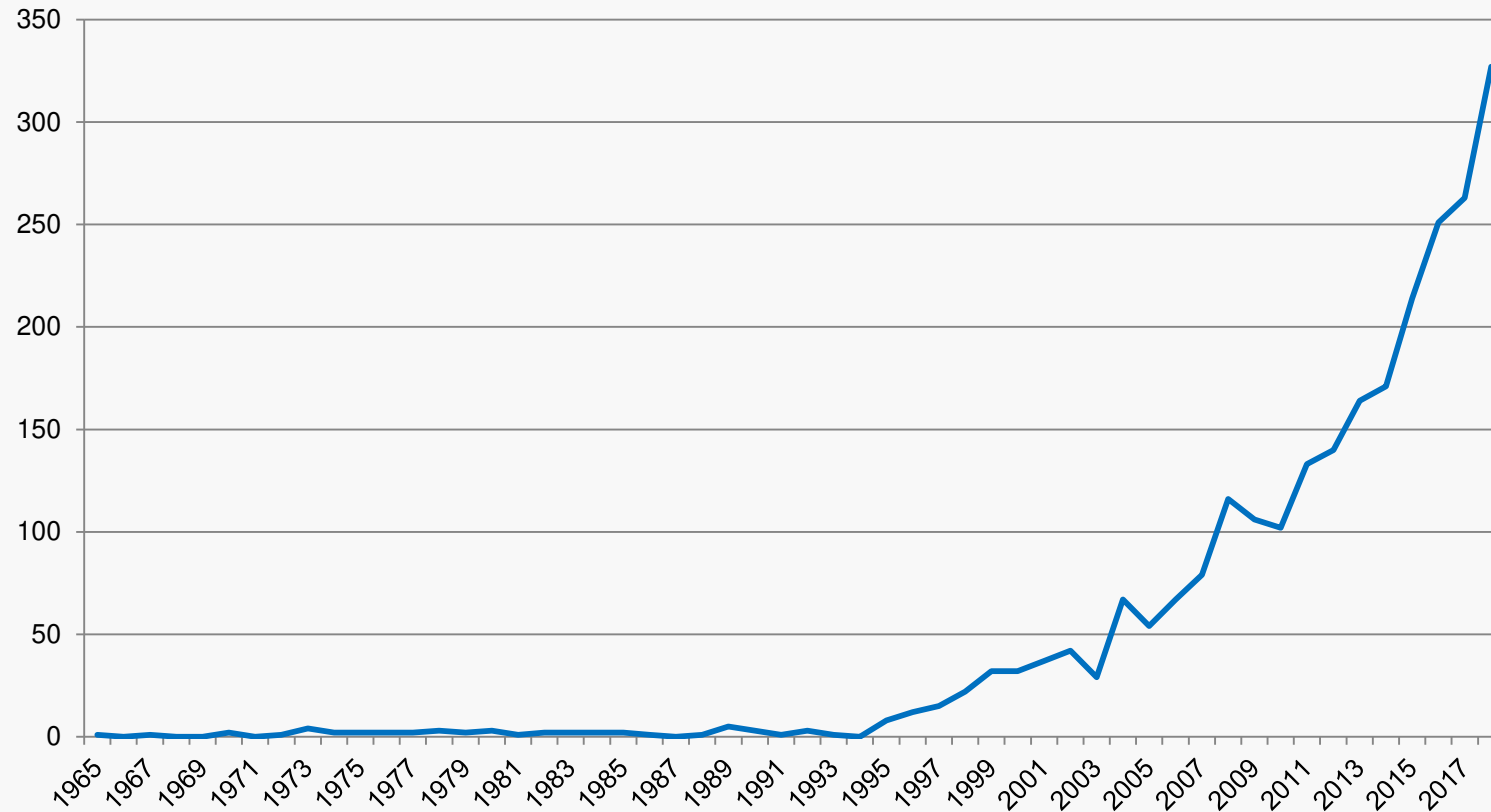
**Modified Atkins Diet**



**Low Glycemic Index Treatment**



# Ketogenic Diet Studies Published




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## BRIEF COMMUNICATION

### A blinded, crossover study of the efficacy of the ketogenic diet

\*John M. Freeman, \*Eileen P.G. Vining, \*Eric H. Kossoff, \*Paula L. Pyzik, \*Xiaobu Ye, and †Steven N. Goodman

