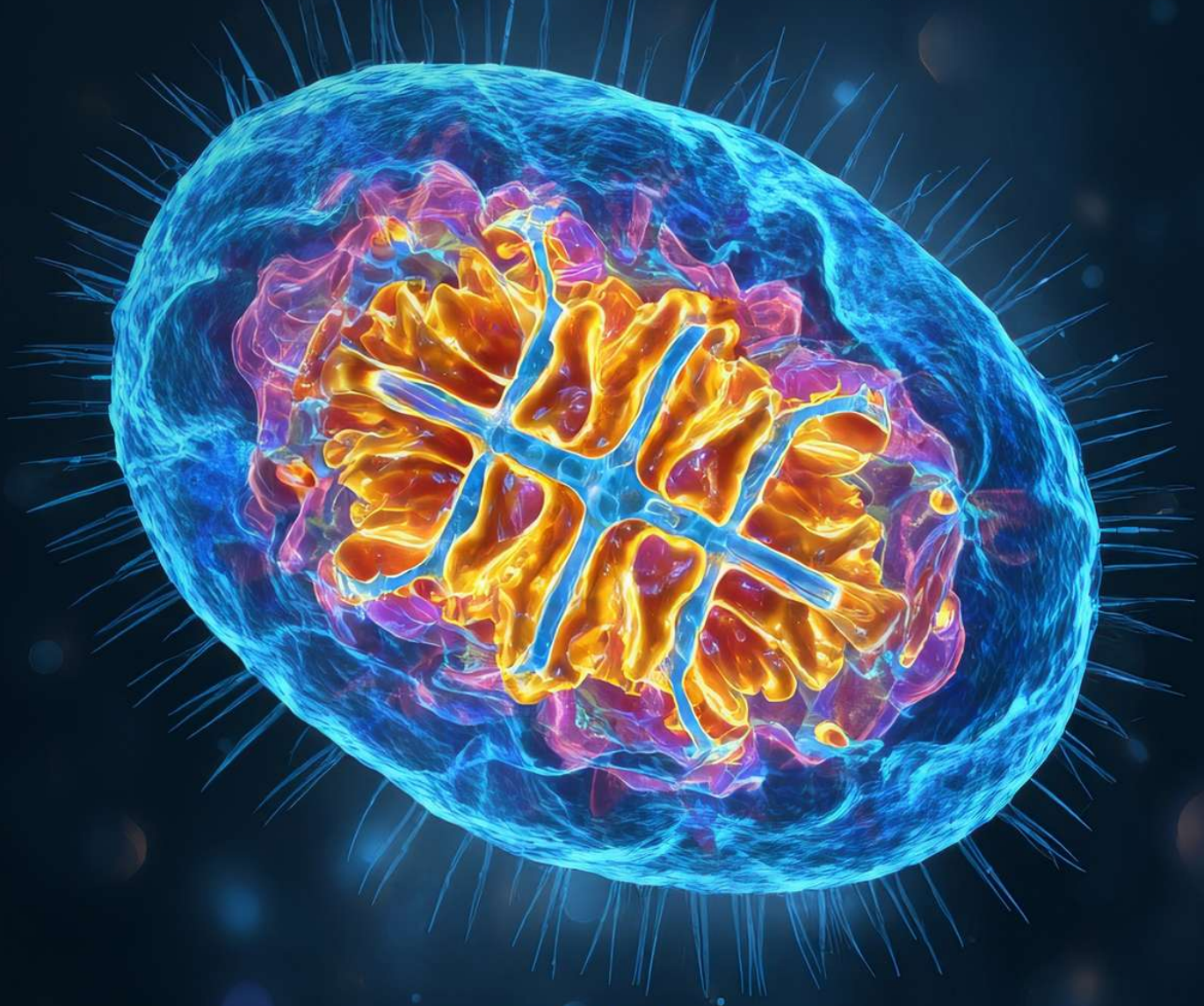
metabolic
health initiative

Ketogenic Metabolic Therapy

An overview of **research** and **advances** in **ketogenic metabolic therapy**.



VOLUME 4

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At Metabolic Health Initiative, our mission is to deliver evidence-based education that elevates the role of nutrition and metabolism in treating disease, extending healthspan, and enhancing human performance. In service of this mission, we've created the 4th volume of our Ketogenic Metabolic Therapy eBook as a user-friendly guide to highlight recent discoveries in our rapidly evolving field.

Think of this publication as an overview—a springboard to help you dive deeper into the literature. For the 150+ primary research articles summarized, you'll find at-a-glance details on study design, key findings, and conclusions. You can click each highlight for quick access to the full citation, abstract, and options for obtaining the article. Additionally, each content section includes curated lists of review articles to help you build a more comprehensive understanding of specific topics.

We hope you enjoy exploring these exciting advances as much as we enjoyed assembling them. Thank you for being part of our community. Here's to revolutionizing medicine, together!

Angela Poff, PhD & Victoria Field
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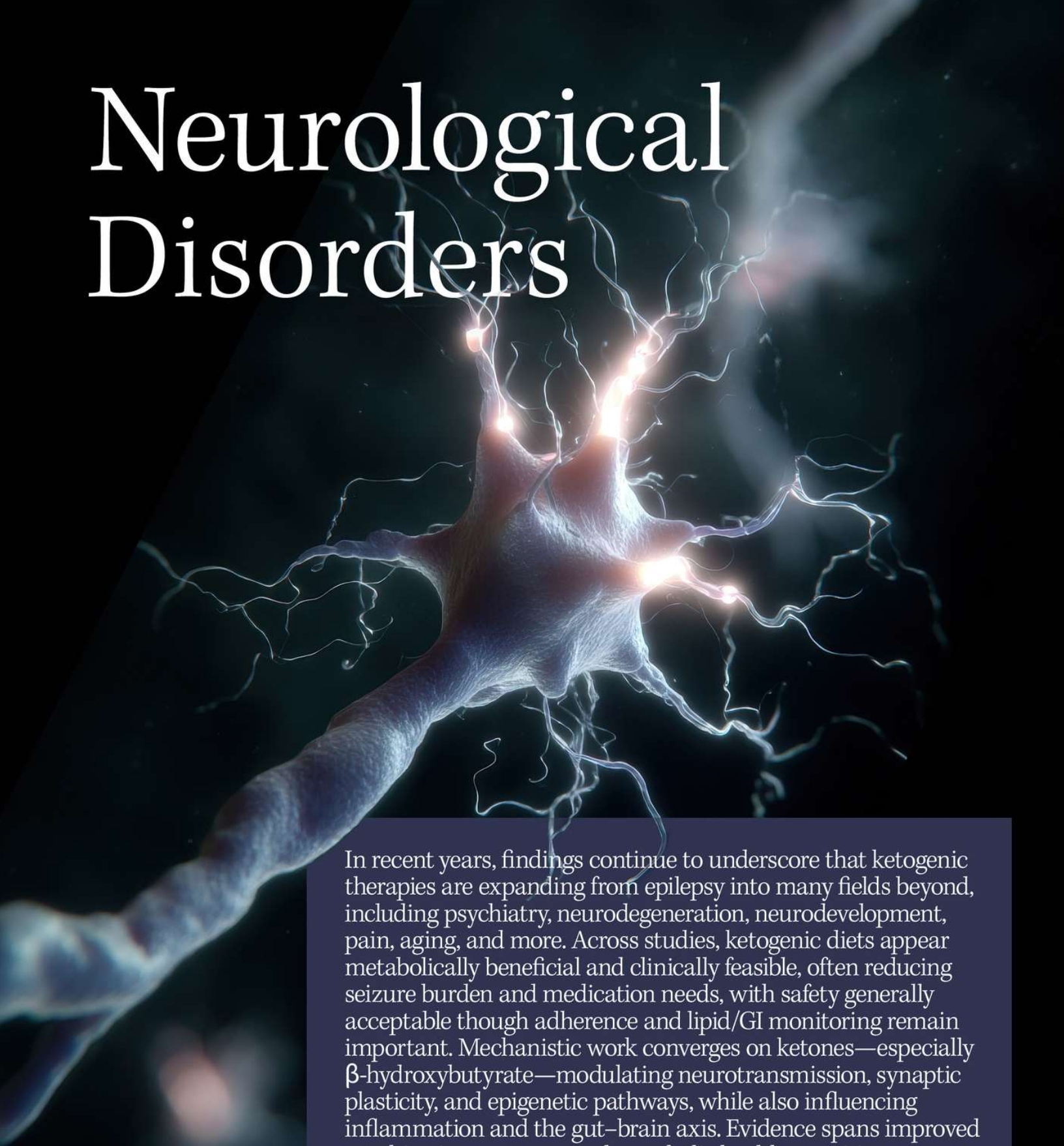
Neurological Disorders



In recent years, findings continue to underscore that ketogenic therapies are expanding from epilepsy into many fields beyond, including psychiatry, neurodegeneration, neurodevelopment, pain, aging, and more. Across studies, ketogenic diets appear metabolically beneficial and clinically feasible, often reducing seizure burden and medication needs, with safety generally acceptable though adherence and lipid/GI monitoring remain important. Mechanistic work converges on ketones—especially β-hydroxybutyrate—modulating neurotransmission, synaptic plasticity, and epigenetic pathways, while also influencing inflammation and the gut–brain axis. Evidence spans improved psychiatric symptoms and metabolic health, cognitive support in Alzheimer's and aging, potential nonmotor benefits in Parkinson's, and anti-allodynic effects in pain models. The adaptability of ketogenic approaches and the rise of human clinical data suggest growing promise as adjunctive strategies across diverse neurological and psychiatric conditions.

A pilot study examining a ketogenic diet as an adjunct therapy in college students with major depressive disorder; Decker et al

- The study enrolled 24 young adults with major depressive disorder (MDD) to follow a 10–12 week ketogenic diet (KD) with partial food provision and frequent dietary coaching, including daily capillary R-BHB tracking, to assess mood, metabolic health, and cognition.
- Among 16 completers, nutritional ketosis was achieved 73% of the time, and depressive symptoms declined by 69–71% (PHQ-9 and HRSD), with improvements in global well-being, body composition (loss of fat and total mass), and cognitive performance.
- These findings suggest that a well-monitored ketogenic diet may be a feasible adjunctive therapy for mild-to-moderate depression, associated with substantial mood and metabolic benefits.

A pilot study of a ketogenic diet in bipolar disorder: clinical, metabolic and magnetic resonance spectroscopy findings; Campbell et al

- The study enrolled euthymic individuals with bipolar disorder in a 6–8 week single-arm open pilot of a modified ketogenic diet, assessing clinical, metabolic, and MR spectroscopy outcomes before and after the intervention.
- In completers (n=20), weight and BMI decreased, systolic blood pressure fell, and daily ketone levels were modestly associated with improved mood and energy and reduced impulsivity and anxiety; MRS showed decreases in brain glutamate plus glutamine in the anterior and posterior cingulate cortices.
- Overall, the ketogenic diet was associated with favorable metabolic changes and brain biochemistry, with small mood associations, supporting further replication and randomized trials.

Exploring diet-induced ketosis with exogenous ketone supplementation as a potential intervention in post-traumatic stress disorder: a feasibility study; Edwards et al

- The study tested a 4-week ketogenic diet with exogenous ketone supplementation (KD-KS) in adults with PTSD, focusing on feasibility, ketosis attainment, safety, and treatment acceptance, with exploratory aims on PTSD symptoms and health-related QoL.
- Among four eligible patients, three were enrolled, two completed the 4-week intervention, ketosis was achieved quickly and maintained on most intervention days, and there were no serious adverse reactions, though adverse events occurred on about 70% of intervention days; PTSD symptoms improved modestly and QoL showed mixed gains in completers.
- Overall, the results suggest the KD-KS approach is feasible and tolerable in PTSD and may yield clinically meaningful symptom improvements, justifying larger, controlled feasibility and pilot studies.

NEUROLOGICAL DISORDERS

Effect of ketogenic diet on Alzheimer's disease to improve cognitive function: A literature review; Khoiroh et al

- A systematic literature review was performed to analyze studies on ketogenic diet interventions in Alzheimer's patients or animal models.
- The ketogenic diet was found to enhance cognitive function by providing ketone bodies that serve as an alternative energy source for brain cells and improve memory performance.
- Chronic ketogenic diet intervention significantly improved cognitive test scores and is considered a safe and feasible therapeutic approach for Alzheimer's disease.

Ketogenic diet and ketone bodies against ischemic injury: Targets, mechanisms, and therapeutic potential; Makievskaya et al

- This study systematically analyzed research from 1980 to 2022 on ketogenic diets and ketone bodies in ischemia–reperfusion injury across organs.
- Ketogenic diets and β-hydroxybutyrate were found to protect against ischemic damage, whereas high-calorie or high-fat diets worsened outcomes.
- The variability in diet composition and treatment protocols contributed to inconsistent results across studies.

Understanding the experiences of ketogenic metabolic therapy for people living with varying levels of depressive symptoms: a thematic analysis; Bellamy et al

- The study used a reflexive thematic analysis of nine participants who followed a non-calorie-restricted ketogenic diet (≤50 g carbs/day) for at least 12 weeks, splitting them into healthy adults and those with depressive symptoms to explore experiences and well-being.
- Five core themes emerged, including psychological well-being improvements, increased self-esteem and purpose, and the diet becoming a sustainable lifestyle, though initial implementation difficulties and hunger/cravings were common; participants generally reported that benefits outweighed side effects.
- Overall, the qualitative findings suggest the KD can be a feasible adjunctive approach that enhances mood and psychological well-being for some individuals with depressive symptoms, warranting further research.

Ketogenic diet protects MPTP-induced mouse model of Parkinson's disease via altering gut microbiota and metabolites; Jiang et al

- Researchers fed an MPTP-induced Parkinson's disease mouse model a ketogenic diet for 8 weeks.
- KD improved motor function, reduced neuronal loss and inflammation, and reversed gut microbiota dysbiosis.
- Fecal transplants from KD-treated mice conferred neuroprotection, implicating the gut–brain axis.

Efficacy of low carbohydrate and ketogenic diets in treating mood and anxiety disorders: systematic review and implications for clinical practice; Dietch et al

- A systematic review was conducted to evaluate the efficacy of low-carbohydrate and ketogenic diets in adults with mood and anxiety disorders.
- Limited evidence from heterogeneous studies suggested possible benefits in bipolar disorder, schizoaffective disorder, and possibly depression/anxiety, though limited high-quality data existed at the time of analysis (2022).
- Robust studies are needed to confirm efficacy, identify appropriate patient groups, and assess risks of relapse after discontinuation.

