



Ketogenic Diets for Mental Health: Clinical Trials

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Nutritional and Metabolic Psychiatry

www.diagnosisdiet.com

Insulin Resistance and/or Cerebral Glucose Hypometabolism

Depression¹

Post-traumatic stress disorder²

Bipolar disorder³

Schizophrenia⁴

Attention deficit hyperactivity disorder
(childhood onset)⁵

Borderline personality disorder⁶

Obsessive compulsive disorder
(hoarding type)⁷

Anxiety disorders in children with
obesity⁸

Alzheimer's disease⁹

Autism¹⁰

Metabolic Dysfunction and Mental Health

Pre-diabetes

2.7 X

more likely to develop major depression¹

Newly diagnosed bipolar disorder

3.5 X

more likely to have metabolic syndrome²

Newly diagnosed **schizophrenia**

3.7 X

more likely to have insulin resistance³

IR Associated with Bipolar Severity

Bipolar (types 1 and 2)

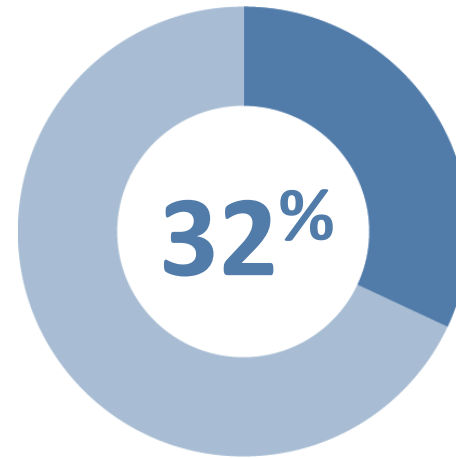
n=121 patients, age 30's–50's

More likely:

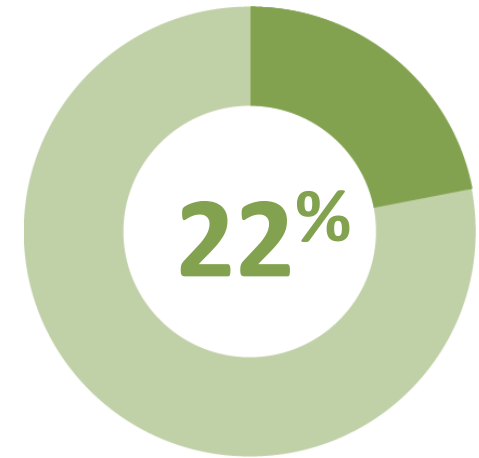
Rapid cycling

Chronic symptoms

Lithium-refractory (BMI predictive)



IR



DMII

IR Reversal Eases Bipolar Depression

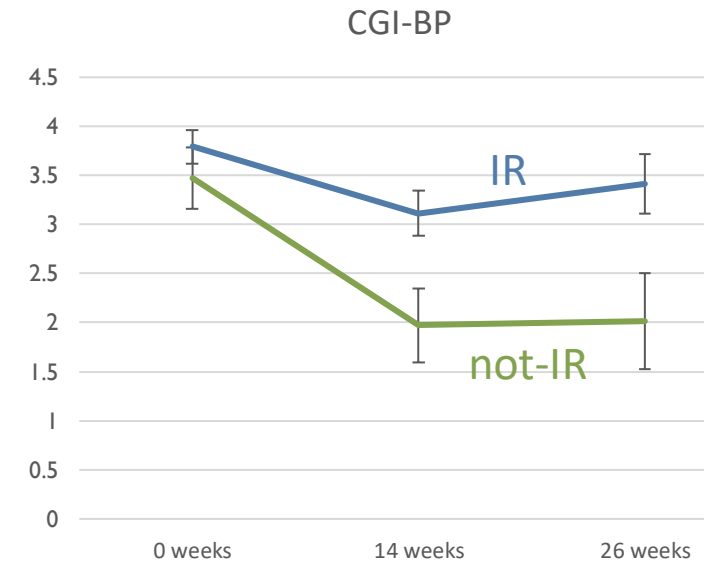
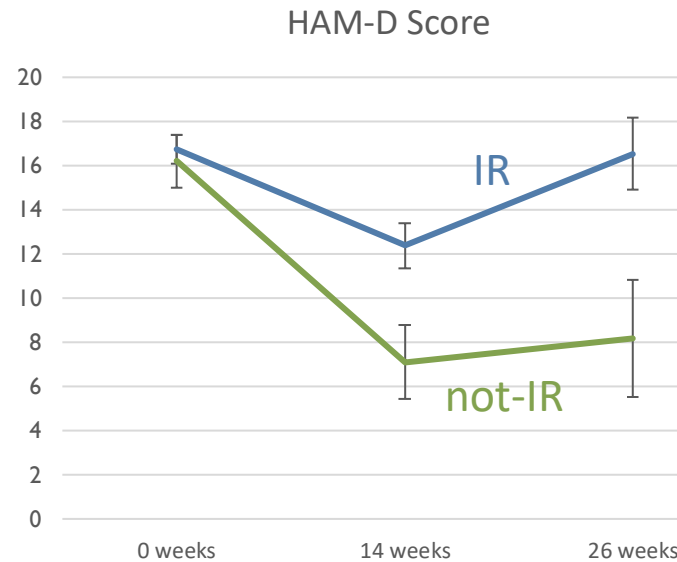
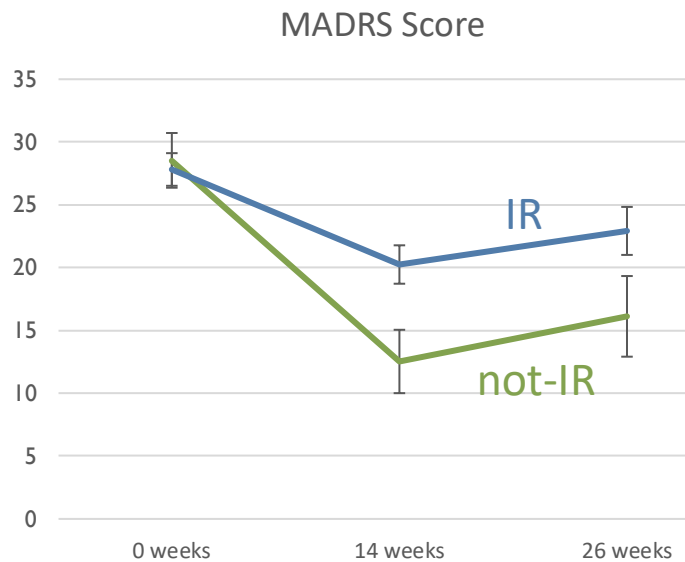
N=45 patients with bipolar disorder and insulin resistance