 The ketogenic diet for the treatment of childhood epilepsy: a randomised controlled trial

Elizabeth C Neal, Hannah Chaffe, Ruby H Schwartz, Margaret S Lawson, Nicole Edwards, Georgina Fitzsimmons, Andrea Whitney, J Helen Cross

## FULL-LENGTH ORIGINAL RESEARCH

### Use of the modified Atkins diet for treatment of refractory childhood epilepsy: A randomized controlled trial

\*<sup>1</sup>Suvasini Sharma, \*<sup>2</sup>Naveen Santhyan, \*Sheffali Gulati, and †Anuja Agarwala

DOI: 10.1111/epi.14407

## FULL-LENGTH ORIGINAL RESEARCH

### Effect of modified Atkins diet in adults with drug-resistant focal epilepsy: A randomized clinical trial

Magnhild Kverneland<sup>1,2,3</sup> | Ellen Molteberg<sup>1</sup> | Per O. Iversen<sup>2,3,4</sup> | Marit B. Veierød<sup>3,5</sup> | Erik Taubøll<sup>3,6</sup> | Kaja K. Selmer<sup>1,3,7</sup> | Karl O. Nakken<sup>1</sup>

Epilepsia

Iranian Journal  
of Neurology

Original Paper

Iran J Neurol 2017; 16(2): 72-7

### Modified Atkins diet in adult with refractory epilepsy: A controlled randomized clinical trial

Mohammad Zare<sup>1</sup>, Ali Asghar Okhovat<sup>2</sup>, Ahmad Esmailzadeh<sup>3</sup>, Jafar Mehvari<sup>1</sup>, Mohammad Reza Najafi<sup>1</sup>, Mohammad Saadatnia<sup>1</sup>

Neurologica

Acta Neurol Scand DOI: 10.1111/ane.12592

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ACTA NEUROLOGICA  
SCANDINAVICA

### A randomized controlled trial of the ketogenic diet in refractory childhood epilepsy

Lambrechts DAJE, de Klerken RJA, Vies JSH, de Louw AJA, Aldenkamp AP, Majije HJM. A randomized controlled trial of the ketogenic diet in refractory childhood epilepsy. Acta Neurol Scand. DOI: 10.1111/ane.12592. © 2016 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

D. A. J. E. Lambrechts<sup>1</sup>, R. J. A. de Klerken<sup>2,3,4</sup>, J. S. H. Vies<sup>1,2,3</sup>, A. J. A. de Louw<sup>2,3</sup>, A. P. Aldenkamp<sup>3,5,6,7</sup>, H. J. M. Majije<sup>1,2,3,8</sup>

Wiley: European Journal of Epilepsy 30 (2015) 150–158



Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

Journal homepage: [www.elsevier.com/locate/seizure](http://www.elsevier.com/locate/seizure)



### Improving compliance in adults with epilepsy on a modified Atkins diet: A randomized trial<sup>a</sup>

Tanya J.W. McDonald<sup>a</sup>, Bobbie J. Henry-Barron<sup>b</sup>, Elizabeth A. Felton<sup>c</sup>, Eric G. Gutierrez<sup>c</sup>, Joanne Barnett<sup>c</sup>, Rebecca Fisher<sup>c</sup>, Mon'Yi Lwin<sup>c</sup>, Amanda Jan<sup>c</sup>, Diane Viethum<sup>c</sup>, Eric H. Kossoff<sup>d,e</sup>, Mackenzie C. Cervenka<sup>d,e</sup>



<sup>a</sup>Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, United States  
<sup>b</sup>Section for Clinical and Translational Research, Johns Hopkins University, Baltimore, MD, United States  
<sup>c</sup>Department of Neurology, University of Missouri, Columbia, MO, United States  
<sup>d</sup>Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD, United States