Ketogenic diet attenuates neuroinflammation and restores hippocampal neurogenesis to improve CUMS induced depression-like behavior in mice; Liang et al

- Mice exposed to chronic unpredictable mild stress (CUMS) were treated with a ketogenic diet (KD) to assess its antidepressant effects and mechanisms.
- KD alleviated depression-like behaviors, reduced neuroinflammation by inhibiting the TLR4/MyD88/NF-κB pathway, and enhanced hippocampal neurogenesis via BDNF/TrkB/CREB and Wnt/β-catenin signaling.
- These results support KD as a potential dietary therapy for depression.

Ketogenic diet mitigates age-related cognitive decline and neuroinflammation in rats, while antibiotics exacerbate brain health risks; Sayin et al

- Aging rats were fed a ketogenic diet (KD), with or without antibiotic-induced gut microbiota depletion, to examine effects on cognition and neuroinflammation.
- KD improved cognitive performance, increased BDNF and anti-inflammatory IL-10, and reduced pro-inflammatory cytokines, even in microbiota-disrupted groups.
- These findings suggest KD enhances brain resilience during aging independent of gut microbiota status.

Effects of the ketogenic diet on dentate gyrus and CA3 KCC2 expression in male rats with electrical amygdala kindling-induced seizures; Granados-Rojas et al

- Male rats with amygdala kindling-induced seizures were fed a ketogenic diet (KD) to study its effects on KCC2 expression and seizure activity.
- KD reduced after-discharge duration, increased latency to generalized seizures, and prevented kindling-induced reductions in KCC2 expression in hippocampal regions.
- Higher KCC2 levels correlated with shorter generalized seizure duration, indicating a neuroprotective role for KD in epilepsy.

Ketamine sustains and enhances the protective effects of a ketogenic diet against relapses in an anorexia mouse model; Dong et al

- Activity-Based Anorexia (ABA) model mice were treated with ketogenic diet (KGD) and sub-anesthetic ketamine to study relapse prevention in anorexia nervosa.
- KGD alone protected against relapses only when maintained, while ketamine enhanced and sustained KGD's protective effects even after withdrawal.
- KGD increased GABAergic synapse length, potentially reducing ABA vulnerability through enhanced synaptic regulation.

Ketogenic diet-induced alterations in neuronal signaling-related proteins are not due to differences in synaptosome protein levels; Fletcher et al

- Aging rats were fed a ketogenic diet (KD) or control diet, and synaptosomes from hippocampus and prefrontal cortex were analyzed for synaptic signaling proteins.
- KD did not alter synaptosomal protein levels but disrupted age-related protein correlations and altered excitatory/inhibitory balance in prefrontal cortex, suggesting KD increases synaptic abundance without changing synaptic biochemical composition.

Ketogenic diet and quercetin promote the recovery of motor function in rats with spinal cord injury; Liu et al

- Spinal cord injured rats were treated with ketogenic diet (KD), quercetin, or their combination to assess motor function recovery.
- Combined KD and quercetin treatment significantly improved motor performance, reduced cavity volume and inflammation, and enhanced neurite preservation compared to single treatments.
- These benefits were mediated through inhibition of the NF-κB/NLRP3 pathway, suggesting a synergistic therapeutic approach for spinal cord injury.

Ketogenic diet intervention on metabolic and psychiatric health in bipolar and schizophrenia: A pilot trial; Sethi et al

- A 4-month pilot study tested the effects of a ketogenic diet (KD) in 23 individuals with schizophrenia or bipolar disorder and pre-existing metabolic abnormalities.
- The KD eliminated metabolic syndrome in all participants, reducing weight (12%), visceral fat (36%), insulin resistance (27%), and triglycerides (25%), while also improving psychiatric symptoms—32% reduction in schizophrenia severity, 31% lower overall illness severity, and gains in life satisfaction (17%) and sleep quality (19%).
- These results highlight the dual metabolic and psychiatric benefits of KD as a potential adjunct therapy for serious mental illness.

Effect of the ketogenic diet as a treatment for refractory epilepsy in children and adolescents: a systematic review of reviews; Díez-Arroyo et al

- This systematic review of 21 existing reviews (8 systematic, 13 unsystematic) evaluated the use of ketogenic diets (KDs) for refractory epilepsy in children, analyzing four KD types.
- Systematic reviews found over 50% seizure reduction in approximately half of patients, while unsystematic reviews reported 30%–60% efficacy.
- Adverse effects like vomiting, constipation, and diarrhea were common, and KD effectiveness was comparable across variations, suggesting adaptability to patient needs.

Ketogenic diet-produced β-hydroxybutyric acid accumulates brain GABA and increases GABA/glutamate ratio to inhibit epilepsy; Qiao et al

- The study investigated the antiepileptic mechanisms of the ketogenic diet (KD) using pentetrazol-induced epilepsy in mice and focused on β-hydroxybutyric acid (BHB), a key KD metabolite.
- Results revealed that BHB inhibited HDAC1/HDAC2, upregulated SIRT4 and glutamate decarboxylase 1 (GAD1), and increased the brain GABA/glutamate ratio to suppress neuron excitation.
- BHB alone mimicked the KD's effects, reducing seizures in mice and suggesting its potential as a therapeutic alternative to the KD.

Ketogenic diet and BHB rescue the fall of long-term potentiation in an Alzheimer's mouse model and stimulates synaptic plasticity pathway enzymes; Di Lucente et al

- The study examined the effects of a 7-month ketogenic diet (KD) on Alzheimer's disease (AD) in APP/PS1 mice, comparing outcomes to a control diet.
- KD restored long-term potentiation (LTP) to wild-type levels without altering amyloid-β, linked to increased β-hydroxybutyrate (BHB), which itself rescued LTP and activated synaptic plasticity pathways (e.g., p-ERK, p-CREB, BDNF).
- These findings suggest KD and BHB, as approved interventions, could therapeutically target synaptic dysfunction in early AD stages like mild cognitive impairment.

Ketogenic diet induced shifts in the gut microbiome associate with changes to inflammatory cytokines and brain-related mirnas in children with autism spectrum disorder; Allan et al

- This pilot study evaluated a modified ketogenic diet (KD) in seven children with autism spectrum disorder (ASD), analyzing gut microbiota, inflammation markers, and microRNAs before and after a 4-month dietary intervention.
- The KD reduced plasma levels of proinflammatory cytokines (IL-12p70, IL-1β) and brain-derived neurotrophic factor (BDNF), altered gut microbiome composition, increased gut butyrate kinase expression, and modified BDNF-associated miRNAs.
- These changes suggest the KD may improve ASD-related social behaviors by mitigating inflammation, restoring gut microbial balance, and influencing BDNF pathways linked to brain function.

Ketogenic diet administration later in life improves memory by modifying the synaptic cortical proteome via the PKA signaling pathway in aging mice; Acuña-Catalán et al

- The study investigated the effects of a short-term ketogenic diet (KD) administered to elderly mice on brain function through behavioral tests, synaptic plasticity assessments, and proteomic analysis.
- The KD enhanced working memory and hippocampal long-term potentiation (LTP) while increasing BDNF levels and activating the PKA signaling pathway, mirroring molecular changes seen with long-term KD.
- These results indicate that even brief, late-life KD interventions can promote synaptic plasticity and mitigate age-related cognitive decline via conserved mechanisms like PKA activation.

The relationship of ketogenic diet with neurodegenerative and psychiatric diseases: A scoping review from basic research to clinical practice; Mentzelou et al

- A scoping review examined basic and clinical research on ketogenic diets in neurodegenerative and psychiatric diseases over the past 20 years.
- Basic research identified multiple neuroprotective mechanisms, such as reduced neuroinflammation and oxidative stress, while clinical evidence remained limited, heterogeneous, and often short-term.
- More controlled, long-term clinical studies are needed to validate these findings.

Effects of ketogenic diet on cognitive function of patients with Alzheimer's disease: a systematic review and meta-analysis; Rong et al

- This meta-analysis of 10 randomized controlled trials (691 Alzheimer's disease patients) evaluated the ketogenic diet's (KD) effects on cognitive function over 3–15 months.
- KD significantly improved mental state (NM scale), cognitive scores (MMSE, ADAS-Cog), and elevated ketone bodies (β-hydroxybutyrate), but also increased triglycerides and LDL cholesterol.
- While KD shows promise for enhancing cognitive function in Alzheimer's patients, its potential lipid-related risks warrant caution, though its overall efficacy and safety support clinical consideration.

Advances in ketogenic diet therapies in pediatric epilepsy: A systematic review; Parveen et al

- This systematic review analyzed 12 studies to assess the effects of ketogenic diets (KD) on epilepsy in children and adolescents, following a PubMed literature search based on PRISMA guidelines.
- KD and its variants significantly reduced seizure frequency and severity but were associated with manageable adverse effects like gastrointestinal issues, dyslipidemia, and metabolic disturbances.
- The findings suggest KD can serve as an effective alternative or complementary treatment for pediatric epilepsy, contingent on patient adherence and comorbidities.

Ketogenic diet modifies ribosomal protein dysregulation in KMT2D Kabuki syndrome; Tsang et al

- This study analyzed molecular mechanisms in Kabuki syndrome (KS) patients and controls using single-cell RNA sequencing and proteomics, alongside a case study of a 12-year-old boy with KS on a ketogenic diet.
- Mutations in KMT2D were linked to ribosomal protein dysregulation and immune disturbances, while the ketogenic diet improved cognitive function and corrected ribosomal transcriptomic profiles in the patient.
- The findings highlight ketones' epigenetic potential to modulate chromatin and address molecular deficits in neurodevelopmental disorders like KS.

A randomized feasibility trial of medium chain triglyceride-supplemented ketogenic diet in people with Parkinson's disease; Choi et al

- This study evaluated a medium-chain triglyceride-supplemented ketogenic diet (MCT-KD) in 16 Parkinson's disease (PD) patients through a one-week randomized controlled trial (MCT-KD vs. standard diet) followed by a two-week open-label extension.
- The MCT-KD was feasible and acceptable (15/16 completion rate), safely inducing ketosis by day 4, though no significant differences emerged in mobility (TUG test) or most clinical measures between groups.
- Nonmotor symptoms improved more in the KD group after three weeks, suggesting potential symptomatic benefits warranting further research to confirm efficacy.

Ketogenic diet alleviates mechanical allodynia in the models of inflammatory and neuropathic pain in male mice; Eto et al

- This study tested the effects of a ketogenic diet on mechanical allodynia in male mice with formalin-induced chronic inflammatory pain and nerve injury-induced neuropathic pain.
- The ketogenic diet reduced mechanical allodynia in both the injured and uninjured hind paws, prevented formalin-induced edema, and alleviated neuropathic pain caused by nerve injury.
- These results demonstrate that the ketogenic diet has therapeutic potential for chronic pain associated with inflammation and nerve damage.

Efficacy and safety of ketogenic diet in infants with epilepsy: KIWE RCT; Schoeler et al

- This randomized trial compared the ketogenic diet to additional antiseizure medications in 136 infants (1–24 months) with drug-resistant epilepsy.
- Reduction of daily seizure frequency did not differ significantly between the KD compared to the antiseizure medication group, and both groups showed similar rates of serious adverse events.
- Three deaths occurred in the KD group but all were considered unrelated to treatment.
- The KD is safe and offers a viable alternative for infants whose seizures persist after two antiseizure medications, despite not demonstrating superior efficacy.

Ketogenic diet therapy leads to antiseizure medication reduction in children and adults with drug-resistant epilepsy; He et al

- This study evaluated the safety of reducing or discontinuing anti-seizure medications (ASMs) in 56 adults and children with drug-resistant epilepsy undergoing KD for ≥6 months.
- Over 64% successfully reduced or withdrew at least one ASM, with comparable rates between children/adults and responders/non-responders, while adults showed a 24.5% average reduction in ASM load without adverse outcomes.
- The results demonstrate that ASM withdrawal via KD is safe and achievable for most patients, irrespective of age or seizure reduction.

Efficacy of anti-seizure medications and alternative therapies (ketogenic diet, CBD, and quinidine) in KCNT1-related epilepsy: A systematic review; Gras et al

- This study reviewed 43 articles involving 197 patients with KCNT1-related epilepsy (EIMFS, [AD]SHE, DEE) to assess treatment efficacy for drug-resistant seizures.
- The KD showed benefit in 62.5% of EIMFS and some DEE cases, while cannabidiol (CBD) and quinidine (QUIN) had partial effectiveness, but conventional anti-seizure medications were rarely effective (5–25% benefit).
- KD and CBD are viable options for KCNT1-related epilepsy, though further research is needed to optimize treatment strategies and identify predictive factors.

Impact of a ketogenic diet on sleep quality in people with relapsing multiple sclerosis; Perlman et al

- This study evaluated the effects of a 6-month KD on sleep in 45 patients with relapsing multiple sclerosis (MS), using the Epworth Sleepiness Scale (ESS) and Sleep Disorders Symptom Checklist-25 (SDS) for assessment.
- KD significantly reduced daytime sleepiness (ESS score decreased by 1.90, $p < 0.001$) and improved symptoms of insomnia, obstructive sleep apnea, and restless leg syndrome, though sleep duration remained unchanged.
- The findings suggest KD may enhance sleep quality in MS patients, supporting dietary interventions as a therapeutic strategy for sleep disorders in neurological conditions.

The ketogenic diet mitigates opioid-induced hyperalgesia by restoring short-chain fatty acids-producing bacteria in the gut; Crawford et al

- This study tested the effects of a KD on opioid-induced hyperalgesia (OIH) in male mice chronically treated with morphine, using 16S rRNA sequencing and short-chain fatty acid (SCFA) supplementation.
- The KD reversed morphine-induced pain sensitivity and restored gut microbiota disrupted by opioids, particularly SCFA-producing bacteria, while SCFA supplementation delayed OIH onset, linking gut microbiome health to pain modulation.
- These findings suggest KD could complement chronic opioid therapy by targeting the gut microbiome, though results are limited to male mice.