20 received Metformin
IR resolved in 10/20

25 received placebo
IR resolved in 1/25

34 remained IR

11 resolved IR





Almost 90% of the patients in the TRIO-BD study had not had a single remission in 25 years. It has been a relief to discover a new mechanism-based treatment that can get these patients better.

—Dr. Cynthia Calkin

Ketogenic Diets for Schizophrenia

1965: 10 hospitalized women, KD x 2 wks¹ “Significant improvement”

.....

2009: 70-yo woman with lifelong schizophrenia KD x 12 mos²

Long-term resolution of visual/auditory hallucinations, medications discontinued

2017: 33-yo man, 31-yo woman³

Improved symptoms within one month

2018: Two 22-yo opposite-sex twins, KD x 6 wks⁴

~10 percent reduction in PANSS score

2019: 39-yo woman, KD x 5 yrs⁵

Long-term resolution of psychotic symptoms, medications discontinued

1. Pacheco A, Easterling W, Pryer M. *Am J Psychiatry*. 1965.

2. Kraft BD, Westman EC. *Nutr Metab*. 2009.

3. Palmer C. *Schizophr Res*. 2017.

4. Gilbert-Jaramillo J, et al. *Clin Nutr & Metab*. 2018.

5. Palmer CM et al. *Schizophr Res*. 2019.

Ketogenic Diets for Binge Eating

30g carbohydrate per day:

Patient	Binge episodes/week at start	Binge episodes/week after 6 months	Weight loss
54 yo woman	14+	0	37 lbs
34 yo man	8-11	0	44 lbs
62 yo woman	8-10	0	22 lbs

Ketogenic Diet for Anorexia


Eating and Weight Disorders - Studies on Anorexia, Bulimia and Obesity

<https://doi.org/10.1007/s40519-022-01455-x>

BRIEF REPORT



Ketogenic diet and ketamine infusion treatment to target chronic persistent eating disorder psychopathology in anorexia nervosa: a pilot study

Lori Calabrese¹ · Barbara Scolnick² · Beth Zupec-Kania³ · Caroline Beckwith⁴ · Kayla Costello⁵ · Guido K. W. Frank⁶ 

Received: 26 May 2022 / Accepted: 19 July 2022

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Abstract

Purpose Anorexia nervosa (AN) is a severe psychiatric disorder, and shape and weight concerns are often chronic despite weight normalization. No specific treatments exist for those preoccupations that interfere with recovery and trigger relapse.

