

Fuel Selection, Tissue Function and Recovery

A targeted evidence review for EPK

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Abstract

This review examines selected evidence connecting dietary composition, substrate use, tissue function and recovery with questions raised by the Energy Per Kilogram (EPK) framework. Human feeding and cortisol studies are considered alongside genetic-disease research, endurance observations, animal experiments and cellular mechanisms. The evidence motivates measuring function and tolerability beyond body mass, but does not establish a universal advantage of glucose oxidation, a protective dietary PUFA ceiling, a requirement for a fixed energy surplus, or clinical efficacy of EPK. A distinction between an experimental mechanism and a practical intervention is maintained throughout. A proposed research programme separates energy provision, dietary composition and meal timing, with direct functional outcomes and transparent reporting of negative findings. No new participant data, pooled estimates or treatment recommendations are reported.

Scope and method

Sources were selected through user-submitted publications and targeted web searches of PubMed-indexed records, journal websites and reference leads, assessed through 2 October 2026. Search themes included fat oxidation versus fat loss, cortisol and carbohydrate intake, adipocyte dysfunction, PUFA and translation, fasting and regeneration, and exercise-related oxidative stress. This is a selected narrative review, not a systematic search, meta-analysis or formal risk-of-bias assessment. Selection reflects the questions under discussion and is vulnerable to selection bias.

Accessible full texts were used where available. The endurance paper was assessed at published-abstract level; the pulmonary-exercise paper at indexed-summary level; the 1992 cell study at abstract level; Stimson at abstract level. These access limits constrain appraisal. Reported mechanisms are not treated as clinical outcomes.

1. Interpreting the evidence

EPK links dietary energy planning to body mass, activity and estimated expenditure. The present review does not validate that calculation. It instead asks which outcomes should accompany an evaluation: body composition, physical function, psychological burden, recovery and the ability to sustain an eating pattern. A mechanism can suggest a measurement or hypothesis without predicting a programme's effect.

Three distinctions guide the synthesis. First, a measured fuel-oxidation rate is not the same as net change in stored body fat. Second, total dietary energy is not equivalent to cellular ATP supply or sport-specific energy availability. Third, results in a selected tissue, mouse strain or cultured-cell preparation cannot be treated as effects of eating a particular food in a general human population.

The evidence notes below are deliberately bounded. They identify study type, a finding and an inference that remains untested. References are numbered in the order of the notes. Their purpose is to define useful research questions rather than accumulate apparently supportive citations.

2. Selected evidence notes

Less body fat does not always mean better metabolic health [1]

Human tissue and animal experiments

Human biopsies and mouse experiments linked LMNA-related lipodystrophy to disturbed lipid pathways, inflammation and regional adipocyte loss. Established human disease combined lower total fat with worse glucose and triglyceride measures. Direct respiratory impairment was demonstrated in particular mouse fat depots.

Boundary: This small genetic-disease study does not show that ordinary dieting produces lipodystrophy, or that additional calories treat it. Human gene-expression changes are not direct measurements of mitochondrial ATP output.

Low-fat diets: carbohydrate source matters [2]

Animal intervention

Six mice per group received two approximately 9%-fat diets for 16 weeks. Replacing sucrose with additional corn starch was associated with poorer glucose tolerance, altered microbiota and intestinal/liver inflammation, without a body-weight difference.

Boundary: The diets changed carbohydrate source, not simply sugar presence. Microbiome mediation was not established. This does not prove humans need added sucrose, or that every low-fat diet is beneficial or harmful.

Selected evidence notes - continued

Dietary fat, brain inflammation and mood [3]

Animal and cell experiments

Male mice consuming 60% versus 10% of calories from fat developed behavioural and inflammatory differences. Arachidonic-acid experiments reproduced aspects of the phenotype; aspirin improved some behavioural outcomes and inflammatory measures.