Mediterranean ketogenic diet accounts for reduced pain frequency and intensity in patients with chronic migraine: A pilot study; Olivito et al

- This study evaluated the effects of a combined Mediterranean-ketogenic diet administered to chronic migraine patients over 4 (T1) and 8 weeks (T2), measuring migraine frequency/intensity, anthropometric data, and biochemical parameters.
- The diet significantly reduced migraine frequency and intensity within 4 weeks ($p < 0.01$), alongside decreased fat mass ($p < 0.001$), insulin levels ($p < 0.01$), and Homa index ($p < 0.05$) by T2.
- These findings suggest the Mediterranean-ketogenic diet is a promising non-pharmacological intervention for migraine management, with additional metabolic and body composition benefits.

Association between seizure reduction during ketogenic diet treatment of epilepsy and changes in circulatory metabolites and gut microbiota composition; Dahlin et al

- Serum metabolomes and gut microbiomes of children with drug-resistant epilepsy were analyzed before and after a 3-month ketogenic diet (KD).
- Plasmalogens, neuroprotective lipids positively linked to *Faecalibacterium* and *Christensenella* species, correlated with seizure reduction, while *E. coli* strains and infant-type *Bifidobacteria* showed negative associations.
- Findings suggest microbiota-metabolite interactions (e.g., plasmalogen production) contribute to KD's anti-seizure effects, highlighting potential therapeutic targeting of gut microbes or metabolites.

The evidence for diet as a treatment in migraine - A review; Nguyen et al

- This study reviewed evidence from PubMed on whether diets or specific foods can prevent migraines, evaluating various dietary interventions.
- Reports found that ketogenic and DASH-style diets, low-fat vegan with elimination, elimination diets (including IgG-guided) and gluten-free diets can reduce attack duration, frequency, severity, and medication use in some patients.
- However, due to small sample sizes and heterogeneous study designs, the overall evidence is limited and more rigorous randomized controlled trials are needed to confirm these associations.

Ketogenic diet reduces a neurobiological craving signature in inpatients with alcohol use disorder; Wiers et al

- This study conducted a secondary analysis of fMRI data from adults with alcohol use disorder randomized to a ketogenic diet or standard American diet during 3 weeks of inpatient alcohol detox, examining brain responses to alcohol cues and a neurobiological craving signature (NCS).
- It found that the KD group showed lower NCS expression to alcohol versus food cues across all weeks, and self-reported wanting for alcohol cues decreased more with KD, though this reduction did not correlate with NCS.
- The authors conclude that a ketogenic diet reduces cue-induced craving signals and self-reported alcohol wanting during detox, but NCS may not fully reflect ongoing non-cue-related alcohol desire.

A high MCT-based ketogenic diet suppresses Th1 and Th17 responses to ameliorate experimental autoimmune encephalomyelitis in mice by inhibiting GSDMD and JAK2-STAT3/4 pathways; Zhang et al

- The study evaluated the therapeutic potential of a ketogenic diet (KD) in experimental autoimmune encephalomyelitis (EAE), reporting that KD reduces demyelination and microglial activation and shifts T cell responses away from Th1/Th17 toward Th2/Treg in the CNS and spleen.
- It also shows KD suppresses GSDMD activation and lowers p-JAK2/JAK2, p-STAT3/STAT3, and p-STAT4/STAT4 signaling, correlating with reduced chemokine expression and T cell infiltration into the CNS.
- The authors conclude that KD may be an effective strategy to treat MS by modulating pyroptosis and inflammatory signaling pathways to dampen pathogenic T cell responses.

Ketogenic diet attenuates cognitive dysfunctions induced by hypoglycemia via inhibiting endoplasmic reticulum stress-dependent pathways; Li et al

- The study fed one-month-old mice a ketogenic diet for 2 weeks and used a hypoglycemia model to assess cognitive function, gut microbiota changes (16S rRNA sequencing), and brain structure/function via immunofluorescence, Western blot, TEM, and Golgi staining.
- It found KD altered gut microbiota (increased Dorea, decreased Rikenella), alleviated anxiety-like behavior, improved hippocampal dendritic spine density and synaptic proteins (SPN, PSD95, SYP), and promoted hippocampal neural stem cell proliferation while reducing apoptosis by dampening ER stress pathways (IRE1-XBP1 and ATF6).
- The authors conclude that KD may mitigate hypoglycemia-induced cognitive impairment by modulating gut microbiota, enhancing synaptic plasticity, and reducing ER stress in the hippocampus.

Ketogenic diet improves sleep quality and daytime sleepiness in chronic migraine: A pilot study; Tereshko et al

- This study followed 26 chronic migraine patients assigned to a 2:1 ketogenic diet (n=11) or a low-glycemic-index diet (LGID, n=15) for 6 months, assessing sleep quality (PSQI), daytime sleepiness (ESS), disability and impact (MIDAS, HIT-6), migraine frequency and intensity, and body composition at baseline, 3 months, and 6 months.
- Both diets significantly improved sleep quality, daytime sleepiness, migraine frequency, migraine intensity, BMI, fat mass, and HIT-6 over time, but MIDAS and fat-free mass did not show significant change; most measures did not differ between 3- and 6-month follow-ups.
- A modest correlation emerged between fat mass reduction and ESS improvement, suggesting greater sleepiness benefits with larger fat loss, while overall the two diets had similar effects on outcomes across the study period.

Bibliometric analysis of global research profile on ketogenic diet therapies in neurological diseases: Beneficial diet therapies deserve more attention; Wang et al

- This study conducted a bibliometric analysis of ketogenic diet therapies (KDTs) in neurology from 2000 to 2021 using WoSCC data and tools like VOSviewer and CiteSpace.
- The findings show a steady rise in publications and citations, with the United States leading in output and Epilepsia as the top journal; key research interests include epilepsy, neuroprotection, and mitochondrial/oxidative stress mechanisms, highlighting a shift from basic research to clinical application.

ADCY3: the pivotal gene in classical ketogenic diet for the treatment of epilepsy; Lin et al

- The study combines a meta-analysis and animal experiments to compare ketogenic diet (KD) with conventional diets for epilepsy, finding KD superior in controlling seizures, especially with the classic KD.
- Transcriptome analysis identifies ADCY3 as a key gene upregulated by KD, and in vivo work shows that ADCY3 activates the cAMP-PKA signaling pathway, enhancing neuronal inhibition and improving epilepsy outcomes.
- The authors conclude that KD may exert its anti-epileptic effects through the ADCY3-initiated cAMP signaling axis, supporting ADCY3 as a potential mechanism mediating KD efficacy.

Ketogenic diet effectiveness is superior for drug resistant epilepsy with causative genetic mutation than those without genetic etiology; Hsieh et al

- The study retrospectively compared ketogenic diet therapy (KDT) responsiveness in children with genetic epilepsy versus non-genetic epilepsy using a GRAD-KD initiation, tracking monthly seizure frequencies and reduction after 3 and 6 months.
- It found that while both groups showed reduced seizure frequencies by 6 months, the seizure reduction was significantly greater in the genetic epilepsy group, with non-DEE patients also showing greater reductions than DEE (developmental and epileptic encephalopathy) patients.
- The authors conclude that KDT may be more effective for seizure burden in genetic etiologies (especially non-DEE) and suggest earlier KDT consideration for these patients.

The effects of ketogenic dietary therapies on sleep: A scoping review; Pasca et al

- This study conducted a scoping review to identify and map evidence on the effects of ketogenic dietary therapies (KDTs) on sleep in neurological conditions, using PubMed and Scopus to June 2023 and including 20 papers after screening 277 records.
- The findings show high variability in study design and sleep outcomes, but overall improvements were observed in sleep quality, ease of falling asleep, nighttime awakenings, daytime sleepiness, and an increase in REM sleep, with potential physiological explanations and future directions discussed.

Efficacy and tolerability of classical and polyunsaturated fatty acids ketogenic diet in controlling paediatric refractory epilepsy - A randomized study; Ray et al

- The randomized study compared a classical ketogenic diet (CKD) with a polyunsaturated fatty acids ketogenic diet (PUFAKD) in 52 children with refractory epilepsy over up to 12 months, assessing seizure frequency reductions and tolerability (vomiting, nausea, lethargy, constipation).
- Both diets produced significant seizure reductions (~71% average) with no significant difference between CKD and PUFAKD in efficacy, though higher compliance correlated with greater seizure improvement across all participants.
- PUFAKD showed poorer tolerability, with higher rates of nausea and vomiting, suggesting CKD is the preferable option for pediatric refractory epilepsy pending further trials of PUFA compositions.

Ketogenic effect of coconut oil in ALS patients; Carrera-Juliá et al

- This pilot study evaluated a Mediterranean diet (MeDi) augmented with nicotinamide riboside (NR), pterostilbene (PTER), and/or coconut oil in ALS patients, aiming to assess effects on anthropometric outcomes.
- Findings suggest that MeDi plus NR, PTER, and coconut oil produced the greatest benefits in anthropometric measures among the interventions tested, with the rationale that ketone bodies from coconut oil may support energy supply for motor neurons.
- The authors discuss the potential of a coconut oil–enriched MeDi to elevate circulating ketone bodies as a therapeutic energy source in ALS, acknowledging ongoing controversy over coconut oil–related ketogenic effects.

Time-restricted ketogenic diet in amyotrophic lateral sclerosis: a case study; Philips et al

- This report documents a single bulbar-onset ALS patient who followed a time-restricted ketogenic diet (TRKD) for 18 months, reporting improvements in ALS-related function, pulmonary measures (FEV, FVC), mood, stress, fatigue, and quality of life, with swallowing and neurocognitive status remaining stable.
- Some functions declined (general physical function, maximal inspiratory and expiratory pressures), but weight loss was limited and no significant adverse effects occurred; the patient remained functionally independent after 45 months since symptom onset.
- The authors note this as the first documented case of combining fasting/ketogenic approaches in TRKD for ALS and suggest potential benefits in energy metabolism and symptom management, while acknowledging the need for broader evidence.

Metabolic reprogramming in astrocytes results in neuronal dysfunction in intellectual disability; Zhang et al

- The study uses SNX27R196W knock-in mice to model an ID-associated mutation, showing impaired synaptic function and learning, linked to disrupted astrocytic glucose uptake via GLUT1, reduced lactate production, and a shift from homeostatic to reactive astrocytes.
- Lactate supplementation or a ketogenic diet restored neuronal oxidative phosphorylation and reversed cognitive deficits in SNX27R196W mice, indicating that astrocyte-derived lactate supports neuron function and cognition.
- The authors conclude that astrocytic SNX27 is crucial for glucose supply and glycolysis, and that correcting astrocytic metabolism can ameliorate ID-related cognitive impairments, proposing metabolic interventions as potential therapies.

REVIEW ARTICLES ON NEUROLOGICAL DISORDERS

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The ketogenic diet and metabolic treatments for neuropsychiatric disorders; Palmer

Ketogenic diet in the treatment of epilepsy; Borowicz-Reutt, et al

Ketogenic diet and behavior: insights from experimental studies; Grabowska, et al

Sleep, mood disorders, and the ketogenic diet: potential therapeutic targets for bipolar disorder and schizophrenia; Choi et al

Exploring the ketogenic diet's potential in reducing neuroinflammation and modulating immune responses; Monda et al

Ketogenic diet and neuroinflammation: Implications for neuroimmunometabolism and therapeutic approaches to refractory epilepsy; Guerreiro et al

Ketogenic diet as a therapeutic approach in autism spectrum disorder: a narrative review; Öztürk et al

Drug resistant epilepsy and ketogenic diet: A narrative review of mechanisms of action; Mishra et al

The potential effects of the ketogenic diet in the prevention and co-treatment of stress, anxiety, depression, schizophrenia, and bipolar disorder: From the basic research to the clinical practice; Chrysafi et al

The impact of microbiota and ketogenic diet interventions in the management of drug-resistant epilepsy; Diaz-Marugan et al

Ketogenic diet as a nutritional metabolic intervention for obsessive-compulsive disorder: A narrative review; Lounici et al

The potential role of the ketogenic diet in serious mental illness: Current evidence, safety, and practical advice; Rog et al

Nutritional strategies in major depression disorder: From ketogenic diet to modulation of the microbiota-gut-brain axis; Nikdasti et al

Exogenous ketone bodies and the ketogenic diet as a treatment option for neurodevelopmental disorders; Omori et al

A side-by-side comparison of fine-tuning options for treatment of medically refractory epilepsy: Antiseizure medications, vagus nerve stimulation and ketogenic diet therapies; Bonno et al

Linking mitochondrial dysfunction, neurotransmitter, and neural network abnormalities and mania: Elucidating neurobiological mechanisms of the therapeutic effect of the ketogenic diet in bipolar disorder; Freyberg et al

Ketogenic therapy towards precision medicine for brain diseases; Liu et al

Neurodevelopment is dependent on maternal diet: Placenta and brain glucose transporters GLUT1 and GLUT3; Daida et al

Metabolic Disorders

Across obesity, metabolic diseases, and inflammatory conditions, research on ketogenic metabolic therapy continues to reveal multifaceted effects spanning the microbiome, bile acids, hormones, immune signaling, and more. Evidence pointed to weight loss driven by reduced calorie absorption via microbiome–bile acid shifts, appetite-regulating ketone metabolites, and a liver PPAR–GDF15 axis. In obesity and PCOS, KDs generally improved weight, waist, and inflammatory markers, and may aid NAFLD through time-dependent antioxidant pathways, while modulating leptin and enhancing monocyte mitochondrial function. Compared with sugar restriction or Mediterranean diets, KDs may confer distinct anti-inflammatory and disease-modifying benefits but also show early, adaptive trade-offs in glucose tolerance, lipids, and gut diversity. Overall, KMT appears to be a potent tool, but condition- and context-dependent metabolic tools require individualized oversight.

Ketogenic diet and ketone salts differentially improve cardiometabolic complications in an HFpEF rat model; Gonçalves et al

- HFpEF rats were treated with a ketogenic diet (KD) or ketone salts (KS) for 10 weeks to evaluate cardiometabolic improvements.
- Both interventions improved structural echocardiographic parameters, reduced glycemia and lipid profiles, and ameliorated fibrosis and hypertrophy, though diastolic function remained unchanged in vivo.
- Ex vivo, cardiomyocytes showed enhanced calcium handling and relaxation, with KS offering a more practical and effective therapeutic option.