Carnivore Diet for Anorexia

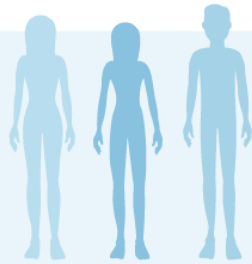
“All foods fit” unrestricted diet is standard of care focus



vs



Animal-based ketogenic diet



Three patients with **severe anorexia (BMI 10.7 - 13.0 kg/m²)** that was refractory or resistant to standard of care therapy adopted **animal-based ketogenic diets**



Improvements in **mental health, body image, and well-being**



At least **≥20 kg** of weight gain



Continued remission lasting **1 to 5 years**

Alcohol Dependence

2021 Randomized controlled trial

3-week inpatient alcohol withdrawal management program

19 pts on classic 4:1 KD vs 14 pts on SAD
(serum BHB 1.6 mM rising to >4 mM)

Fewer cravings

and

Required ~50% less benzodiazepine
(oxazepam/Serax)



Autism Spectrum Conditions

Three 6-month clinical trials (plus two case reports^{1,2})

- 2003: n=30, cyclical KD. 18/23 completers experienced 10 – 33% improvement³ (serum BHB 0.8 to 2.2 mM)
- 2017 RCT: n = 45. KD outperformed a gluten-free/casein-free diet vs. no benefit on balanced diet⁴ (in ketosis by urine testing)
- 2018: Substantial improvement in 8/15 children on gluten-free KD + MCT oil⁵ (in ketosis by urine testing)

1. Herbert MR, Buckley JA. *J Child Neurol.* 2013;28(8):975-982.

2. Żarnowska, I et al. *Metab Brain Dis.* 2018;33:1187-1192.

3. Evangelidou A et al. *J Child Neurol.* 2003;18(2):113-118.

4. El-Rashidy O et al. *Metab Brain Dis.* 2017;32(6):1935-1941.

5. Lee RWY et al. *Physiol Behav.* 2018;188:205-211.

Mild Cognitive Impairment /Early Alzheimer's

2012: 23 pts w MCI; ~34g CHO/day x 6wks¹

Small, statistically significant improvement on long-term memory tests

2018: 10 pts w early AD; ~45g CHO/day + MCT oil x 6wks²

Small, statistically significant improvements on cognitive tests in 9/10

2019: n=27 pts w MCI and early AD

RCT of modified Atkins vs low-fat Mediterranean diet x 6wks³

Small, statistically significant improvement in memory testing

2021: 21 pts w mild AD; crossover study KD (~.95mM) vs low-fat diet x 6 wks⁴

Sig. improvement on tests of daily function and quality of life

No improvement on cognitive tests

1. Krikorian R. *Neurobiol Aging*. 2012.

2. Taylor MK et al. *Alzheimers Dement (N Y)*. 2018.

3. Brandt J, et al. *J Alzheimers Dis*. 2019.

4. Phillips MCL, et al. *Alzheimers Res Ther*. 2021

Dementia in the Context of Down Syndrome

47 yo woman with Down Syndrome and obesity (BMI 47)

Rapidly progressing dementia, paranoia, and seizures x 4 years

ADL dropped from 57/78 to 34/78

KD x 6 wks
(BHB 0.8 mM – 3.0 mM):

- Seizures stopped
- Paranoia resolved
- ADL score 58
- Vocabulary expanded

VIRTA: Ketogenic Diet for Depression

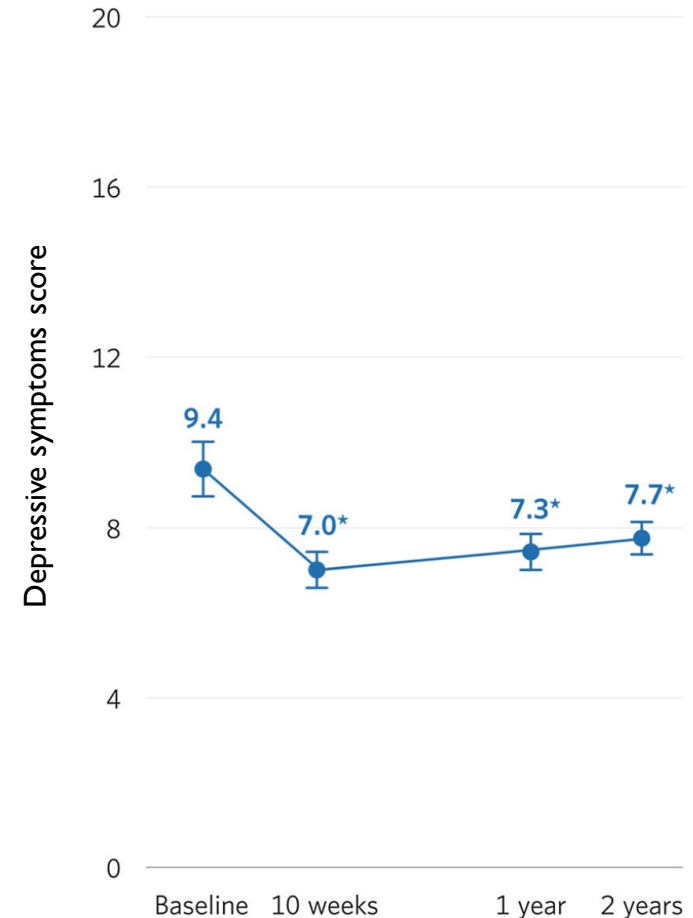
Non-randomized, uncontrolled study

262 outpatients with T2DM;
36 with mild clinical depression

Mildly ketogenic diet

Mood improved modestly in all patients

More than half with clinical depression had
achieved remission at week 10



KD for Serious Mental Illness (2022)

