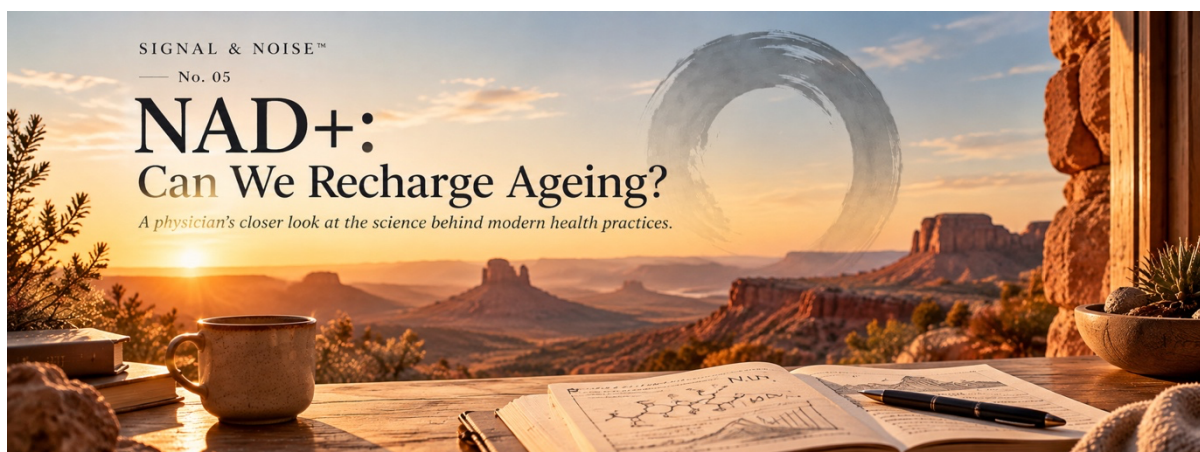




Few molecules have acquired as much importance in the modern longevity conversation as NAD⁺. It appears in discussions of mitochondrial function, cellular energy, DNA repair, metabolism and ageing. Supplements designed to increase it are widely available, NAD⁺ clinics offer intravenous infusions, and compounds such as NMN and NR are increasingly presented as ways of restoring something that ageing takes away.

There is real science behind this interest. NAD⁺ is essential to human biology, and experiments in animals have produced compelling evidence that manipulating NAD metabolism can influence several processes associated with ageing. Human studies also show that we can alter NAD-related biomarkers.

But that leaves a much bigger question unanswered. If we can raise NAD⁺, does doing so actually make humans healthier — and is there any evidence that it slows ageing?

The Claim

Nicotinamide adenine dinucleotide, or NAD⁺, is a molecule found in virtually every cell. It participates in the chemical reactions that allow nutrients to be converted into usable energy, but its role extends well beyond energy metabolism. NAD⁺ is also consumed by enzymes involved in DNA repair, cellular signalling, stress responses and regulation of gene expression.

Interest in NAD⁺ and ageing grew partly from research showing that NAD⁺ availability can decline with age in animal models and in at least some human tissues. This generated an appealing hypothesis: perhaps declining NAD⁺ contributes to some aspects of ageing, and restoring it might preserve cellular function.

Taking NAD⁺ itself orally is not the principal strategy studied in clinical research. Instead, researchers have largely investigated **precursors** that the body can use to synthesize NAD⁺. Two have attracted particular attention: **nicotinamide riboside (NR)** and **nicotinamide mononucleotide (NMN)**.

The commercial proposition that followed is easy to understand. If NAD⁺ falls with ageing, and NMN or NR can restore it, perhaps supplementation can restore some of the physiology associated with youth.

The first two parts of that argument have considerable biological support. It is the final step that requires much more scrutiny.

Why Might It Work?

NAD⁺ occupies an unusually central position in cellular metabolism. In its NAD⁺/NADH forms, it transfers electrons during reactions involved in glycolysis, the citric-acid cycle and oxidative phosphorylation — processes through which cells ultimately generate ATP.

It is also required by several families of enzymes with particular relevance to ageing biology. These include **sirtuins**, which influence metabolic regulation and cellular stress responses, and **PARPs**, which participate in DNA repair. Another NAD-consuming enzyme, CD38, has been implicated experimentally in age-associated changes in NAD metabolism.

This creates a plausible biological story. Ageing may alter NAD production and consumption; lower NAD availability may compromise cellular processes; restoring NAD might therefore improve cellular resilience.

Animal experiments have made that story considerably more compelling. Increasing NAD⁺ availability through NMN, NR or manipulation of NAD-related pathways has produced improvements in metabolic function, mitochondrial biology, inflammation and physical function in numerous rodent models.

But animal ageing experiments are hypothesis-generating evidence for human longevity, not proof of it. The important question is what happens when the same pathway is manipulated in people.

Can We Actually Raise NAD⁺ in Humans?