The ketogenic diet promotes triacylglycerol recycling in white adipose tissue and uncoupled fat oxidation in brown adipose tissue, but does not reduce adiposity in rats; Da Eira et al

- Male Wistar rats were fed a ketogenic diet for 8 or 16 weeks to study adipose tissue metabolism.
- KD enhanced triacylglycerol recycling in white fat and uncoupled oxidation in brown fat but did not reduce overall adiposity.
- Insulin sensitivity and lipolytic capacity were preserved despite weight gain.

Sex-specific anti-inflammatory effects of a ketogenic diet in a mouse model of allergic airway inflammation; Ekpruke et al

- Male and female mice with house dust mite-induced allergic airway inflammation were fed a ketogenic diet (KD) for 12 weeks to assess sex-specific immune responses.
- KD reduced eosinophils and altered immune cell populations preferentially in males, with minimal effects in females.
- These findings demonstrate sex-specific anti-inflammatory effects of KD in allergic airway disease.

Ketogenic diet-associated worsening of osteoarthritis histologic secerity, increased pain sensitivity and gut microbiome dysbiosis in mice; Dyson et al

- Mice with surgically-induced knee osteoarthritis were fed a ketogenic diet (KD) to evaluate effects on OA severity, pain sensitivity, and gut microbiome.
- KD worsened OA histologic severity, increased mechanical allodynia, and caused gut microbiome dysbiosis with specific bacterial clades correlating with both histological damage and pain sensitivity.

A long-term ketogenic diet causes hyperlipidemia, liver dysfunction, and glucose intolerance from impaired insulin secretion in mice; Gallop et al

- This study evaluated the long-term metabolic effects of ketogenic diets (KD) in male and female mice. KD initially prevented weight gain and promoted weight loss but over time caused hyperlipidemia, hepatic steatosis, severe glucose intolerance, and impaired insulin secretion, despite maintained insulin sensitivity compared with high-fat diet controls.
- Mechanistically, islet transcriptomics show ER/Golgi stress and disrupted trafficking, with electron microscopy revealing a dilated Golgi and defective insulin granule secretion.
- Of note, a lard-based KD formulation was used in this study, causing some researchers to question the relevancy of the results.

Minimum dietary fat threshold for effective ketogenesis and obesity control in mice; Shou et al

- Multiple KD formulations (80–95% fat) were tested in wild-type and diet-induced obese mice to assess ketogenesis thresholds.
- Diets exceeding 85% fat induced robust ketosis and weight loss, while moderate KDs (80–85%) failed to trigger ketosis and resembled high-fat diets.
- Intestinal ketone production emerged as a key contributor to systemic ketosis, especially in obesity.

Ketogenic diet ameliorates MASLD via balancing mitochondrial dynamics and improving mitochondrial dysfunction; You et al

- A 2-week ketogenic diet (KD) was administered to high-fat diet-induced MASLD mice, and mitochondrial dynamics were studied in vitro using HepG2 cells.
- KD partially improved hepatic lipid deposition and mitochondrial dysfunction by reducing fission proteins (Fis1, Drp1) and enhancing fatty acid oxidation.
- β-hydroxybutyrate (β-OHB) attenuated palmitate-induced mitochondrial fission and lipid accumulation in cells, an effect reversed by mitochondrial fusion inhibition.

A pseudo-ketogenic sugar-ghee-enriched diet induces metabolic and immune alterations in rats: a model of flawed ketogenic diet practice; Ismail et al

- A sugar-ghee-enriched diet (SGED), mimicking a flawed ketogenic diet, was fed to Wistar rats to study metabolic and immune effects.
- The diet, low in ketogenic ratio, induced hyperlipidemia, insulin resistance, and altered immune parameters despite promoting weight loss.
- This highlights potential risks of improperly applied ketogenic diets in real-world settings.

Vegetal oil-based ketogenic diet improves inflammation and fibrosis in experimental metabolic dysfunction-associated steatohepatitis; Provera et al

- A vegetal oil-based ketogenic diet (KD) was administered to mice with Western Diet-induced MASH for eight weeks.
- KD increased ketone production, reduced liver weight, and improved glucose/lipid metabolism, steatosis, injury, and fibrosis.
- These benefits were linked to reduced hepatic pro-inflammatory and pro-fibrotic markers and improved gut dysbiosis.

Ketogenic diet-induced bile acids protect against obesity through reduced calorie absorption; Li et al

- This study investigated gut microbiota and bile acid changes in mice and humans (416 observational, 25 interventional) on a ketogenic diet (KD), focusing on *Lactobacillus murinus* and bile salt hydrolase (BSH) activity.
- KD reduced *L. murinus* abundance, increasing bile acids TDCA/TUDCA, which inhibited intestinal carbonic anhydrase 1 to limit energy absorption, driving weight loss and lower fasting glucose. These bile acids also protected against obesity in mice.
- The findings reveal a gut microbiome-mediated mechanism for KD's effects and identify TDCA/TUDCA as potential therapeutic agents for metabolic disorders.

The effect of a ketogenic diet versus mediterranean diet on clinical and biochemical markers of inflammation in patients with obesity and psoriatic arthritis: A randomized crossover trial; Lambadiari et al

- A crossover trial involving 26 patients with psoriasis (PSO) and psoriatic arthritis (PSA) compared the effects of an 8-week Mediterranean diet (MD) and ketogenic diet (KD), separated by a 6-week washout period.
- Both diets significantly improved metabolic markers (weight, BMI, fat mass), but only the KD reduced disease severity (PASI, DAPSA) and inflammatory cytokines (IL-6, IL-17, IL-23).
- The anti-inflammatory and disease-modifying benefits observed over the 22-week program were primarily linked to the ketogenic diet, suggesting its unique therapeutic potential for PSO/PSA.

Ketogenic diet but not free-sugar restriction alters glucose tolerance, lipid metabolism, peripheral tissue phenotype, and gut microbiome: RCT; Hengist, et al

- Healthy adults were randomized to either a free-sugar-restricted diet or a ketogenic (carbohydrate-restricted) diet for 12 weeks to assess effects on metabolism, energy expenditure, and gut microbiome compared to a control group.
- Both diets reduced fat mass without altering energy expenditure, but the ketogenic diet initially impaired glucose tolerance, raised markers like C-reactive protein and apolipoprotein B, and altered gut microbiome diversity—effects that normalized by week 12, suggesting metabolic adaptation. In contrast, sugar restriction lowered LDL cholesterol without significant metabolic or microbiome changes.
- While both diets reduced energy intake, they diverged in metabolic impacts, highlighting trade-offs between carbohydrate restriction approaches.

Effects of ketogenic diet on weight loss parameters among obese or overweight patients with polycystic ovary syndrome: a systematic review and meta-analysis of randomized controlled trials; Xing et al

- This meta-analysis of 11 randomized controlled trials evaluated the KD's impact on weight, BMI, waist circumference, and fat mass in obese/overweight women with polycystic ovary syndrome (PCOS).
- The KD significantly reduced weight, BMI, waist circumference, and fat mass compared to control diets, with marked improvements across all metrics.
- The findings underscore KD's potential for managing PCOS-related obesity and the critical role of healthcare providers in addressing nutritional strategies for these patients.

The effects of the ketogenic diet for the management of type 2 diabetes mellitus: A systematic review and meta-analysis of recent studies; Choy et al

- A systematic review and meta-analysis was conducted on randomized controlled trials comparing the ketogenic diet to a control diet for managing type 2 diabetes.
- The analysis found no significant difference in improvements for glycemic control or body weight. However, the ketogenic diet did lead to greater increases in HDL cholesterol and greater reductions in triglycerides.

Effects of a ketogenic diet on body composition in healthy, young, normal-weight women: A Randomized controlled feeding trial; Burén et al

- This randomized crossover trial compared a 4-week ketogenic low-carbohydrate high-fat (LCHF) diet to a standard control diet in 17 healthy, young, normal-weight women, using DXA scans and blinded analysis.
- The ketogenic diet significantly reduced both lean mass (–1.45 kg) and fat mass (–0.66 kg) compared to the control, despite matched energy intake and activity levels.
- The findings suggest ketogenic diets are effective for weight loss in this population, but may disproportionately decrease lean body mass, highlighting the importance of combining such diets with strength training to preserve muscle.

Effect of weight-maintaining ketogenic diet on glycemic control and insulin sensitivity in obese T2D subjects; Merovci et al

- This study assigned 29 overweight/obese individuals to one of three 10-day weight-maintaining diets (standard, ketogenic, or ketogenic plus β-hydroxybutyrate supplementation) to assess metabolic effects independent of weight loss.
- While the ketogenic diets doubled plasma ketones and shifted substrate metabolism toward fat oxidation, they did not improve glucose tolerance, insulin sensitivity, blood lipids, or blood pressure compared to the standard diet.
- The findings indicate that the metabolic benefits of ketogenic diets on glucose and insulin regulation depend on weight loss rather than ketosis itself.

Does the ketogenic diet mediate inflammation markers in obese and overweight adults? A systematic review and meta-analysis of randomized clinical trials; Rondanelli et al

- This meta-analysis and systematic review evaluated the effects of a ketogenic diet on inflammatory biomarkers (e.g., CRP, IL-6) across seven randomized controlled trials involving 218 overweight or obese individuals over 8 weeks to 2 years.
- The ketogenic diet significantly reduced CRP levels (–0.62 mg/dL) but showed only a marginal, non-significant decrease in IL-6 (–1.31 pg/mL), with mixed results for other biomarkers.
- The findings suggest that a ketogenic diet may help modulate inflammation in obese/overweight populations, particularly through CRP reduction, though further research is needed on broader inflammatory pathways.

Intermittent fasting, calorie restriction, and a ketogenic diet improve mitochondrial function by reducing lipopolysaccharide signaling in monocytes during obesity: A randomized clinical trial; Guevara-Cruz et al

- This randomized clinical trial compared the effects of calorie restriction (CR), intermittent fasting (IF), ketogenic diet (KD), and a habitual diet (AL) over two months (with rifaximin) on mitochondrial function in monocytes and gut microbiota in 44 individuals with obesity.
- CR, IF, and KD improved monocyte mitochondrial respiration, reduced reliance on glycolysis (IF/KD), and lowered lipopolysaccharide (LPS)-producing gut bacteria and serum LPS levels, linked to enhanced metabolic and inflammatory profiles.
- The findings suggest dietary interventions enhance monocyte bioenergetics and gut microbiota diversity, positioning monocyte mitochondrial health as a potential biomarker for metabolic status in obesity.

The effect of ketogenic diet on adipokines levels: a systematic review and meta-analysis of randomized-controlled trials; Xiao et al

- This meta-analysis of 22 controlled trials evaluated the effects of a ketogenic diet (KD) on adipokine levels, including leptin, adiponectin, and ghrelin.
- The KD significantly reduced leptin levels compared to control diets, particularly in individuals with obesity (BMI >30 kg/m^2) and in interventions lasting ≤8 weeks, but showed no notable impact on adiponectin or ghrelin.
- These findings suggest KD may serve as a supplementary therapy to modulate leptin, which is implicated in metabolic disorders, though further research is needed to clarify its broader adipokine-related effects.

Ketogenic diet time-dependently prevents NAFLD through upregulating the expression of antioxidant protein metallothionein-2; You et al

- This study examined the effects of varying durations (1–6 weeks) of a ketogenic diet (KD) on NAFLD in mice, combining proteomics, MT2 knockdown via AAV/siRNA, and assessments of lipid metabolism, oxidative stress, and PPARα signaling.
- KD for 2 weeks optimally improved NAFLD by reducing liver fat and oxidative stress, mediated by β-hydroxybutyrate (β-OHB)-induced upregulation of nuclear MT2, which enhanced PPARα activity.
- MT2 knockdown abolished KD's benefits, identifying MT2 as a critical effector linking ketosis to metabolic improvements in NAFLD.

The effect of acute and 14-day exogenous ketone supplementation on glycaemic control in adults with type 2 diabetes: two randomized controlled trials; Falkenhain et al

- In this study, researchers conducted two randomized controlled trials testing acute and 14-day thrice-daily premeal ketone monoester supplementation in adults with type 2 diabetes.
- Neither acute ingestion nor repeated supplementation lowered blood glucose or improved overall glycemic control.
- Although acute ketone intake temporarily raised insulin and reduced fatty acids, these changes did not translate into sustained glucose-lowering benefits.

A β-hydroxybutyrate shunt pathway generates anti-obesity ketone metabolites; Moya-Garzon et al

- This study discovered a novel metabolic pathway where β-hydroxybutyrate (BHB) conjugates with amino acids via the enzyme CNDP2, producing BHB-amino acids that regulate energy balance.
- BHB-Phe, the most abundant metabolite, reduces food intake by activating hypothalamic and brainstem neurons, while mice lacking CNDP2 show increased appetite and weight gain under ketogenic conditions.
- The pathway is conserved in humans, linking ketone metabolism to bioactive compounds that influence energy homeostasis.

A ketogenic diet alleviates the apoptosis of granulosa cells by inhibiting the activation of cGAS-STING signaling pathway in PCOS mice; Zhao et al

- This study examined the effects of a KD in a letrozole-induced PCOS mouse model and testosterone-treated KGN cells, focusing on ovarian function and molecular pathways.
- The KD reduced body weight, improved ovarian function in some mice, and mitigated mitochondrial damage and inflammation by suppressing the cGAS-STING-NF-κB pathway, which was activated by hyperandrogenism.
- The findings suggest ketone bodies like BHB protect ovarian cells by inhibiting this pathway, highlighting KD's potential to alleviate PCOS-related ovarian dysfunction through metabolic and anti-inflammatory mechanisms.

GDF15 is a major determinant of ketogenic diet-induced weight loss; Lu et al

- This study investigated the KD's mechanism for obesity management using humans, pigs, and mice, including genetic models lacking GDF15 or its receptor GFRAL.
- KD elevated hepatic GDF15 production via PPARγ activation, which directly binds the Gdf15 promoter, and GDF15-GFRAL signaling was essential for weight loss, as its absence abolished KD's effects.
- Restoring GDF15 in PPARγ-deficient mice rescued obesity management, revealing a liver-PPARγ-GDF15 axis critical to KD's efficacy.