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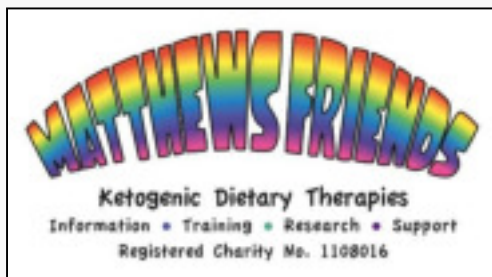
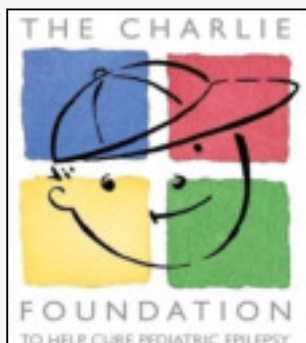
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SPECIAL REPORT

**Optimal clinical management of children receiving dietary  
therapies for epilepsy: Updated recommendations of the  
International Ketogenic Diet Study Group**

<sup>1</sup>Eric H. Kossoff, <sup>2</sup>Beth A. Zupec-Kania, <sup>3</sup>Stéphane Auvin , <sup>4</sup>Karen R. Ballaban-Gil,  
<sup>5</sup>A.G. Christina Bergqvist, <sup>6</sup>Robyn Blackford, <sup>7</sup>Jeffrey R. Buchhalter, <sup>8</sup>Roberto H. Caraballo ,  
<sup>9</sup>J. Helen Cross, <sup>10</sup>Maria G. Dahlin, <sup>11</sup>Elizabeth J. Donner, <sup>12</sup>Orkide Guzel, <sup>13</sup>Rana S. Jehle,  
<sup>14</sup>Joerg Klepper, <sup>15</sup>Hoon-Chul Kang, <sup>16</sup>Danielle A. Lambrechts, <sup>17</sup>Y.M. Christiana Liu,  
<sup>18</sup>Janak K. Nathan, <sup>19</sup>Douglas R. Nordli Jr, <sup>20</sup>Heidi H. Pfeifer, <sup>21</sup>Jong M. Rho, <sup>22</sup>Ingrid E. Scheffer,  
<sup>23</sup>Suvasini Sharma, <sup>24</sup>Carl E. Stafstrom, <sup>20</sup>Elizabeth A. Thiele, <sup>25</sup>Zahava Turner,  
<sup>24</sup>Maria M. Vaccarezza, <sup>27</sup>Elles J.T.M. van der Louw, <sup>28</sup>Pierangelo Veggiotti, <sup>29</sup>James W. Wheless,  
<sup>30</sup>Elaine C. Wirrell, The Charlie Foundation, Matthew's Friends, and the Practice Committee of  
the Child Neurology Society

*Epilepsia Open*, 3(2):175–192, 2018  
doi: 10.1002/epi4.12225



WORKSHOP:  
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**Table 1. Epilepsy syndromes and conditions (listed alphabetically) for which KDT has been consistently reported as more beneficial (>70%) than the average 50% KDT response (defined as >50% seizure reduction).**

Angelman syndrome<sup>56,57</sup>  
Complex I mitochondrial disorders<sup>51,55</sup>  
Dravet syndrome<sup>35,36</sup>  
Epilepsy with myoclonic–atonic seizures (Doose syndrome)<sup>34,37,38</sup>  
Glucose transporter protein I (Glut-I) deficiency syndrome (Glut1DS)<sup>27,29–32</sup>  
Febrile infection–related epilepsy syndrome (FIRES)<sup>44–47</sup>  
Formula-fed (solely) children or infants<sup>48,49</sup>  
Infantile spasms<sup>10,39,40</sup>  
Ohtahara syndrome<sup>50–52</sup>  
Pyruvate dehydrogenase deficiency (PDHD)<sup>28</sup>  
Super-refractory status epilepticus<sup>44,46,53,54</sup>  
Tuberous sclerosis complex<sup>41–43</sup>



# The Problem for Patients and Families...

- A strict diet where a small indiscretion of carbohydrates can have major implications
- Education about diets max 1-3 days
  - Then families are mostly on their own
- Epilepsy is a private disorder
  - Eating foods is NOT
- In adults, ~50% noncompliance by 6 months
- Even neurologists refer to it as a “unpalatable” diet



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# New KetoCal 2.5:1 Liquid – Questions & Answers

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We are pleased to introduce the first and only nutritionally complete ketogenic formula in a 2.5:1 ratio with MCT, specifically developed for adults and children 8 years of age and older. Below is a collection of common questions and answers about KetoCal 2.5:1 Liquid.