Clinique du Castelvieu
Castelmarrou, France



The Ketogenic Diet for Refractory Mental Illness: A Retrospective Analysis of 31 Inpatients



Albert Danan¹,



Eric C. Westman²,



Laura R. Saslow³ and



Georgia Ede^{4*}

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² Department of Medicine, Duke University Medical Center, Durham, NC, United States

³ Department of Health Behavior and Biological Sciences, School of Nursing, University of Michigan, Ann Arbor, MI, United States

⁴ Independent Researcher, Northampton, MA, United States

Background and Hypothesis: The robust evidence base supporting the therapeutic benefit of ketogenic diets in epilepsy and other neurological conditions suggests this same metabolic approach may also benefit psychiatric conditions.

85,088

Total views



ORIGINAL RESEARCH article

Front. Psychiatry, 06 July 2022

Sec. Public Mental Health

<https://doi.org/10.3389/fpsy.2022.951376>

Study Participants

31
enrolled



28
>2 weeks
on the
keto diet



Bipolar disorder
n=12



Schizophrenia
n=10



Major Depression
n=6

Average hospital stay: 85 days

Average diet duration: 59 days

Study Participants

71% female; 29% male

Average age: 50 years old (27-73)

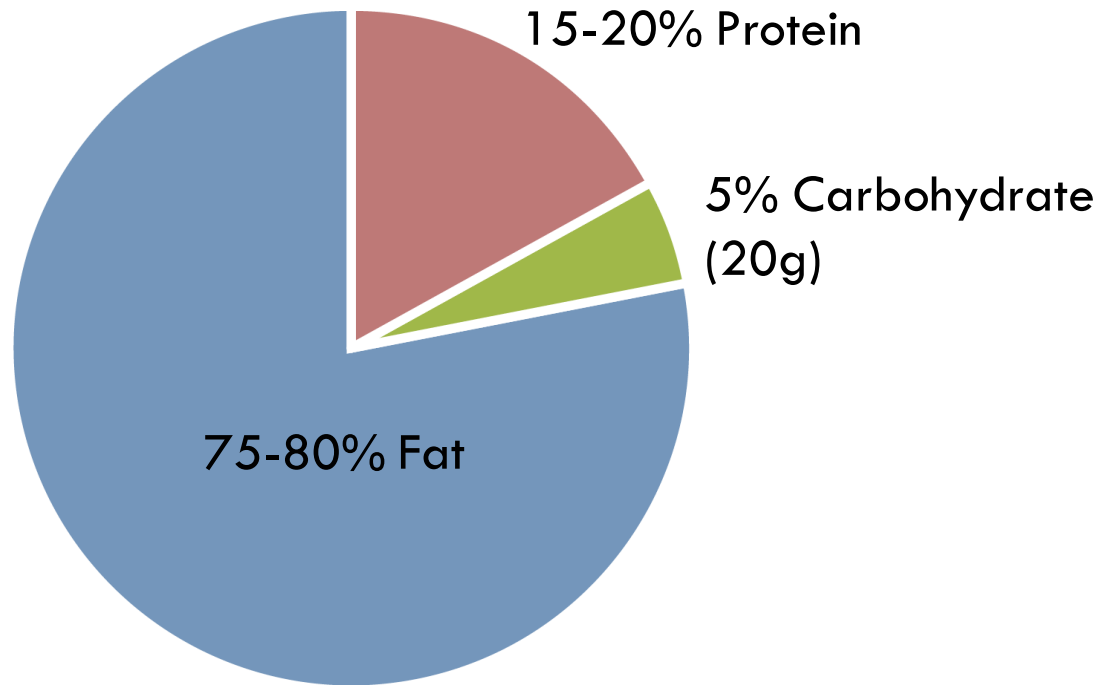
Average duration of care : 10 years (5 mos – 30 years)

Average number of medications: 5

(25/28 taking at least one antipsychotic medication)