The effects of ketogenic diet on metabolic and hormonal parameters in patients with polycystic ovary syndrome: a systematic review and meta-analysis of clinical trials; Eshaghhosseiny et al

- This meta-analysis of 10 clinical trials evaluated the effects of a KD on 408 women with PCOS, focusing on hormonal, glycemic, and lipid parameters.
- KD significantly reduced triglycerides (–44.03 mg/dL), total cholesterol (–18.95 mg/dL), LDL (–18.11 mg/dL), fasting glucose (–10.30 mg/dL), HOMA-IR (–1.93), luteinizing hormone (–3.75 mIU/mL), and testosterone (–7.71 ng/dL), while increasing follicle-stimulating hormone (0.43 mIU/mL).
- These results highlight KD's potential to improve metabolic and hormonal imbalances in women with PCOS.

Ketogenic diet improves fertility in patients with polycystic ovary syndrome: a brief report; Tsushima et al

- This retrospective study analyzed 30 women with PCOS who followed a ketogenic diet (KD) for ≥3 months to assess menstrual cycle regularity and fertility outcomes.
- All participants (100%) restored regular menstrual cycles, and 55.6% of those seeking pregnancy (n=18) achieved conception, with significantly higher pregnancy rates among women not using metformin (100% vs. 38.5%).
- The results suggest KD may enhance fertility in PCOS beyond weight loss, though further research is needed to confirm these findings.

A 3-week ketogenic diet increases skeletal muscle insulin sensitivity in individuals with obesity: A randomized controlled crossover trial; Luong et al

- This randomized crossover trial examined the effects of a 3-week KD versus a standard diet on organ-specific insulin sensitivity in 11 individuals with obesity.
- The KD increased skeletal muscle insulin sensitivity (measured via hyperinsulinemic-euglycemic clamp) and induced weight loss but reduced adipose tissue insulin sensitivity (impaired lipolysis suppression) without affecting hepatic insulin sensitivity.
- These findings suggest KD enhances glycemic control through muscle-specific mechanisms while altering lipid metabolism regulation.

Effects of ketone supplements on blood β-hydroxybutyrate, glucose and insulin: A systematic review and three-level meta-analysis; Yu et al

- This study conducted a three-level meta-analysis of randomized crossover/parallel trials to assess acute effects of exogenous ketone supplementation on blood BHB, glucose, and insulin, using 327 data points from 30 studies (408 participants).
- It found that ketone supplements robustly raise blood BHB, lower glucose, and increase insulin in non-athlete healthy populations (with no insulin increase in obesity/prediabetes), and identified dose-response and time-dependent relationships for these parameters.
- Overall, dose and time modulate metabolic responses to ketone supplementation, with clinically relevant glucose-lowering effects that do not necessarily raise insulin in certain populations.

The effects of ketogenic diet on brain gene expressions in type 2 diabetes background; Ren et al

- This study examined the effects of a KD on gene expression in the brains of T2DM model (db/db) mice over six months, comparing KD-fed mice to those on a normal diet.
- KD reduced fasting glucose and body weight while altering 189 brain genes linked to inflammatory pathways (e.g., NF-κB, cytokine interactions) and biosynthesis processes (lipid/amino acid metabolism, proteasomal activity).
- These findings suggest KD may mitigate neuroinflammation and enhance metabolic pathways in T2DM, supporting its potential as a strategy to prevent neurodegenerative diseases in diabetic patients.

Ketogenic diet alleviates β-cell dedifferentiation but aggravates hepatic lipid accumulation in db/db mice; Zhang et al

- This study investigated the effects of a ketogenic diet (KD) on β-cell function and liver health in diabetic *db/db* mice compared to normal diet (ND) and calorie-restricted (CR) groups over 4 weeks.
- The KD improved glucose tolerance, reduced fasting blood glucose and insulin levels, and reversed β-cell dedifferentiation by restoring β-cell numbers and transcription factors, but increased hepatic lipid accumulation and inflammation (e.g., elevated *Cd36* and inflammatory genes).
- While KD demonstrated metabolic benefits for β-cell function, it exacerbated liver steatosis and inflammatory responses diabetic mice.

Ketogenic diet ameliorates high-fat diet-induced insulin resistance in mouse skeletal muscle by alleviating endoplasmic reticulum stress; Ma et al

- High-fat-diet (HFD)-induced insulin-resistant mice and palmitic acid-exposed C2C12 muscle cells were treated with a ketogenic diet (KD) or β-hydroxybutyrate (β-OHB).
- The KD reversed HFD-induced ER stress, reactivated the AKT/GSK3β pathway, and restored Glut4 membrane translocation in muscle; β-OHB similarly alleviated ER stress and improved glucose uptake in cells, indicating that KD improves insulin sensitivity by suppressing ER stress and enhancing insulin signaling.

Ketogenic diet and endocrine and metabolic diseases: A bibliometric study and visualization analysis; Zhang et al

- This study performed a bibliometric analysis of 508 ketogenic diet–related papers from 2003–2023 using Web of Science data, VOSviewer, bibliometrix in R, and CiteSpace to map trends and collaborations.
- It found rapid growth in publications, with the United States as the leading contributor and Nutrients as a key journal, while obesity, ketogenic diet, and weight loss were the most frequent keywords, highlighting current and emerging research directions in endocrine/metabolic contexts.

Ketogenic diet preserves muscle mass and strength in a mouse model of type 2 diabetes; Park et al

- This study tested whether a ketogenic diet (KD) preserves muscle mass and strength in a mouse model of type 2 diabetes, using lean controls, diabetes controls, and KD-fed groups after inducing diabetes with high-fat feeding plus STZ/NAM, followed by 6 weeks of KD and assessments of glucose tolerance and grip strength.
- KD improved muscle mass, grip strength, and muscle fiber area in diabetic mice and modulated muscle gene expression related to NLRP3 inflammasome and ER stress.
- The authors conclude that KD enhances muscle mass and function in this T2DM model, potentially through reductions in inflammasome activation and ER stress pathways in skeletal muscle.

Role of liver FGF21-KLB signaling in ketogenic diet-induced amelioration of hepatic steatosis; Guo et al

- This study examined whether a ketogenic diet (KD) improves hepatic steatosis in mice and whether FGF21-KLB signaling in the liver is required for these benefits, using chow, high-fat, and KD groups with liver-specific KLB knockdown.
- KD reduced liver fat by boosting fatty acid oxidation and reducing lipogenesis, with strong activation of the FGF21 pathway (KLB and FGFR1); knocking down hepatic KLB attenuated KD's improvements in fatty liver, insulin resistance, and lipid metabolism.
- The authors conclude that liver FGF21-KLB signaling is critical for KD-induced alleviation of hepatic steatosis, highlighting a key mechanistic link between KD and liver metabolism.

Gender differences in liver steatosis and fibrosis in overweight and obese patients with metabolic dysfunction-associated steatotic liver disease before and after 8 weeks of very low-calorie ketogenic diet; Rinaldi et al

- The study examined the impact of an eight-week very low-calorie ketogenic diet (VLCKD) in 112 overweight/obese patients, focusing on gender differences in liver steatosis (CAP) and fibrosis (FibroScan) before, during, and after treatment.
- At baseline, men had higher liver steatosis, liver stiffness, and worse metabolic/liver markers than women; after VLCKD, both genders showed broad improvements, but only men showed significant reductions in liver stiffness, AST, creatinine, and CRP.
- Overall, men retained higher levels of steatosis and fibrosis than women despite VLCKD, suggesting gender-specific factors (e.g., hormonal/metabolic differences) may necessitate tailored therapeutic approaches.

Adherence to ketogenic diet in lifestyle interventions in adults with overweight or obesity and type 2 diabetes: a scoping review; Li et al

- A scoping review was conducted to map out the methods used to assess adherence to the ketogenic diet and physical activity in lifestyle interventions for adults with overweight/obesity and type 2 diabetes.
- The review found that participants typically consumed more carbohydrates and less fat than the ketogenic regimen required, indicating poor adherence. It also identified a lack of standardized tools for measuring diet adherence and physical activity, creating inconsistencies across studies.

Efficacy and safety of long-term ketogenic diet therapy in a patient with type 1 diabetes; Koutnik et al

- This case report describes a 10-year experience with a long-term ketogenic diet (≤50 g carbs/day) in a person with type 1 diabetes, showing excellent glycemic control with HbA1c 5.5%, median CGM glucose 98 mg/dL, and 90% time-in-range 70–180 mg/dL, plus a 43% reduction in daily insulin requirements.
- Lipid changes included an increase in LDL cholesterol, but small-dense LDL remained below 90 nmol/L, and there were no adverse effects on thyroid, kidney, or bone mineral density.
- The authors conclude that prolonged KD can yield meaningful metabolic benefits in type 1 diabetes without detectable short- to mid-term safety concerns, highlighting the need for broader studies to assess long-term feasibility and risk.

Oreo cookie treatment lowers LDL cholesterol more than high-intensity statin therapy in a lean mass hyper-responder on a ketogenic diet: A curious crossover experiment; Norwitz et al

- A single-subject crossover trial compared the effects of short-term carbohydrate supplementation (100g/day via Oreo cookies) versus high-intensity statin therapy (rosuvastatin) on LDL cholesterol (LDL-C) in a "Lean Mass Hyper-Responder" (LMHR) adhering to a ketogenic diet.
- Oreo supplementation reduced LDL-C by 71% (from 384 to 111 mg/dL), significantly outpacing the 32.5% reduction from statins (284 mg/dL), consistent with the lipid energy model linking elevated LDL-C to energy demands during carbohydrate restriction.
- This striking response underscores the model's plausibility but emphasizes the need for broader research, as findings are preliminary and not prescriptive.

Impact of the ketogenic diet as a dietary approach on cardiovascular disease risk factors: a meta-analysis of randomized clinical trials; Wang et al

- This meta-analysis of 27 randomized controlled trials (1278 participants) compared the effects of ketogenic and control diets on cardiovascular disease (CVD) risk factors.
- Overall, the ketogenic diet increased total cholesterol, LDL cholesterol, and HDL cholesterol levels and reduced triglycerides, blood glucose, insulin, diastolic blood pressure, weight, and BMI.

Effect of ketogenic diet on blood pressure: A GRADE-Assessed systematic review and meta-analysis of randomized controlled trials; Amini et al

- This meta-analysis of 23 randomized controlled trials (1664 participants) examined the effects of KDs on blood pressure (BP), synthesizing data from four databases up to November 2022.
- The results showed no significant reductions in systolic or diastolic BP with KDs, and subgroup/dose-response analyses found no associations between fat intake proportion and BP changes.
- The current data suggests that KDs do not improve BP, further research is needed to determine optimal fat intake levels for potential cardiovascular benefits.

REVIEW ARTICLES ON METABOLIC DISORDERS

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Effect of ketogenic diet on obesity and other metabolic disorders: Narrative review; Baylie et al

Does a ketogenic diet have a place within diabetes clinical practice? Review of current evidence and controversies; Firman et al

Very low calorie ketogenic diet: What effects on lipid metabolism?; Suarez et al

Ketogenic diet and its potential role in preventing type 2 diabetes mellitus and its complications: A narrative review of randomized controlled trials; Alluwyam et al

Beneficial effects of the ketogenic diet on nonalcoholic fatty liver disease (NAFLD/MAFLD); Dyńka et al

Obesity and obesity-related thyroid dysfunction: any potential role for the very low-calorie ketogenic diet (VLCKD)?; Chapela et al

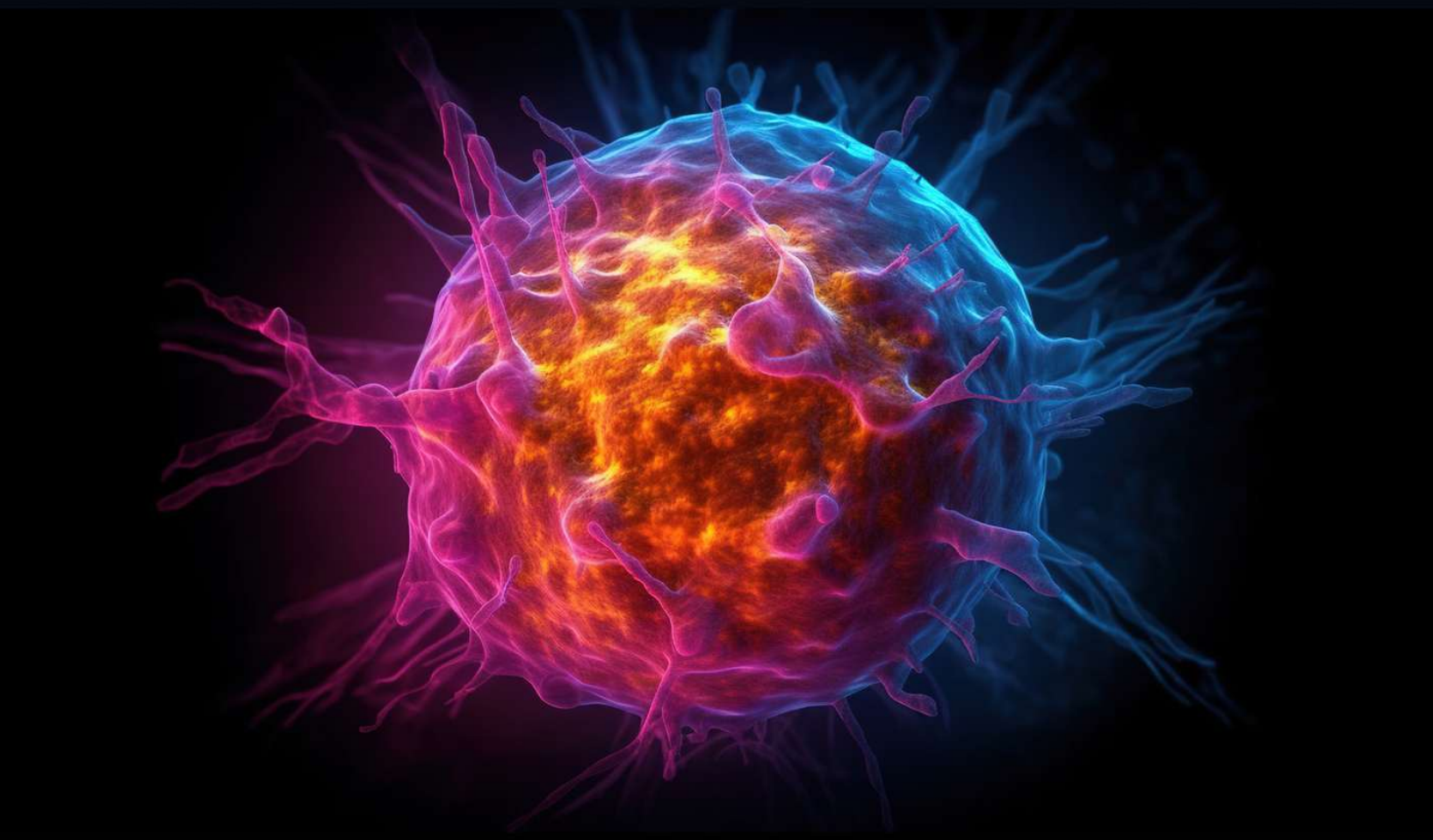
Common and divergent molecular mechanisms of fasting and ketogenic diets; Paoli et al