## 1. What is KetoCal 2.5:1 Liquid?

KetoCal 2.5:1 Liquid is a convenient, ready-to-feed ketogenic formula with a 2.5:1 ratio, with added medium-chain triglyceride (MCT) oil, fiber, and DHA. It is available in great-tasting vanilla.

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## Prospective Study of the Modified Atkins Diet in Combination With a Ketogenic Liquid Supplement During the Initial Month

Eric H. Kossoff, MD<sup>1</sup>, Jennifer L. Dorward, RD<sup>1</sup>,  
Zahava Turner, RD<sup>1</sup>, and Paula L. Pyzik, BA<sup>1</sup>


Journal of Child Neurology  
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DOI: 10.1177/0883073810375718  
http://jcn.sagepub.com  
SAGE

- 30 children
- Open-label, prospective
- Modified Atkins Diet with supplemental 60 g/day of ketogenic 4:1 powder for 1<sup>st</sup> month
  - 87% drank as liquids
- Month 2 – MAD alone



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DOI: 10.1177/0883073810375718  
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- 24/30 (80%) with >50% seizure reduction
- Continued into month 2 even without the supplement
- Significant factor: FAT
  - Ratio increased from 1:1 to 1.8:1
  - Not ketosis



Contents lists available at ScienceDirect

## Seizure: European Journal of Epilepsy

journal homepage: [www.elsevier.com/locate/seizure](http://www.elsevier.com/locate/seizure)



### Improving compliance in adults with epilepsy on a modified Atkins diet: A randomized trial<sup>☆</sup>



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<sup>a</sup> Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, United States

<sup>b</sup> Institute for Clinical and Translational Research, Johns Hopkins University, Baltimore, MD, United States

<sup>c</sup> Department of Neurology, University of Wisconsin, Madison, WI, United States

<sup>d</sup> Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD, United States

RCT : 40 KetoCal, 40 MAD alone

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Table e-2. Compliance, ketosis, constipation, and survey results by treatment arm.

	Control	Treatment	P-value <sup>c</sup>
Diet duration, m (SD)	10.7 (9.7)	13.4 (13.2)	0.335 <sup>a</sup>
Continued MAD, n (%)	5/29 (17.2)	13/30 (43.3)	<b>0.047<sup>b</sup></b>
<b>Achieved ketosis, n (%):</b>			
1 Month	29/33 (87.9)	27/34 (79.4)	0.512 <sup>b</sup>
2 Month	25/31 (80.6)	20/33 (60.6)	0.104 <sup>b</sup>
Median time to ketosis, d (IQR)	4.0	4.5	0.747
Constipation, n (%)	7/33 (21.2)	2/35 (5.7)	0.079 <sup>b</sup>
<b>MAD median survey score (IQR):</b>			
Convenience	6.0	7.0	0.163
Taste	8.0	8.0	0.533
Texture	8.0	8.3	0.683
Tolerance	8.0	8.0	0.852
<b>Ketocal median survey score (IQR):</b>			
Convenience	9.0	9.5	0.866
Taste	6.0	6.0	0.478
Texture	7.0	8.0	0.615
Tolerance	9.3	9.0	0.981

<sup>a</sup>Student t test.<sup>b</sup>Fisher's Exact test.<sup>c</sup>Mann-Whitney U test.

d= days, IQR= interquartile range, m= months, SD= standard deviation



4.5 Witloof met mozzarella en spek



- Ingrediënten:
- 85 gr witloof
  - 10 gr mozzarella
  - 25 gr spek
  - 15 gr Bece| bakken en braden



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☆ 做法：1. 將蛋打成蛋液，約用 MCT oil 5g 做蛋皮，

將紅蘿蔔及小黃瓜切條汆燙待用。

2. 飯加代糖、醋拌勻。

3. 蛋皮包所有材料捲起，切斜塊即可。



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# Regulatory (insurance) issues for me...