All had at least one marker of poor metabolic health

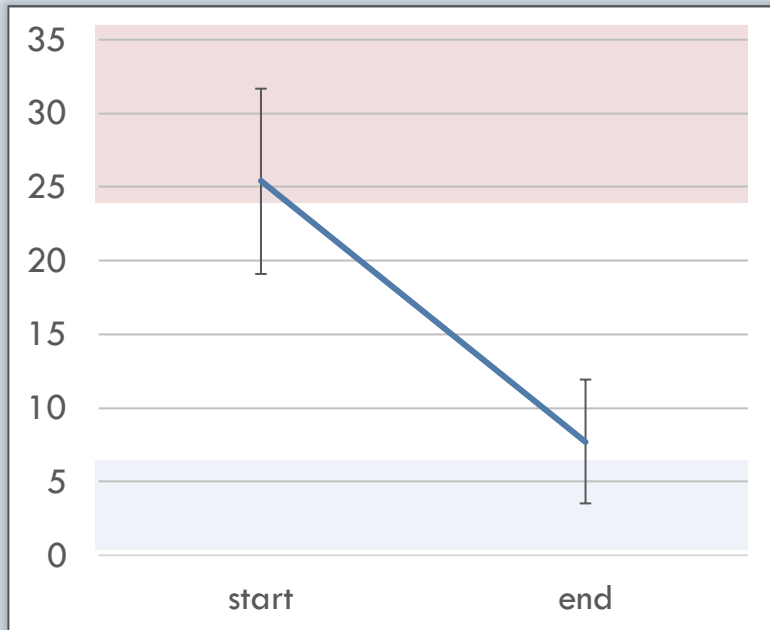
Dietary Intervention



- Meat, seafood, poultry, eggs
- 2 cups salad vegetables per day
- 1 cup cooked non-starchy vegetables per day
- 1 snack box (e.g. nuts, cheese, boiled egg)

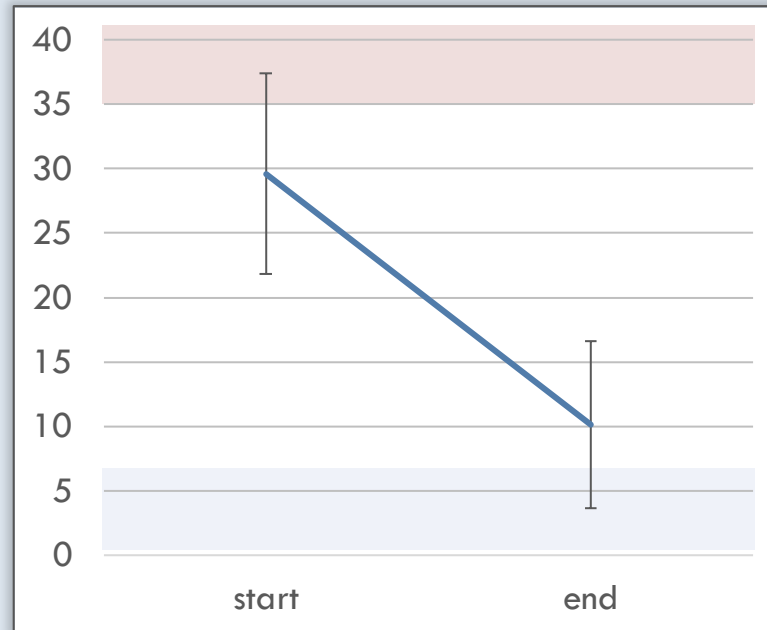
Mental Health Measures

**Hamilton Depression
Rating Scale
(HAM-D)**



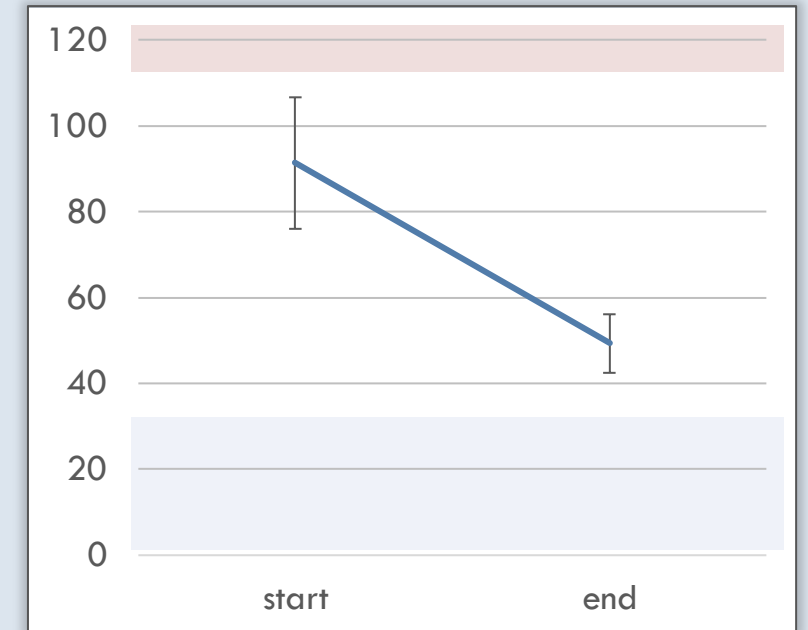
Scale of 0 – 52
 ≤ 7 no depression
 ≥ 24 severe depression