Misalignment of circadian rhythms in diet-induced obesity; Engin et al

Impact of ketogenic diet on cardiovascular disease; Zaghloul et al

Understanding the relationship between the ketogenic diet and the heart: A novel therapeutic potential for cardiovascular health; Shah et al

Cancer



KMT research continues to advance our understanding of the complex biological effects of therapeutic ketosis in oncology, with accumulating evidence suggesting modulation of cancer metabolism and immune pathways, alongside both potential benefits and context-dependent risks. Mechanistically, ketone-driven protein modifications and epigenetic effects can suppress glycolysis and mTOR signaling, remodel tumor and immune cells, and shift neutrophils toward anti-tumor states—enhancing responses to checkpoint blockade and targeted therapies in several models. Ketone bodies may also restore treatment sensitivity and, when paired with metabolic inhibitors, expose tumor dependencies. Diet composition matters: fish oil–based KDs showed stronger chemopreventive signals than other fats, while some breast cancer models indicated KD safety and potential benefit. Conversely, specific stress pathways (BACH1/ATF4) and systemic effects like p53-dependent senescence highlight potential hazards, particularly with prolonged or poorly tailored protocols. Overall, KD appears to be a powerful, modulable adjuvant in oncology, best applied with precision—considering tumor type, therapy pairing, diet formulation, and timing—to maximize benefit while mitigating risk.

Long-term effects of a ketogenic diet for cancer; Egashira et al

- A long-term follow-up study analyzed 55 advanced cancer patients adhering to a ketogenic diet for varying durations.
- Longer diet adherence (≥12 months) significantly improved overall survival compared to shorter use.
- Median survival was 55.1 months in the long-adherence group versus 12 months in the short-adherence group.

Ketogenic diet reshapes cancer metabolism through lysine β-hydroxybutyrylation; Qin et al

- Researchers analyzed mouse liver proteins under a ketogenic diet (KD) to study lysine β-hydroxybutyrylation (Kbhb) and developed a bioinformatics tool (pFunK) to predict critical modification sites, then tested these findings in hepatocellular carcinoma cells.
- Kbhb modification at aldolase B (ALDOB) Lys108, enhanced by KD or β-hydroxybutyrate, inhibited ALDOB activity, disrupted glycolysis and mTOR signaling, and suppressed cancer cell proliferation—effects replicated by a Kbhb-mimicking mutation.
- This study highlights Kbhb's role in cancer metabolism and introduces pFunK as a broadly applicable method for identifying functionally significant lysine modifications.

Ketogenic diet promotes tumor ferroptosis but induces relative corticosterone deficiency that accelerates cachexia; Ferrer et al

- Experiments used a ketogenic diet (KD) in IL-6-producing murine cancer cachexia models.
- KD delayed tumor growth by inducing ferroptosis but accelerated host cachexia and reduced survival due to corticosterone deficiency.
- Dexamethasone administration restored metabolic balance and extended survival while preserving reduced tumor growth.

Targeting fatty acid oxidation enhances response to HER2-targeted therapy; Nandi et al

- The study shows that in ErbB2-positive breast cancer, loss of Cpt1a impairs LCFA oxidation, delaying tumor onset and growth but forcing a switch to glucose dependence, which increases oxidative stress and activates Nrf2-driven survival.
- Inhibiting Nrf2 or reducing its activity in Cpt1a-deficient cells reduces proliferation and glucose consumption, and combining Cpt1a deficiency with a ketogenic LCFA-rich diet or anti-ErbB2 therapy markedly slows tumor growth, promotes apoptosis, and decreases lung metastasis.
- In an immunocompetent model, Cpt1a inhibition also enhances antitumor immunity, improving the efficacy of anti-ErbB2 monoclonal antibodies, suggesting that targeting fatty acid oxidation alongside HER2-targeted therapy could overcome resistance in HER2-positive breast cancer.

Ketogenic diet alters the epigenetic and immune landscape of prostate cancer to overcome resistance to immune checkpoint blockade therapy; Murphy et al

- This study tested combinations of immune checkpoint inhibitors (anti-PD1/anti-CTLA4) with cyclic ketogenic diet (CKD), ketone body BHB, or HDAC inhibitor vorinostat in ICB-resistant prostate cancer models.
- CKD and BHB supplementation slowed tumor growth by boosting adaptive immunity and modulating immune cells (e.g., enhancing CD8+ T-cell recruitment, rebalancing macrophages), while HDAC inhibition and ketogenesis improved ICB efficacy via upregulated MHC-I in cancer cells and reduced immunosuppressive neutrophils.
- These findings highlight CKD and BHB as dietary strategies to sensitize prostate tumors to immunotherapy through epigenetic and immune remodeling.

An unexpected role for the ketogenic diet in triggering tumor metastasis by modulating BACH1-mediated transcription; Su et al

- This study investigated the effects of a KD on cancer metastasis using mouse models, focusing on the roles of BACH1 and ATF4 in regulating pro-metastatic genes.
- The KD promoted metastasis by elevating ATF4, which bound BACH1 to activate genes like cell migration-inducing hyaluronidase 1, while genetic or pharmacological inhibition of BACH1 abolished these effects.
- These findings reveal a dietary risk for cancer progression and highlight the BACH1/ATF4 axis as a critical driver of KD-induced metastasis.
- Of note, a Crisco-based KD formulation was used in this study, causing some researchers to question the relevancy of the results.

A ketogenic diet sensitizes pancreatic cancer to inhibition of glutamine metabolism; Hajihassani et al

- This study examined the effects of a ketogenic diet combined with glutamine metabolism inhibitors (DON, CB839) on pancreatic cancer using murine models and in vitro systems simulating ketogenic metabolic conditions.
- The ketogenic diet increased TCA cycle and glutamine-associated metabolites, driving tumor reliance on glutamine-mediated anaplerosis, which rendered pancreatic cancer cells vulnerable to glutamine inhibitors.
- Combining the ketogenic diet with glutamine-targeted therapies resulted in robust antitumor effects, suggesting this metabolic approach could enhance clinical outcomes for pancreatic cancer.

Ketogenic diet enhances the anti-cancer effects of PD-L1 blockade in renal cell carcinoma; Richard et al

- This study examined the effects of ketone bodies (KB) *in vitro* and a ketogenic diet (KD) *in vivo* on renal cancer cells (ACHN and Renca) and their interaction with anti-PDL1 immunotherapy in mice.
- KB reduced tumor cell proliferation and enhanced mitochondrial metabolism, while KD slowed tumor growth, upregulated PDL-1 expression, and improved anti-PDL1 treatment efficacy.
- The findings suggest combining KD with immunotherapy could enhance therapeutic outcomes in renal cancer, though further clinical studies are needed to validate these results.

Anti-tumor effects of ketogenic diets and their synergism with other treatments in mice: Bayesian evidence synthesis of 1755 individual mouse survival data; Klement et al

- A systematic review and meta-analysis of 43 mouse studies was performed to evaluate the anti-tumor effects of a ketogenic diet (KD) alone and in combination with chemotherapy (CT), radiotherapy (RT), or targeted therapies (TT).
- The analysis found that KD monotherapy significantly prolonged survival, and combining KD with RT or TT led to a further 20-30% increase in survival time.
- The anti-tumor effects were particularly significant in models of pancreatic cancer, gliomas, head and neck cancer, and stomach cancer.

The ketogenic diet modulates tumor-associated neutrophil polarization via the AMOT-YAP/TAZ axis to inhibit colorectal cancer progression; Mi et al

- This study investigated the effects of a KD and its metabolite BHB on colorectal cancer (CRC) using a mouse model (AOM/DSS-induced) and clinical patient data.
- KD and BHB shifted tumor-associated neutrophils (TANs) from pro-tumor N2 to anti-tumor N1 polarization, suppressing tumor growth/metastasis via BHB's interaction with HDAC3, which inhibits pro-carcinogenic signaling through the AMOT-YAP/TAZ axis.
- Clinical data confirmed that higher BHB levels in CRC patients correlated with reduced lymph node involvement and increased N1-TAN infiltration, suggesting BHB as a prognostic marker and KD as a potential therapeutic strategy for CRC.

A ketogenic diet rich in fish oil is superior to other fats in preventing NNK-induced lung cancer in A/J mice; Elisia et al

- This study compared multiple ketogenic diets enriched with different fats (MCTs, milk fat, palm oil, olive oil, corn oil, fish oil) and control diets in mice to evaluate their ability to reduce nicotine-derived nitrosamine ketone (NNK)-induced lung cancer.
- It found that all KDs reduced lung nodules more than controls, with the fish oil–KD (FO-KD) being the most effective; FO-KD mice also had lower blood glucose, higher β-hydroxybutyrate, lower liver FAS/CPT1a ratio, and a dramatic increase in fecal Akkermansia, without liver damage.
- The authors conclude that FO-KD is superior among tested fats in suppressing NNK-induced lung cancer, potentially by shifting whole-body metabolism away from glucose toward fat utilization.

Ketogenic diet does not promote triple-negative and luminal mammary tumor growth and metastasis in experimental mice; Grube et al

- This study evaluated the effects of a ketogenic diet on growth and metastasis of triple-negative 4T1 mammary tumors and progression of luminal breast tumors in MMTV-PyMT mice.
- KD did not promote metastasis and, in vivo, modestly reduced 4T1 primary tumor growth and proliferation, with ketosis only robustly achieved in female mice at higher ketogenic ratios than typically seen in humans.
- The authors conclude that KD appears safe regarding tumor progression in these models and may be advantageous for certain breast cancer contexts, while highlighting the need to verify ketosis levels and sex-specific responses in future KD studies.

Metabolomics reveals the implication of acetoacetate and ketogenic diet therapy in radioiodine-refractory differentiated thyroid carcinoma; Wang et al

- The study compared metabolomic profiles of radioiodine-refractory (RAIR) differentiated thyroid carcinoma (DTC) to non-RAIR DTC, identifying ketone body metabolism as a key differentiator with acetoacetate (AcAc) markedly reduced in RAIR and linked to lower radioiodine uptake and tumor aggressiveness.
- In cellular and in vivo models, AcAc increased NIS and TSHR expression, enhanced radioiodine uptake, and suppressed proliferation, migration, and invasion while promoting apoptosis; ketogenic diet–induced AcAc elevations produced similar antitumor effects and improved NIS/TSHR signaling.
- The authors conclude that ketone body metabolism, particularly AcAc, may be exploited therapeutically to improve iodine uptake and reduce tumor growth in RAIR-DTC, proposing KD as a potential new treatment strategy.

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The effects of the ketogenic diet on cancer treatment: a narrative review; Deng et al

Systematic review and clinical insights: The role of the ketogenic diet in managing glioblastoma in cancer neuroscience; Valerio et al

Clinical research framework proposal for ketogenic metabolic therapy in glioblastoma; Duraj et al

Diet as an adjunct therapy in reducing chemotherapy toxicities and improving patients quality of life: A systematic review and meta-analysis; Abene et al

Therapeutic potential of β-hydroxybutyrate in the management of pancreatic neoplasms: exploring novel diagnostic and treatment strategies; Vaezi et al

Overcoming immunosuppression in cancer: how ketogenic diets boost immune checkpoint blockade; Stefan et al

Ketogenic diet in clinical populations-a narrative review; Zemer et al

European Association for the Study of Obesity (EASO) position statement on medical nutrition therapy for the management of individuals with overweight or obesity and cancer; Muscogiuri et al

Effect of ketogenic diets on insulin-like growth factor (IGF)-1 in humans: A systematic review and meta-analysis; Rajakumar et al

Effects of nutritional interventions on cognitive function in adult cancer survivors: A systematic review; Lu et al

Effects of ketogenic diets on cancer-related variables: A systematic review and meta-analysis of randomised controlled trials; Salido-Bueno et al

Emerging Applications

Across diverse settings, KMT approaches show broad, context-dependent signals: small case series and preclinical models suggest symptom relief in inflammatory bowel disease, immune modulation attenuates autoimmune and infectious pathology, and metabolic effects spanning fat browning, improved mitochondrial function, and enhanced drug responsiveness (for example, with antifungals and in sepsis care). Observational data link ketogenic eating to better mental well-being and lower all-cause mortality risk, while athletic strength appears largely maintained. Disease-specific findings are mixed: notable renal protection in cystinosis models contrasts with safety concerns in some mitochondrial myopathy genotypes, and benefits in alcohol withdrawal and ocular neuroprotection remain preclinical. Rapid immune and microbiome shifts underscore diet-specific signatures (distinct from vegan patterns), mediated in part by ketone-driven pathways like AMPK–SIRT1–PGC-1α and Treg/Th17 rebalancing. Overall, the growing body of research points to a rapidly diversifying field of potential applications, with strategies that appear promising but require individualized monitoring, attention to genotype and clinical context, and validation in larger, controlled human trials.

EMERGING APPLICATIONS

Effects of ketogenic diet on health outcomes: an umbrella review of meta-analyses of randomized clinical trials; Patikorn et al

- An umbrella review of meta-analyses assessed the effects of ketogenic diets on health outcomes using GRADE criteria.
- High-quality evidence supported reduced triglycerides and seizure frequency but increased LDL cholesterol, while moderate-quality evidence indicated benefits for weight, respiratory exchange ratio, and HbA1c.
- Many associations were of low or very low quality, warranting longer-term trials to evaluate clinical outcomes like cardiovascular events.