Boundary: Mouse behavioural tests are not human depression diagnoses. The comparison establishes neither a human fat threshold nor harm from all PUFA. Aspirin was an experimental intervention, not an established dietary-mood treatment.

Endurance exercise, red blood cells and recovery [4]

Human observational study; abstract assessed

Before-and-after sampling around 40-km and 171-km trail races found oxidative and inflammatory signatures in red blood cells, with molecular changes associated with impaired deformability. Assessment here is based on the published abstract.

Boundary: The study did not establish that under-fuelling caused these changes or that extra carbohydrate prevents them. Red-cell ageing signatures are not evidence that running shortens human lifespan. No 15% surplus was tested.

Selected evidence notes - continued

Fat oxidation is not the same as body-fat loss [5]

Human controlled feeding

In 19 adults studied under controlled feeding, carbohydrate restriction increased fat oxidation, but equal-calorie fat restriction produced greater calculated net fat loss over six days. Substrate use and net storage are different outcomes.

Boundary: This short experiment cannot establish long-term superiority. Both interventions restricted energy. It does not demonstrate fat loss at maintenance intake or validate an EPK target.

The Biggest Loser follow-up adds evidence about metabolic adaptation and substantial regain, with participants still lighter on average at six years. It does not establish universal diet failure. [6]

PUFA tracking: what cellular research can tell us [7]

Cell experiment

Direct fatty-acid exposure inhibited protein synthesis in cultured cells, with arachidonic acid generally most potent among those tested. Calcium regulation contributed, and effects were reversible.

Boundary: Cell exposure is not dietary intake. The experiment measured neither human muscle growth nor a safe dietary ceiling. It cannot justify converting micromolar concentrations into grams per day.

Selected evidence notes - continued

Carbohydrate intake can change cortisol metabolism [9]

Human crossover interventions

Crossover studies in 17 men and a six-man isocaloric group compared 66%-fat/4%-carbohydrate with 35%-fat/35%-carbohydrate diets. The very-low-carbohydrate diet increased cortisol regeneration and reduced clearance, without changing plasma cortisol or its salivary rhythm.

Boundary: Subcutaneous abdominal 11 β -HSD1 was unchanged. Small male-only studies do not demonstrate clinical harm, abdominal-fat gain, or a benefit from a particular EPK prescription. Neither comparator was a 20%-fat diet.

Fasting, hair regeneration and energy supply [10]

Animal experiments and small human trial

Mouse experiments linked fasting to local fatty-acid release, oxidative stress and loss of activated hair-follicle stem cells. A short human trial also found slower hair growth; only 26 of 49 randomised participants had hair-growth measurements.

Boundary: This does not establish permanent human baldness or universal harm from fasting. Timing and calorie reduction must be distinguished. Human participants were healthy young adults, and long-term hair outcomes were not established.

Selected evidence notes - continued

Cortisol signalling depends on tissue and context [11]

Animal intervention; indexed summary assessed

A mouse experiment reported increased lung 11 β -HSD1 expression alongside reduced obesity-associated pulmonary inflammation after exercise training. This review uses the indexed publication summary.

Boundary: It does not establish lasting systemic cortisol excess or that exercise is harmful. Local glucocorticoid activity and clinical outcomes cannot be inferred from a single circulating measurement.

NAD precursors and evidence for energy support [12]

Small human crossover pilot

A short crossover pilot tested a combined nicotinamide/D-ribose product and reported changes in NAD-related biomarkers. Fifty people were screened; the intention-to-treat population was 18 and the per-protocol population 17.

Boundary: A combination product does not isolate niacinamide. Biomarker changes do not establish treatment of insulin resistance, durable functional benefit or equivalence to DCA. Independent replication and longer follow-up are needed.

3. An EPK research programme

Energy provision. Compare a clearly specified EPK pathway with an equally supported comparator. Record the difference between prescribed intake and achieved intake; wearable expenditure remains an estimate. Do not infer an energy surplus simply because a prescribed target is above a device reading. Document device use, missingness, fallback calculations and changes in body mass over time.