**Montgomery-Åsberg
Depression Rating Scale
(MADRS)**



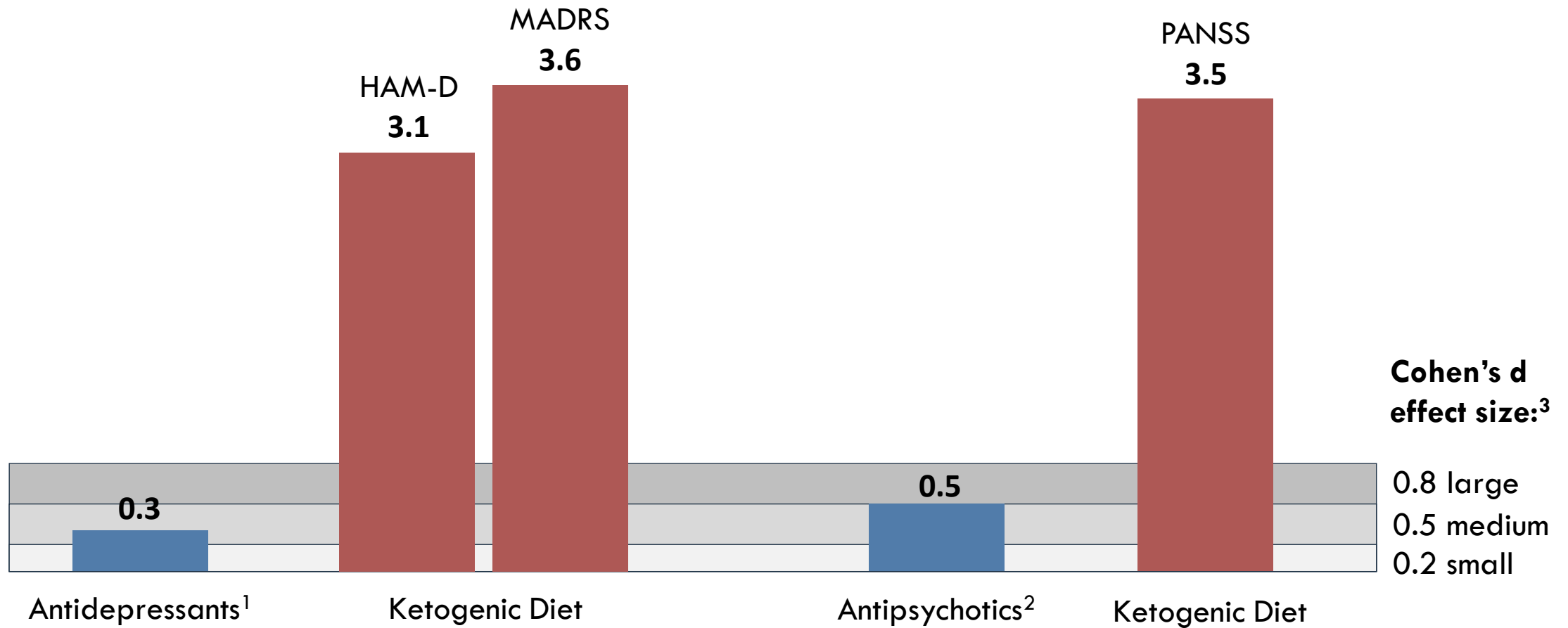
Scale of 0 – 60
 ≤ 6 no depression
 ≥ 35 severe depression

**Positive and Negative
Syndrome Scale
(PANSS)**



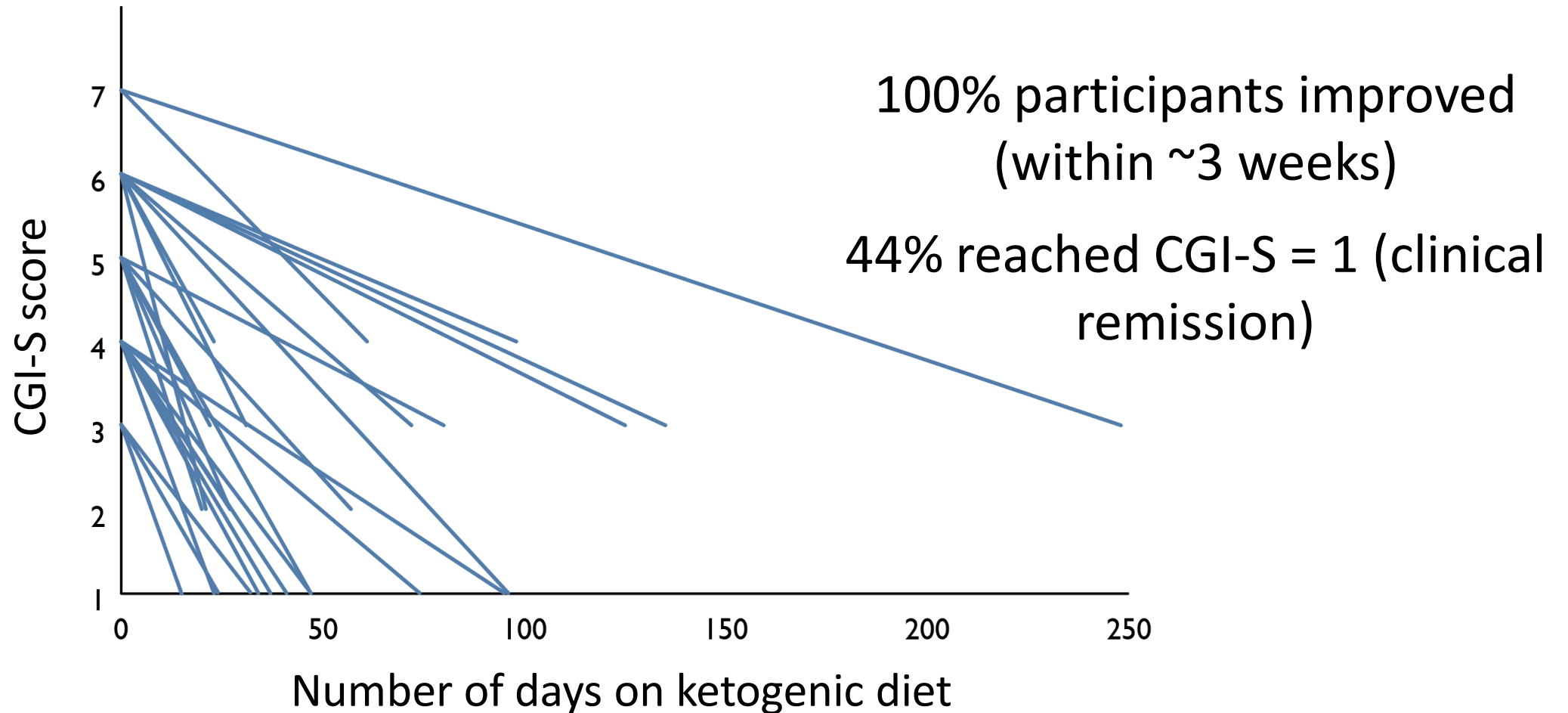
Scale of 30 – 210
30 = least severe
 ≥ 116 severely ill