Ketogenic diet and multiple health outcomes: An umbrella review of meta-analysis; Chen et al

- This umbrella review synthesized meta-analyses on ketogenic diets and health outcomes, finding increases in LDL-C, total cholesterol, HDL-C, and respiratory exchange rate, and decreases in testosterone.
- Combining ketogenic diets with exercise reduced weight but increased LDL-C and cortisol.
- Evidence strength was generally weak, highlighting the need for rigorous, longer-duration studies.

A ketogenic diet substantially reshapes the human metabolome; Effinger et al

- A prospective intervention studied 40 healthy volunteers on a three-week ketogenic diet.
- KD reduced insulin and triglycerides while increasing anti-inflammatory fatty acids and shifting metabolism toward fatty acid oxidation.
- No metabolic risks were identified, supporting KD as a safe immunometabolic intervention.

The effect of a ketogenic diet on weight loss in CKD: a randomized controlled trial in obese stage G1–3a CKD patients; Zoccali et al

- A multicenter randomized controlled trial evaluated a ketogenic diet in obese stage G1–3a chronic kidney disease (CKD) patients.
- The diet group experienced significant weight loss and improved metabolic markers compared to controls.
- Kidney function remained stable, suggesting KD may be a viable weight-loss strategy in early-stage CKD.

From glucose to histone modification: sex-specific metabolic responses to ketogenic therapy in VM/Dk mice; Moss et al

- Sex-specific metabolic responses to ketogenic therapies were assessed in VM/Dk mice, focusing on glucose/ketone metabolism and histone modifications.
- Significant differences were observed between males and females in body weight, circulating metabolites, insulin levels, and histone modification profiles.
- These findings underscore the importance of considering sex in metabolic and preclinical ketogenic therapy studies.

Sex differences in ketogenic diet response reveal gonadal hormone interaction with FGF21 in mice; Zhang et al

- Male and female C57BL/6J mice were fed a ketogenic diet (KD) to examine sex-specific metabolic and hormonal responses.
- Males lost weight with increased energy expenditure and insulin sensitivity, while females gained fat mass and developed glucose intolerance, with gonadal hormones and FGF21 signaling mediating these divergent effects.

Eating a ketogenic diet enhances sensitivity of rats to the effects of methamphetamine, but not dopamine D2/D3 receptor agonist quinpirole; Elsey et al

- Rats fed standard, high-fat, or ketogenic diets were tested for sensitivity to dopaminergic drugs quinpirole and methamphetamine.
- Unlike the high-fat diet, the ketogenic diet did not enhance sensitivity to quinpirole but increased sensitivity to methamphetamine-induced locomotion, indicating distinct behavioral effects between diet types.

Combined effects of ketogenic diet and aerobic exercise on skeletal muscle fiber remodeling and metabolic adaptation in simulated microgravity mice; Chen et al

- Hindlimb-unloaded mice simulating microgravity were treated with ketogenic diet (KD) and aerobic exercise to study skeletal muscle adaptation.
- Combined intervention attenuated muscle atrophy, increased oxidative fiber proportion (MyHC-I), upregulated lipid metabolism genes (CPT-1b, HADH, PGC-1α), and improved exercise endurance, highlighting synergistic benefits for disuse conditions.

Effects of soy protein on liver and adipose tissue inflammation and gut microbiota in mice fed with ketogenic diets; Li et al

- Mice were fed ketogenic diets (KD or soy protein-substituted KS) for 18 weeks to assess tissue inflammation and gut microbiota.
- Both KD and KS reduced mesenteric fat, adipose inflammation, and NLRP3 expression but induced hyperlipidemia and hepatic inflammation.
- Soy protein altered gut microbiota composition but did not significantly differ from casein in modulating tissue inflammation.

Case report: Carnivore-ketogenic diet for the treatment of inflammatory bowel disease: A case series of 10 patients; Norwitz et al

- This study analyzed 10 cases of inflammatory bowel disease (IBD) patients—6 with ulcerative colitis and 4 with Crohn's disease—who adopted ketogenic or carnivore diets, primarily meat-based, to manage symptoms without medication.
- All participants reported significant clinical improvements in IBD symptoms (measured by IBDQ scores of 72–165), enhanced quality of life, and dietary sustainability.
- The findings align with research suggesting reduced intestinal inflammation via elevated ketones and microbiota-modulating effects of low-residue, high-fat diets, supporting their therapeutic potential for IBD.

Divergent sex-specific effects on a ketogenic diet: Male, but not female, mice exhibit oxidative stress and cellular senescence; Wei et al

- A ketogenic diet (KD) was administered to male and female mice to evaluate sex-specific effects on oxidative stress and cellular senescence.
- KD induced oxidative stress, mitochondrial protein acetylation, and cellular senescence only in male mice, effects that were prevented by estrogen or antioxidant treatments.
- These findings highlight significant sex differences in KD response, with implications for personalized dietary interventions.

Effects of the ketogenic diet on strength performance in trained men and women: A systematic review and meta-analysis; Vargas-Molina et al

- This meta-analysis assessed the effects of a ketogenic diet (KD) combined with resistance training on 1-repetition maximum (1-RM) strength in trained individuals, evaluating 106 participants for squats and 119 for bench press.
- While no significant differences in 1-RM performance emerged between KD and control groups, the KD group showed a marginally higher effect size.
- The results indicate that KD does not hinder 1-RM strength but suggest 1-RM testing may not optimally measure hypertrophy-driven strength improvements in resistance-trained populations.

Ketogenic diet has a positive association with mental and emotional well-being in the general population; Garner et al

- This cross-sectional study analyzed two online cohorts (n=147 and n=276) to assess associations between a ketogenic diet and mental health outcomes (e.g., stress, depression, anxiety, loneliness) in a general healthy population.
- Results indicated that individuals following a ketogenic diet reported significantly higher levels of calmness, contentedness, and alertness, alongside lower perceived stress, depression, anxiety, and loneliness compared to those on non-specific diets.
- These findings suggest that a ketogenic diet may confer psychological benefits beyond weight loss, enhancing mental well-being in non-clinical populations.

Ketogenic diet improves alcohol withdrawal; Ferreira et al

- This study examined the effects of a ketogenic diet versus ketone supplementation on alcohol withdrawal symptoms in female C57BL/6J mice exposed to alcohol vapor, assessing metabolic, behavioral, and neurochemical changes.
- The ketogenic diet reduced blood glucose, cholesterol, and depressive-like behaviors (e.g., improved tail-suspension test performance, higher saccharin preference) while lowering anxiety-related vocalizations, outperforming ketone esters in mitigating withdrawal symptoms.
- Additionally, the diet partially restored serotonin levels altered by alcohol exposure, suggesting its potential as a non-addictive therapeutic strategy for alcohol withdrawal.

Ketogenic diet and progression of kidney disease in animal models of nephropathic cystinosis; Bellomo et al

- This study tested the effects of a ketogenic diet on kidney disease progression in two animal models (Ctns−/− mice and rats) of nephropathic cystinosis, a lysosomal storage disorder causing renal Fanconi syndrome and chronic kidney disease (CKD).
- The ketogenic diet nearly prevented Fanconi syndrome (reducing proteinuria, glycosuria, and polyuria), mitigated kidney damage (reduced fibrosis, apoptosis, inflammation), and improved autophagic function, even when initiated after kidney impairment had developed.
- These findings suggest the ketogenic diet could serve as a partial therapeutic alternative to cysteamine in regions where cost limits access to standard treatment, offering significant renal protection in cystinosis.

An open-label, randomized controlled trial to assess a ketogenic diet in critically ill patients with sepsis; Rahmel et al

- This single-center randomized controlled trial compared a ketogenic diet (KD) to a standard high-carbohydrate diet in 40 critically ill sepsis patients, evaluating ketosis induction, safety, and clinical/immunological outcomes.
- The KD group achieved stable ketosis (β-hydroxybutyrate levels 1.4 mmol/L higher than controls) with no major adverse effects, required no insulin after day 4, and showed more days free of ventilation, vasopressors, dialysis, and ICU care, alongside reduced T-cell activation and pro-inflammatory cytokine levels.
- These results demonstrate the safety and potential clinical benefits of KD in sepsis, justifying larger trials to explore its impact on organ dysfunction and immune modulation.

Ketogenic diet in adult patients with mitochondrial myopathy; Zweers et al

- This study assessed a twelve-week Modified Atkins Diet (MAD) in 20 patients with mitochondrial myopathy (MM), evaluating feasibility, safety, and efficacy through ketone levels, adverse events, and physical performance tests.
- While 40% of participants discontinued due to adverse events (e.g., rhabdomyolysis, fatigue), completers showed improvements in aerobic capacity, muscle strength, fatigue, and metabolic parameters, though patients with mtDNA deletions experienced severe muscle-related side effects.
- The diet proved most feasible for those with the m.3243A>G mutation, highlighting the need for personalized monitoring and caution in MM patients with mtDNA deletions.

EPOtential target for endurance performance: The effect of exogenous ketone supplementation on circulating erythropoietin levels; Robertson et al

- Recreationally active adults underwent 3 weeks of intensified, twice-daily exercise with either a ketone monoester supplement or a calorie-matched control, to examine effects on skeletal muscle angiogenesis, signaling, and circulating erythropoietin (EPO).
- Ketone monoester ingestion appeared to raise serum EPO by about 26% around 12 hours after the final training session, whereas the control did not show this increase, suggesting a potential link between exogenous ketones and elevated EPO.
- Importantly, exercise volume and study conditions can also influence EPO levels, and therefore further work is needed to clarify mechanisms, dose/type effects, and to determine whether chronic KB supplementation could raise red blood cell mass.

Ketogenic diet modulates immune cell transcriptional landscape and ameliorates experimental autoimmune uveitis in mice; Duan et al

- This study used single-cell RNA sequencing and flow cytometry to examine the effects of a ketogenic diet (KD) on immune cells in lymph nodes and retinas of healthy mice and those with experimental autoimmune uveitis (EAU).
- KD promoted regulatory T cell (Treg) differentiation in healthy mice and alleviated uveitis symptoms by reducing pathogenic CD4+ T cells, correcting the Th17/Treg imbalance, and decreasing retinal Th17 cells while increasing Tregs.
- These results suggest KD may modulate immune responses from lymph nodes to the retina, positioning it as a potential therapeutic strategy for uveitis.

A ketogenic diet enhances fluconazole efficacy in murine models of systemic fungal infection; Palmucci et al

- This study tested a ketogenic diet combined with fluconazole in mouse models of *Cryptococcus neoformans* and Candida albicans infections, comparing fungal burden and drug efficacy between ketogenic and conventional diets.
- The ketogenic diet significantly enhanced fluconazole's effectiveness, reducing fungal load in the brain, lungs, and kidneys by 1.7–2.7 log units and improving drug pharmacodynamics by enabling lower doses to achieve therapeutic effects.
- These findings highlight the ketogenic diet's potential to amplify antifungal treatment efficacy, offering a novel dietary strategy to combat invasive fungal infections.

Differential peripheral immune signatures elicited by vegan versus ketogenic diets in humans; Link et al

- This study analyzed the effects of a 2-week vegan or ketogenic diet in 20 participants, using multiomics data to assess impacts on immunity and the microbiome.
- The KD upregulated adaptive immune pathways and reduced microbial activity, while the vegan diet enhanced innate immunity and antiviral responses, with both diets altering amino acid metabolism and microbiome composition.
- These findings highlight that brief dietary interventions can distinctively reshape immune and microbial profiles, suggesting potential for tailored nutritional strategies in precision health.

Ketogenic diets: A systematic review of current scientific evidence and possible applicability in dogs and cats; Vendramini et al

- A systematic review was performed to evaluate the existing scientific literature on the application of ketogenic diets in dogs and cats.
- The review found evidence that diets with medium-chain triglycerides can increase ketone bodies and improve signs of epilepsy in dogs.
- These diets were noted to have a different macronutrient composition, being higher in carbohydrates and lower in fat, compared to the classic ketogenic diet.

Ketogenic diet with aerobic exercise can induce fat browning: potential roles of β-hydroxybutyrate; Kim et al

- This study investigated the effects of BHB on white adipose tissue (WAT) browning using *in vitro* (3T3-L1 adipocytes) and *in vivo* (rat) models, comparing KD, exercise (EX), and their combination (KE).
- BHB reduced lipid accumulation, activated the AMPK-SIRT1-PGC-1α pathway, and upregulated thermogenic genes (UCP1, PRDM16) and adipokines (FGF21, FNDC5) in adipocytes, while KE in rats synergistically enhanced WAT browning, mitochondrial biogenesis, and metabolic health.
- These findings suggest BHB induction via dietary or exercise interventions promotes fat browning and metabolic benefits through mitochondrial activation and thermogenic pathways.

The ketogenic diet has the potential to decrease all-cause mortality without a concomitant increase in cardiovascular-related mortality; Qu et al

- This study analyzed data from 43,776 U.S. adults in the NHANES (2001–2018) to assess the relationship between dietary ketogenic ratio (DKR) and mortality risks using Cox regression and restricted cubic spline models.
- A higher DKR was linearly associated with a 24% reduced risk of all-cause mortality (HR=0.76, P=0.003), but showed no significant link to cardiovascular disease mortality (HR=1.13, P=0.504).
- The findings suggest a ketogenic diet may lower overall mortality risk without increasing cardiovascular death rates in adults.

The ketogenic diet and hypoxia promote mitophagy in the context of glaucoma; Morgan et al

- This study examined the impact of a ketogenic diet on mitophagy in retinal ganglion cells (RGCs) and Müller glia using MitoQC mice with induced ocular hypertension (OHT) and hypoxia markers.
- Both OHT and the KD increased mitophagy (measured via mitolysosomes), with the diet enhancing mitophagy in RGCs more than OHT alone, while Müller glia showed comparable increases from both factors.
- The findings suggest hypoxia contributes to mitophagy induction, but the KD's cell-specific effects highlight metabolic differences between RGCs and glia, independent of BNIP3/NIX pathways.

Nurture growth: Ketogenic diet therapy and growth velocity in infants under 12 months with epilepsy - A systematic review and infant data study; Maass et al

- This study evaluated the effects of KD on growth in infants under 12 months through a systematic literature review and analysis of a prospective cohort of 63 infants.
- Results showed that with proper nutritional monitoring, KD did not impair growth velocity or height percentiles in the first year, and even led to growth improvements likely due to reduced seizures.
- However, growth velocity declined in the second year for those continuing KD, particularly in infants with earlier epilepsy onset or diet initiation, highlighting the need for long-term monitoring.