Dietary composition. To test a low-fat/high-carbohydrate hypothesis, define the achieved fat and carbohydrate percentages, protein, fibre, food sources and adherence. An intervention changing calories, food quality and fat percentage together tests the package, not the independent effect of fat. A separate matched-energy comparison is required for that narrower question.

Timing. Feeding-window effects should be distinguished from total energy reduction. An exploratory comparison could hold intake and composition constant while varying timing. Outcomes should be selected in advance, with adequate follow-up rather than a collection of favourable biomarkers.

Performance and recovery. Use reproducible strength or endurance tests appropriate to the population, recorded training load, sleep and recovery measures. Extreme endurance observations should not supply expected effects for sedentary adults. A 15% performance allowance remains a programme choice to test, not an amount established by the papers in this review.

Body composition. Include fat and lean tissue with standardised measurement, and region-specific imaging in a feasible subgroup. Fat-free mass includes more than muscle. A lower body mass can be a useful outcome without being sufficient evidence of improved function.

3.1 PUFA tracking as a research variable

The optional PUFA target should record a user preference rather than label an unvalidated threshold as safe or protective. Separate omega-3 and omega-6 where nutrient data permit, display missing nutrient information rather than imputing zero, and preserve essential-fatty-acid adequacy. Nutrient databases estimate intake; they do not measure tissue fatty-acid exposure. The NIH reference identifies linoleic and alpha-linolenic acids as essential. [8]

A prospective comparison could test a specified dietary-fat pattern with equal energy, protein and study support. Baseline status, substitution foods and adverse outcomes should be recorded. Its hypothesis should be stated before results are available. Evidence of cellular effects alone cannot determine the intervention dose.

4. Claims excluded from efficacy conclusions

The reported DCA obesity master's thesis was not located for primary verification. It therefore remains a research lead, not an efficacy source. The associated news account is not used to establish a dietary mechanism. Before inclusion as primary evidence, the original methods, animal numbers, intake controls, allocation, body-composition measurements and complete results would need appraisal.

A nutrient cofactor and a drug acting on enzyme regulation are different interventions. The reviewed material does not establish that B1, magnesium and niacinamide reproduce DCA effects. Nor does a blood NAD marker establish the mitochondrial NAD⁺/NADH ratio in every relevant tissue. Such equivalence requires direct testing.

Cancer case reports and combination protocols are not evidence that DCA reliably induces tumour regression. A phase-I study in advanced solid tumours reported no objective responses among 23 evaluable patients, with neuropathy among adverse effects. [13] Claims of suppressed curative efficacy are not supported by that evidence. The case-report review is listed for transparency, not as proof of efficacy. [14]

4.1 Relation to the seven working papers

EPK-001: define sufficiency using function as well as intake per kilogram. EPK-002: measure mood and behavioural burden directly. EPK-003: distinguish substrate selection from net storage and tissue-specific metabolism. EPK-004: test performance and recovery rather than infer them from biomarkers. EPK-005: separate energy deficiency from meal timing. EPK-006: treat cognitive and mood applications as hypotheses requiring human evidence. EPK-007: allow inflammatory and glucocorticoid effects to be context-dependent.

These are proposed connections and companion commentary. This release does not silently revise the seven existing PDFs or relabel their DOIs.

Conclusion

The selected evidence supports a research agenda that joins adequate energy provision to direct assessment of tissue function, recovery and dietary tolerability. It does not support treating all fat oxidation, all PUFA exposure or every stress response as harmful. EPK should be evaluated with prespecified outcomes, transparent comparators and complete reporting, including findings that contradict its proposed mechanisms.

Disclosure: The author develops EPK and has an intellectual interest in the framework. AI-assisted drafting and source checking were used. This working paper is not externally peer reviewed and reports no new data. Original text: copyright 2026 Billy Craig, CC BY-ND 4.0. Third-party publications retain their own rights.

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