- Improves compliance, but not necessary for most patients
- Helpful...but not required (usually)
  - Not fixing an underlying disorder, nor a cure
- Except for 100% G-tube fed patients, it's not fully reimbursed (and expensive for patients)
- 80% of patients are not on the KD alone
  - However, many can reduce antiseizure drug dosing and save money

# What options do busy, stressed, families have?

1. Ketogenic company products
2. Store-bought foods
3. Charity group offerings
4. *Hire personal chefs*



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## Products

- Broccoli Cheddar Soup
- Broccoli Soufflé
- Butter Almond Cookie Dough
- Cinnamon Donut Delights
- Cheddar Dough
- Creamy Cereal
- Kwik Mix
- Mushroom & Spinach Frittata
- Pizza Petites
- Raspberry Muffins
- Savory Stuffing
- Spinach & Feta Quiche
- Tomato Basil Soup
- Veggie Dip Mix
- Veggie Pattie
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- How to Order
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KetoVie Café Pizza Petites will soon become one of your favorite foods and a part of your everyday.

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Visit Our CA Food Store



Indications Ingredients Select Nutrients Packaging Recipes

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#### Patient Information and Consent

Patient's Name	Date of Birth
If a minor, Parent/Guardian/Consent Name	Diagnosis
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City	State, Zip Code
Email	

**Yes** The patient or guardian consents to the health professional indicated below disclosing personal information to Ajinomoto-Cambrooke, Inc. for the purpose of directing Ajinomoto Cambrooke in providing KetoVie. The patient or guardian also consents to Ajinomoto Cambrooke collecting, using and disclosing the personal information for the purpose of providing the requested product.

#### Health Care Professional

Health Care Professional's Name	License Number
Medical Institution	Health Care Professional's Position
Email	Phone

I hereby confirm that the above patient is authorized to take the selected KetoVie product checked below.  
Signature

#### Sample Request or Order

- Sample Request:** consent for sample request through Ajinomoto Cambrooke.
- Order:** consent to order KetoVie through Ajinomoto Cambrooke.

Product:  KetoVie 4:1 Chocolate  KetoVie 4:1 Vanilla  KetoVie 4:1 Variety (chocolate & vanilla)  KetoVie Peptide 4:1  KetoVie 3:1 Unflavored

#### Form Submission

Please email or fax completed form: [keto vie@cambrooke.com](mailto:keto vie@cambrooke.com) or 978 443 1318

- Intractable epilepsy
- Pyruvate dehydrogenase deficiency (PDH)
- Glucose transporter type-1 deficiency (GLUT1DS)
- Other medical conditions where a ketogenic diet is indicated

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# Ketogenic Products that are not labelled for medical purposes





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## The Definitive Guide to Ketone Esters and Ketone Salts



Help

### Instructions

#### For sport

- HVMN Ketone Ester is most effective for endurance exercise lasting an hour or more
- Drink one serving 30 minutes before exercise with usual pre-workout fuel (carbs, caffeine, etc.)
- For extended endurance exercise (2+ hours), consume an additional serving every 1.5 - 2 hours with usual carbs

#### For cognition

- Use in conjunction or in replacement of your coffee or tea, and expect a mental clarity distinct from a stimulant effect
- Ketones cross the blood-brain barrier and serve as an efficient fuel source for neurons in the brain

#### For recovery

- Drink one serving 30 minutes after exercise with normal post-workout nutrition (protein, carbs, etc.)

#### For fasting and diet

- Elevate your ketone levels to equivalent to 5-10 days of fasting
- Non-insulinogenic calorie source compatible with fasting and ketogenic diets
- High fat diets convert fat into ketones; HVMN Ketone Ester provides ketones directly

**H.V.M.N.™**

## Ketone Ester

This is KETONE ESTER. The nutritional drink is deep berry in a bottle.

Enhance your physical and cognitive performance and endurance, and support your fasting and dietary goals. Use before, during, and/or after activity - daily or as needed.

No caffeine, no sugar, no salt, no fat - just 25g of ketone ester. HVMN Ketone Ester is compliant with fasting, ketogenic diet, and professional sport.

Pick size: HVMN Ketone Ester 3-pack (3 bottles)

Subscribe monthly & save 10% **\$59.88/mo**

One-time order **\$59.88**

**Subscribe - \$59.88**

Shipping is included for orders over \$40.

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★★★★★ (140)

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Our products have been carefully developed to meet the strict standards of the ketogenic diet.

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## Cheddar Crackers

\$8.99

Quantity:

ADD TO CART

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A fan favorite! Our delicious cheddar crackers will satisfy any cheese lover's palate. These crunchy crisps are at a 2:1 ketogenic ratio and contain 2 grams of net carbohydrates per serving. These crisps come in varying shapes and sizes so be sure to carefully read the label when measuring out a serving.