The efficacy of ketogenic diets (low carbohydrate; high fat) as a potential nutritional intervention for lipedema: A systematic review and meta-analysis; Amato et al

- This systematic review and meta-analysis evaluated the impact of a low-carbohydrate, high-fat (LCHF) KD on 329 women with lipedema across seven studies.
- The KD significantly reduced BMI, body weight, waist/hip circumferences, and pain sensitivity, with mean differences of 4.23 (BMI), 7.94 kg (weight), and 1.12 (pain sensitivity) after an average 15.85-week intervention.
- Despite limited studies and participants, the findings suggest LCHF KDs may be beneficial for managing lipedema-related anthropometric and symptomatic outcomes.

Two-month ketogenic diet alters systemic and brain metabolism in middle-aged female mice; Roslund et al

- This study analyzed metabolic changes in 16-month-old female mice after a 2-month KD using targeted 1H-NMR metabolomics across serum, liver, kidney, muscle, and brain regions.
- The KD increased fatty acid catabolism and ketone bodies system-wide, altered glucose-alanine cycle metabolites in muscle, serum, and liver, and induced tissue-specific shifts in one-carbon metabolism and hippocampal myelinogenesis-related metabolites.
- These findings suggest KD may support anti-aging mechanisms in females through metabolic reprogramming, potentially enhancing brain function and energy metabolism.

Effect of acute and chronic ingestion of exogenous ketone supplements on blood pressure: A systematic review and meta-analysis; Marcotte-Chénard et al

- This study performed a systematic review and meta-analysis of exogenous ketone supplements on blood pressure (BP) and resting heart rate (HR), including 10 studies (4 acute, 6 chronic; n=187).
- The results show no significant effect on systolic or diastolic BP for either acute or chronic ingestion, but a potential dose-dependent increase in resting heart rate with higher supplement doses.
- Overall, current data do not support BP modulation by exogenous ketone supplements, and higher-quality studies are needed to confirm these findings and clarify HR effects.

The effect of the ketogenic diet on resistance training load management: a repeated-measures clinical trial in trained participants; Vargas-Molina et al

- This study examined the effects of a 6-week KD combined with resistance training (RT) in 14 trained individuals, assessing variables like volume load, repetitions, perceived exertion (RPE), movement velocity, and exertion index.
- The KD did not impair performance, with increased volume load in later weeks and a slight decrease in RPE, though movement velocity remained unchanged.
- Despite potential performance maintenance, challenges with KD adherence and adaptation were noted, particularly during initial weeks.

Effects of a ketogenic diet on motor function and motor unit number estimation in aged C57BL/6 mice; Padilla et al

- This study investigated the effects of a KD on neuromuscular function in 36 aged C57BL/6 mice, comparing grip strength, motor performance, and neuromuscular integrity over 10 weeks.
- Mice on the KD showed significantly increased hindlimb/all-limb grip strength, rotarod endurance, and motor unit numbers, alongside elevated blood ketone levels, but no improvement in muscle contractility or neuromuscular transmission.
- The findings suggest KD may mitigate age-related neuromuscular decline in mice, warranting further research into its potential for addressing sarcopenia in aging populations.

A diet-dependent host metabolite shapes the gut microbiota to protect from autoimmunity; Alexander et al

- Experiments tested a ketogenic diet (KD) in mice with experimental autoimmune encephalomyelitis (EAE), a multiple sclerosis model.
- The KD reduced disease severity via microbiota-dependent mechanisms, with the host metabolite β-hydroxybutyrate (βHB) and transplantation of βHB-shaped gut microbiota offering protection.
- A Lactobacillus murinus strain and its metabolite indole-3-lactate, enriched by βHB, suppressed pro-inflammatory T helper 17 cells, linking diet-induced host metabolism shifts to microbiome-mediated immunomodulation.

Ketogenic diet ameliorates high-fat diet-induced insulin resistance in mouse skeletal muscle by alleviating endoplasmic reticulum stress; Ma et al

- This study investigates whether a ketogenic diet improves insulin sensitivity in skeletal muscle by alleviating endoplasmic reticulum (ER) stress, using high-fat diet–induced insulin-resistant mice and C2C12 myoblasts treated with palmitic acid.
- Ketogenic diet reversed HFD-induced changes: AKT/GSK3β signaling improved, ER stress markers (IRE1, PERK, BIP) reduced, and Glut4 translocation to the membrane increased, leading to better glucose uptake in muscle cells.
- The authors conclude that KD partially mediates insulin sensitization in skeletal muscle by inhibiting ER stress and upregulating AKT/GSK3β signaling and membrane Glut4 availability.

A maternal ketogenic diet alters oviduct fluid nutrients and embryo histone acetylation in mice; Whatley et al

- This study assessed whether a maternal ketogenic diet alters glucose and β-hydroxybutyrate levels in blood and oviduct fluid and whether this diet affects in vivo embryo development and blastocyst epigenetic marks (H3K27ac).
- It found that KD increased β-hydroxybutyrate in both blood and oviduct fluid without changing glucose, and periconceptional KD delayed blastocyst development and reduced trophectoderm H3K27ac.
- The authors conclude that maternal KD alters reproductive tract nutrients and embryonic development/epigenetics in vivo, suggesting a need for further research on implications for human development and health.

Very low-calorie ketogenic diet (VLCKD) in the management of hidradenitis suppurativa (Acne Inversa): an effective and safe tool for improvement of the clinical severity of disease. Results of a pilot study; Verde et al

- The study prospectively evaluated a 28-day active phase of a very low-calorie ketogenic diet (VLCKD) in 12 treatment-naive women with hidradenitis suppurativa and overweight/obesity, assessing HS severity (Sartorius score) and metabolic markers.
- VLCKD led to significant improvements in anthropometrics and body composition, with a substantial reduction in HS severity and concurrent decreases in TMAO, dROMs, and oxLDL; reductions in Sartorius score correlated with decreases in these metabolic markers.
- The authors suggest VLCKD may be a useful approach for managing HS and related metabolic derangements in this population.

Acute pancreatitis associated with ketogenic diet: A case report; Shanti et al

- This case report documents a 47-year-old woman who developed acute pancreatitis after self-administering a ketogenic diet for weight loss, with confirmed elevated lipase/amylase and CT evidence.
- It highlights a potential link between ketogenic diets and pancreatitis, discusses possible mechanisms and risk factors, and calls for clinician awareness and careful supervision when adopting low-carbohydrate, high-fat diets.

Human milk and breastfeeding during ketogenic diet therapy in infants with epilepsy: Clinical practice guideline; Van der Louw et al

- The paper reports an international expert consensus on incorporating human milk and breastfeeding into ketogenic diet therapy (KDT) for infancy, including practical strategies to overcome barriers and facilitate referrals to experienced centers.
- It concludes that human milk and breastfeeding can be safely included in KDT without reducing its effectiveness, and suggests two practical practice strategies to support continued breastfeeding alongside KDT, along with advocating education on the nutritional benefits of human milk.
- The authors also call for prospective registries to collect real-world data on breastfeeding in KDT and to assess non-seizure outcomes such as quality of life and social-emotional well-being for infants and mothers.

Changes in pediatric referrals after the 2009 ketogenic diet consensus recommendations; Stainman, et al

- The study compared KD referrals for epilepsy at Johns Hopkins Hospital in the 10 years before versus after the 2009 International Ketogenic Diet Study Group recommendations, focusing on whether referrals for indications listed in the table increased.
- After the recommendations, overall referrals meeting indications rose from 44% to 69%, with particularly large increases from JHH neurologists and for specific conditions (Glut-1 deficiency, Dravet syndrome, Rett syndrome, and formula-fed status).
- Seizure reduction among referred patients improved modestly (56% to 61%), but this change was not statistically significant, suggesting referrals increased for more appropriate indications, while efficacy gains remained limited.

A bibliometric analysis of the global trends and hotspots for the ketogenic diet based on CiteSpace; Ye et al

- This bibliometric study analyzed KD-related literature from 2001 to 2022 in Web of Science using CiteSpace to map knowledge structure, trends, and hotspots.
- It found 2,676 publications, with Epilepsia journals producing the most output and Kossoff EH and Rho J as leading authors; the United States and Johns Hopkins institutions dominated contributions, and recurring keywords included epilepsy, metabolism, ketosis, and weight loss.
- The findings highlight the field's focus areas and provide guidance for researchers to identify emerging topics and gaps.

Self-reported menses physiology is positively modulated by a well-formulated, energy-controlled ketogenic diet vs. low fat diet in women of reproductive age with overweight/obesity; Kackley et al

- The study compared precisely designed hypocaloric ketogenic diets (KD) to an isocaloric low-fat diet (LFD) in overweight/obese premenopausal women over six weeks, assessing weight, body composition, metabolic markers, and self-reported menstrual changes.
- Both diets produced meaningful weight loss and fat-mass reduction with improved insulin sensitivity and lipid profiles; KD markedly increased fasting ketones, while inflammatory markers did not differ between groups.
- A subset of KD participants reported increases in menstrual frequency and intensity (including some regaining menses), whereas LFD participants did not report such changes, suggesting potential ketosis-specific effects on menstrual function beyond weight loss.

Effects of different exercises combined with different dietary interventions on body composition: A systematic review and network meta-analysis; Xie et al

- The network meta-analysis compared four combined interventions in healthy adults: exercise with calorie restriction (CR+EX), exercise with time-restricted feeding (TRF+EX), exercise with 5/2 intermittent fasting (5/2F+EX), and exercise with a ketogenic diet (KD+EX), across 78 RCTs and 5219 participants, focusing on body composition outcomes.
- CR+EX most effectively reduced weight and body fat and best preserved lean mass overall; for women, TRF+EX best preserved lean mass, while KD+EX reduced weight but was less effective for fat loss and lean-mass preservation.
- The authors conclude that CR+EX is the optimal pairing for weight and fat reduction with lean-mass maintenance, with sex-specific nuances favoring TRF+EX for women and KD+EX being suboptimal for fat loss and muscle preservation.

Adult inception of ketogenic diet therapy increases sleep during the dark cycle in C57BL/6J wild type and Fragile X mice; Westmark et al

- The study assessed the effects of a ketogenic diet (KD) started in adulthood on sleep-wake patterns in Fmr1KO and WT mice, using EEG to measure sleep architecture and comparing findings to prior light-cycle sleep outcomes and actigraphy validity.
- KD increased NREM sleep during the dark cycle in both genotypes and altered sleep microstructure (wake bout length), but there was no clear light-cycle sleep improvement in Fmr1KO mice, suggesting limited benefit of KD for Fragile X–related sleep disturbances.
- The authors conclude that actigraphy is not a reliable surrogate for EEG in mice and that KD initiated in adulthood may not alleviate Fragile X–associated sleep problems, with only modest weight changes observed.

Carbohydrate ingestion on exercise metabolism and physical performance; Koutnik et al

- Experiments compiled in this review examine carbohydrate ingestion during exercise across 160 studies, focusing on metabolism and performance. The major findings are:
  (1) Exercise-induced hypoglycemia (EIH) correlates with task termination and is not simply caused by muscle glycogen depletion;
  (2) CHO intake preserves blood glucose, reduces liver glycogenolysis, and speeds muscle glycogen breakdown via neuroendocrine pathways, improving performance by preventing EIH even when glycogen is depleted; and
  (3) High-fat–adapted athletes can sustain similar performance with lower CHO oxidation, challenging the idea that glycogen/CHO oxidation are central to performance, with CHO ingestion during exercise most beneficial by preventing EIH in prolonged efforts.

Ketogenic diet induces p53-dependent cellular senescence in multiple organs; Wei et al

- A study tested ketogenic diets (KDs) in mice of varying ages and human trial participants, using genetic knockouts (p53, caspase-2) and inhibitors (AMPK, p21, caspase-2) to explore KD effects on cellular senescence.
- KDs triggered senescence in organs like the heart and kidney via an AMPK-caspase-2-MDM2 pathway, elevating p53/p21 and senescence biomarkers in mice and humans, but this was reversed by senolytic drugs or intermittent KD regimens.
- The findings suggest KDs' effects are context-dependent, highlighting potential risks of prolonged use and the need for personalized dietary strategies to balance benefits and harms.

REVIEW ARTICLES ON EMERGING APPLICATIONS

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International society of sports nutrition position stand: ketogenic diets; Leaf, et al

Molecular mechanisms of healthy aging: the role of caloric restriction, intermittent fasting, mediterranean diet, and ketogenic diet—A scoping review; Surugiu et al

Therapeutic potential of the ketogenic diet: A metabolic switch with implications for neurological disorders, the gut-brain axis, and cardiovascular diseases; Shahpasand et al

Ketogenic diet therapy for epilepsy: Clinical pearls; Pinto, et al

The case for a ketogenic diet in the management of kidney disease; Athinarayanan et al

Mechanisms of ketogenic diet action; Williams, et al

Ketogenic diet in clinical populations - A narrative review; Zemer, et al

Ketogenic diet: A review of composition diversity, mechanism of action and clinical application; Malinowska et al

Is ketogenic diet a "precision medicine"? Recent developments and future challenges; Falsaperla et al

Ketogenic diet for epilepsy and obesity: Is it the same?; Tagliabue et al

Ketogenic nutritional therapy (KeNuT)-a multi-step dietary model with meal replacements for the management of obesity and its related metabolic disorders: a consensus statement from the working group of the Club of the Italian Society of Endocrinology (SIE)-diet therapies in endocrinology and metabolism; Barrea et al

Ketogenic diet: Parental experiences and expectations; Orr et al

Take the bull by the horns and tackle the potential downsides of the ketogenic diet; Meng et al

Dietary influence on drug efficacy: A comprehensive review of ketogenic diet-pharmacotherapy interactions; Marinescu et al

Literature review: Support for caregivers of children on the ketogenic diet for epilepsy and other neurologic disorders; Metzger et al

Human milk and breastfeeding during ketogenic diet therapy in infants with epilepsy: Clinical practice guideline; Van der Louw et al

Impact of ketogenic and low-glycemic diets on inflammatory skin conditions; Roster et al

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