Effect Sizes Compared to Medication



1. Hengartner MP, Plödel M. *Front Psychiatry*. 2018; 2. Leucht S et al. *Schizophr Bull*. 2022; 3. Lakens D. *Front Psychol*. 2013.

Clinical Global Impressions Severity Scale (CGI-S)



Metabolic Health Measures

FBG: ↓8.1%

HbA1c: ↓3.5%

SBP: ↓7.6%

DBP: ↓7.4%

Weight: ↓5.3%

Trig: ↓14.8%

Total Chol: ↓.4%

LDL-C: ↓0.5%

HDL-C: ↑.4%

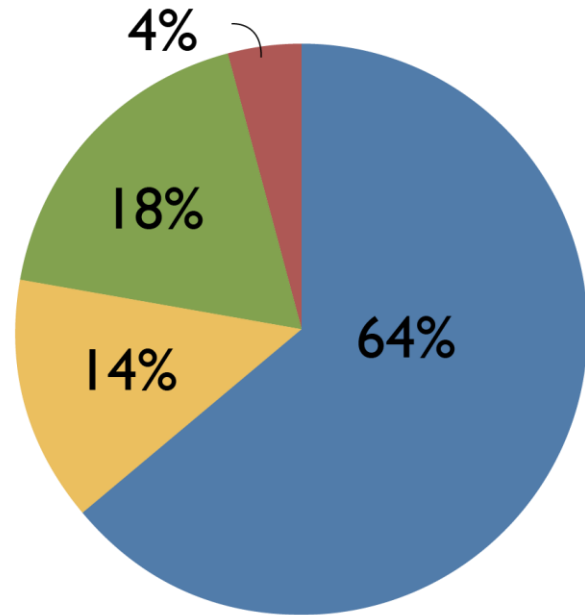
AST: ↓9.0%

GGT: ↓1.0%

ALT: ↓1.4%

Values in **bold** are statistically significant

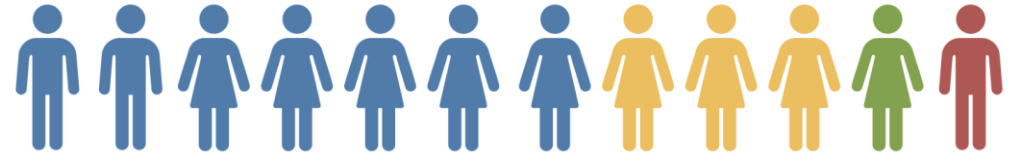
Change in Medication



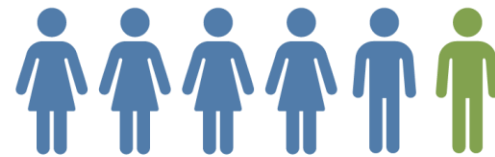
Overall n=28



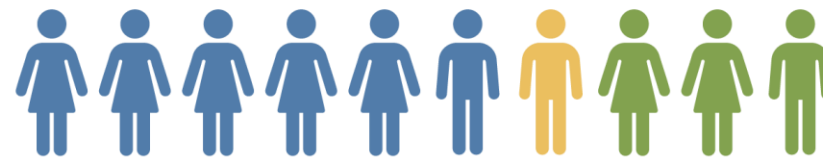
Bipolar disorder n=12



Major depressive disorder n=6



Schizoaffective disorder n=10



Limitation

Study treatment conditions



Prior treatment conditions



No control group



What Can We Say?