To increase the ratio and provide more fat this could easily be paired with an avocado dip or heavy cream as a beverage.

Ingredients: Cheddar Cheese, Butter, Coconut Flour, Contains 2% or less of: Baking Powder (Sodium Bicarbonate, Cornstarch, Monocalcium Phosphate), Salt, Onion Powder



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# What do patients/families ask for?

1. Foods (pre-made) that mimic “normal” snacks
2. Crunch
3. Portable (no refrigeration required)
4. Savory NOT sweet
5. Inexpensive



# Neurologic Uses Other than Epilepsy

Hypoxia-anoxia	2001
Autism	2003
Brain tumors	2003
Depression	2004
Narcolepsy	2004
Glycogenosis Type V	2005
Alzheimer's	2005
Traumatic brain injury	2005
Parkinson's	2005
ALS	2006
Migraine	2006
Sleep disorders	2007
Post hypoxic myoclonus	2007
Schizophrenia	2009
Spinal cord injury	2009
Pain	2009
Sandhoff disease	2010
Huntington's disease	2011
Bipolar disorder	2012
Multiple Sclerosis	2012
Diving CNS toxicity	2014
Alternating hemiplegia of childhood	2015
Kabuki syndrome	2016
Pelizaeus-Merzbacher disease	2019

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## Can a High-Fat Diet Beat Cancer?

By RICHARD FRIEBE

Monday, Sep. 17, 2007



MARTIN JOPP / ZEPHYRUS CORPIS

The women's hospital at the University of Würzburg used to be the biggest of its kind in Germany. Its former size is part of the historical burden it carries — countless women were involuntarily sterilized here when it stood in the geographical center of Nazi Germany.

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# KETOSIS FOR ALZHEIMERS



PERFECT KETO



## Ketones to combat Alzheimer's disease

Published 10/10/16 by [ScienceDirect](#)



Despite decades of efforts to develop a drug that prevents or cures Alzheimer's disease (AD), the most prevalent form of dementia affecting our aging population, there is currently no treatment for this devastating condition. Emerging research suggests that such a miracle treatment might already exist, not in the form of a pill, but as a simple dietary change. A growing number of studies report that interventions to improve metabolic health can alleviate symptoms and reduce brain pathology associated with AD. A popular theory posits that AD has multiple causes, but that common thread may involve metabolic dysfunction. Instead, markers of your metabolic health, such as diabetes, inflammation and high cholesterol, are major risk factors for AD.

Just like our muscles, the brain requires energy to function properly. Both neurons and muscles have the unique capacity to metabolize ketones as an alternative fuel source when glucose is in short supply for instance during fasting or on a low-carbohydrate diet. In the 1920s scientists discovered that a high-fat diet promoting ketogenesis controlled epilepsy, and ketosis remains one of the most effective treatments for the condition. This opens the possibility that ketones may also be neuroprotective for against



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## Ketogenic diets and Alzheimer's disease

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## Diet & Memory Study



### Can Diet Improve Alzheimer's Disease?



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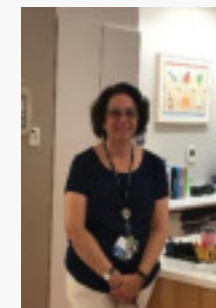
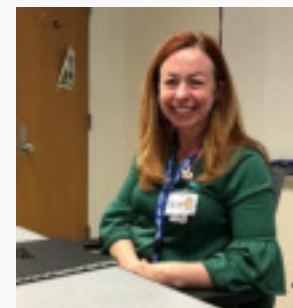
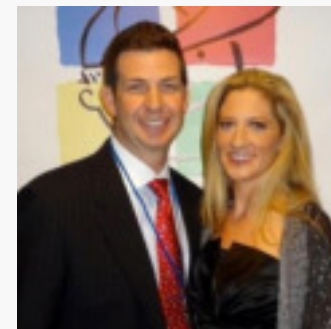
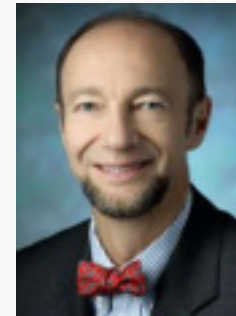
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