NAD+ Research Summary

Research Library Summary — PHX Performance Research

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What the Research Suggests, in Plain Language

NAD+ is a natural molecule found in every cell, where it helps turn food into energy. Levels tend to fall with age. Most human research has not tested NAD+ itself; it has tested related supplements, taken by mouth, that the body converts into NAD+.

• In people, these supplement studies consistently found that NAD+-related levels in the blood went up. Effects on physical function, metabolism and other health measures were mixed: some small studies reported changes, and many found no difference from placebo. No human study has shown that it extends lifespan.

• In animal studies, mostly in mice, results suggest these supplements may be linked to slower age-related decline, better muscle energy use and better blood-sugar control. One mouse study, not yet peer-reviewed, reported a longer median lifespan in female mice but not in males.

• Very few controlled human studies have tested NAD+ itself given directly rather than as a supplement.

In short: the animal results and the mixed human supplement results raise questions for further research. They do not show that NAD+ is safe or effective in people for any purpose.

Overview

NAD+ (nicotinamide adenine dinucleotide) is a coenzyme involved in cellular energy metabolism and redox reactions. Levels decline with age in multiple tissues. Research has examined NAD+ precursors such as nicotinamide riboside (NR) and nicotinamide mononucleotide (NMN). It is not an FDA-approved drug.

What the Research Actually Presents

Human studies (oral NR or NMN precursors):

• Multiple trials report increases in circulating or cellular NAD-related metabolites after supplementation (for example, PMID 29599478, PMID 36482258).

• Effects on physical function, metabolic markers, insulin sensitivity, and other healthspan-related outcomes are mixed. Some individual trials report changes in walking distance or selected markers; many report null results for muscle mitochondrial respiratory capacity or clinical endpoints (for example, PMID 31412242, PMID 29992272).

• No published human trials have demonstrated lifespan extension or consistent anti-aging effects.

Animal studies (mice and other models):

• Long-term NMN administration in aging mice has been reported to mitigate age-associated physiological decline, enhance mitochondrial oxidative metabolism in skeletal muscle, improve insulin sensitivity, and increase physical activity in some models (Mills et al. 2016, PMID 28068222).

• One study reported that long-term NMN supplementation increased median lifespan by approximately 8.5% in female mice (no significant lifespan extension in males in that study). This is a preprint that had not completed peer review when catalogued (Kane et al. 2024, PMID 38979132). Other rodent work has reported lifespan or healthspan changes in specific models.

• These are animal findings. They have not been shown to translate to humans.

Direct NAD+: Very few controlled human studies test NAD+ itself given directly rather than as an oral precursor. A 2026 systematic review identified only an intravenous pharmacokinetic pilot without clinical outcomes (PMID 41655607).

What the Research Suggests

Human trials consistently show that oral NR and NMN raise NAD-related blood markers in the groups studied. Broader effects on energy metabolism, mitochondrial function in muscle, or clinical outcomes remain inconsistent. Animal studies report improvements in mitochondrial function, metabolic parameters, and, in some cases, lifespan or healthspan measures. These animal results do not establish human outcomes.

Mechanism and Signaling Pathways (as described in the literature)

NAD+ participates in redox reactions and serves as a substrate for sirtuins and PARP (poly-ADP-ribose polymerase) enzymes involved in DNA repair and metabolic regulation. Animal studies describe enhanced mitochondrial oxidative metabolism after NMN administration in the models examined.

Research Landscape

Catalog: 398 records — 177 human randomized controlled trials (RCTs, including registry entries; most test precursors), 100 other human, 55 animal, 2 in-vitro, 54 reviews, 6 systematic reviews/meta-analyses, 4 other. 207 ClinicalTrials.gov entries. The catalog focuses on human supplementation and administration studies, reviews, and animal studies of NAD+ given from outside the body, not the full basic-science literature.

Key Studies

• Martens CR et al. 2018 (Nature Communications): randomized, placebo-controlled crossover trial of NR in healthy middle-aged and older adults (PMID 29599478).

• Dollerup OL et al. 2018: randomized, placebo-controlled trial of NR in men with obesity; insulin sensitivity not improved (PMID 29992272).

• Elhassan YS et al. 2019 (Cell Reports): NR in older men, muscle NAD+ measures; 12 men (PMID 31412242).

• Yoshino M et al. 2021 (Science): NMN in women with prediabetes, muscle insulin sensitivity (PMID 33888596).

• Brakedal B et al. 2022 (Cell Metabolism), NADPARK: randomized phase 1 trial of NR in Parkinson’s disease (PMID 35235774).

• Yi L et al. 2023 (GeroScience): randomized trial of NMN in healthy middle-aged adults; 80 participants (PMID 36482258).

• Mills KF et al. 2016 (Cell Metabolism): animal study (mice), long-term NMN (PMID 28068222).

• Systematic reviews: Gindri IM et al. 2024 (PMID 37971292); Gallagher C et al. 2026 (PMID 41655607).

Safety Findings Reported in the Studies

Oral NR and NMN have been described as well tolerated in short- to medium-term human trials. Long-term human safety data remain limited, and safety data for NAD+ given directly are sparse.

Limitations and Evidence Gaps

Most human studies use precursors rather than NAD+ itself. Functional and clinical outcomes in humans are inconsistent. Lifespan and robust mitochondrial findings are limited to animal models.

Regulatory Status

NAD+ and its precursors are not FDA-approved drugs for any indication. Precursors are sold as dietary supplements in some markets.

References

Martens CR et al. 2018 (PMID 29599478). Dollerup OL et al. 2018 (PMID 29992272). Elhassan YS et al. 2019 (PMID 31412242). Yoshino M et al. 2021 (PMID 33888596). Brakedal B et al. 2022 (PMID 35235774). Yi L et al. 2023 (PMID 36482258). Mills KF et al. 2016 (PMID 28068222). Kane AE et al. 2024, preprint (PMID 38979132). Gindri IM et al. 2024 (PMID 37971292). Gallagher C et al. 2026 (PMID 41655607). Full catalog entries available in the research library.

Evidence reviewed through November 2026 (PHX research catalog snapshot of PubMed, ClinicalTrials.gov and Europe PMC).

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