Feasible

Safe

Well-Tolerated*

Low-Risk, High Potential Benefit

*mild keto flu symptoms <2 wks

2/28 pts experienced GI upset <4 weeks

Studies Under Way

Bipolar Disorder

S. Sethi, Stanford Univ

H. & I. Campbell, Univ of Edinburgh

Psychosis

A. Ruusunen, Finland

Z. Sarnyai, James Cook University

J. Ford, UC San Francisco

D. Kelly, Univ of Maryland

Major Depressive Disorder

E. Brietzke, Queens University

Anxiety

A. Soto-Mota, Mexico City

Alzheimer's Disease

R. Swerdlow, Univ of Kansas

S. Craft, Wake Forest Univ

M. Lilimand, Hôpitaux de Paris

Substance Abuse

C. Wiers, U Penn

G-J Wang, NIH

A. Fink-Jensen, Denmark

PTSD

J. Rikardt Andersen, U. Copenhagen

Weight-Restored Anorexia

G. Frank, UC San Diego

Everyone Deserves a Metabolic Evaluation

Fasting glucose (<90 mg/dl, <5.0 mM)

Hemoglobin A1c (<5.7% ideal)

Fasting total insulin (single digits mIU/L ideal)

Waist : height ratio (<0.5 ideal)

Triglycerides (<100 mg/dl or <1.1 mM)

Triglyceride : HDL ratio (< 1.5 ideal)

HOMA-IR (<1 ideal, >3 poor)



Look Before You Leap

Learn more about:

Absolute and relative contraindications

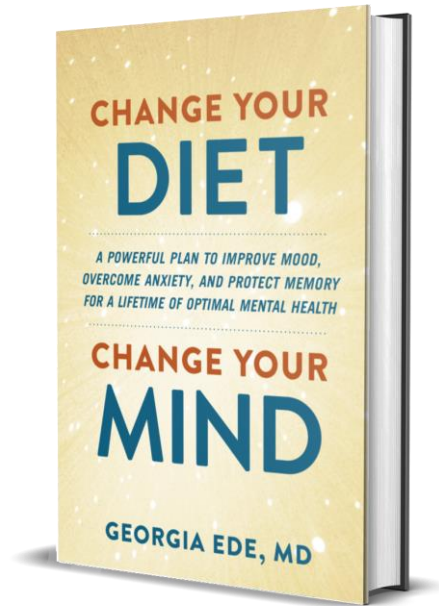
Medication management

Safe navigation of keto-adaptation phase

Medical care coordination



Learn More



January 23, 2024

The graphic has a blue background with a white central box. The title "KETOGENIC DIETS FOR MENTAL HEALTH" is in large, bold, blue letters. Below it, "Clinician Trainings with Dr. Georgia Ede" is in a smaller, gold-colored font. To the right is a circular image of various keto-friendly foods like salmon, avocado, and broccoli. At the bottom, there is a quote in italics: "Expand your offerings. Empower your patients. Transform your practice."/>

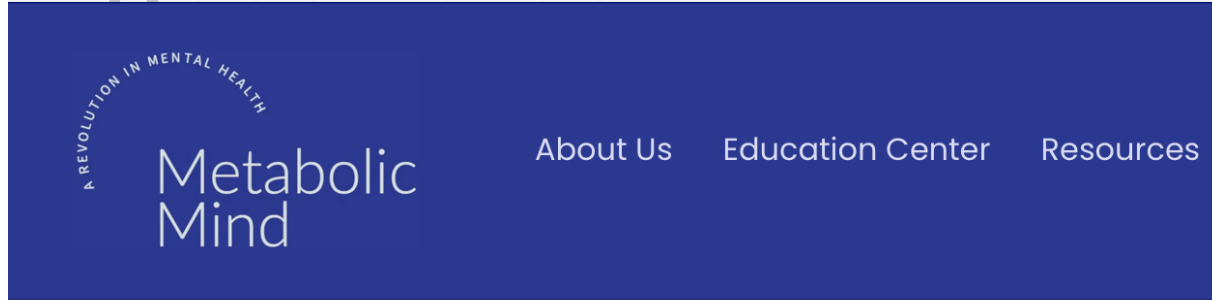
KETOGENIC DIETS FOR MENTAL HEALTH

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Transform your practice.*

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Ketogenic Diets for Mental Health



Metabolic Therapies and Mental Health

Metabolic Mind™ is a non-profit initiative providing education and resources in the emerging field of metabolic psychiatry. Our goal is to help revolutionize treatment of mental disorders through the adoption of metabolic therapies. We explore science and lived experience to highlight the connection between metabolic and mental health.

[MetabolicMind.org](https://www.MetabolicMind.org)

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