Here the evidence is considerably stronger than many other claims in the longevity industry.

A 2026 systematic review examined 113 NAD-related intervention studies, including 33 human studies, 28 of which were randomized trials. Oral NR and NMN consistently demonstrated **biochemical target engagement**: supplementation altered circulating or cellular NAD-related metabolites.

A recent randomized trial provides a particularly clear example. Adults aged 65 years or older received 1,250 mg of NMN daily or placebo for 24 weeks. NMN produced a substantial and sustained increase in circulating NAD⁺ and related metabolites.

Similarly, in a randomized trial involving people with mild cognitive impairment, NR approximately doubled blood NAD⁺.

So one part of the story is increasingly difficult to dispute: **We can manipulate NAD⁺ biology in humans.**

The more important question is what happens next. **What Does the Human Evidence Show?**

This is where the picture becomes considerably less impressive — and considerably more interesting.

The 2026 systematic review found that although NR and NMN reliably affected NAD-related biomarkers, effects on metabolic health, vascular function, physical performance and other outcomes relevant to healthy ageing were heterogeneous and frequently absent.

A separate 2026 systematic review and meta-analysis examined 15 randomized trials of oral NMN, using doses ranging from 250 to 2,000 mg per day. Across the available studies, NMN did not significantly improve body weight, BMI, fasting glucose, HbA1c, lipid profiles or systolic blood pressure. There was a small reduction in diastolic blood pressure and a non-significant trend towards improved HOMA-IR, leaving open the possibility that particular populations or outcomes may prove more responsive.

Individual studies have produced more encouraging signals. Some have reported improvements in measures such as walking ability, muscle function, insulin sensitivity or fatigue. These findings deserve investigation rather than dismissal. But studies have generally been small, relatively short, and heterogeneous in population, dose and outcomes, making replication particularly important.

The recent 24-week high-dose NMN trial illustrates the distinction especially well. NAD⁺ concentrations increased substantially, demonstrating that the intervention reached its biochemical target. Yet there was no significant improvement in the primary endpoint or in physical-performance measures. Several nominal

changes appeared in secondary measures, but they did not remain significant after adjustment for multiple comparisons.

The same pattern has appeared in neurological research. In a small randomized trial in people with mild cognitive impairment, NR doubled blood NAD⁺ but did not improve the primary cognitive outcome.

And in October 2026, a much larger test produced an important result. A randomized JAMA trial followed 410 people with early Parkinson disease for 52 weeks. NR did not slow clinical progression. The primary clinical outcome actually favoured placebo, although the magnitude of the difference was smaller than the prespecified threshold considered clinically important.

Parkinson disease is not normal ageing, and that trial cannot tell us whether NAD augmentation might benefit healthy people in other ways. What it does demonstrate is something scientifically important: **successfully targeting a biologically compelling pathway does not guarantee clinical benefit.**

Where Signal Becomes Noise

The NAD⁺ story contains a genuine scientific signal.

NAD⁺ is fundamental to cellular biology. NAD metabolism appears to change with ageing. Animal experiments provide substantial evidence that manipulating this pathway can affect age-related physiology. And human trials demonstrate that oral NMN and NR can alter NAD-related biomarkers.

The noise begins when these observations are compressed into a much stronger claim:

NAD⁺ declines with age, therefore restoring NAD⁺ reverses ageing.

That conclusion has not been demonstrated.

Increasing the concentration of a molecule associated with younger physiology is not equivalent to making a cell younger. Making a biomarker move in the desired direction is not equivalent to improving organ function. And improving a short-term physiological measurement is still several steps removed from extending healthspan or lifespan.

This distinction matters because the language surrounding NAD⁺ frequently moves between these levels without acknowledging the transitions. “Supports NAD⁺ levels,” “supports cellular energy,” “promotes healthy ageing” and “anti-ageing” can sound like variations of the same claim. Scientifically, they are not.

One can be demonstrated by measuring a molecule in blood. Proving the last would require substantially more evidence.

What About NAD⁺ IV Infusions?

This deserves to be considered separately because intravenous NAD⁺ is increasingly offered by wellness and longevity clinics.

It may sound like the most direct intervention: rather than providing a precursor and relying on cellular metabolism to produce NAD⁺, why not administer NAD⁺ itself?

The problem is that the clinical evidence is considerably thinner.

The 2026 systematic review found **no eligible human outcome trials of intravenous or intramuscular NAD⁺ itself for anti-ageing or wellness indications.** A small pharmacokinetic study and limited

observational evidence exist, but this is very different from demonstrating improvements in energy, cognition, recovery or ageing.

That produces an unusual inversion of the marketing intuition. The intervention that may appear the most medically sophisticated — an intravenous infusion — currently has a weaker clinical evidence base for wellness outcomes than oral NR or NMN.

Safety and Trade-offs

Short-term oral supplementation appears reasonably reassuring. The 2026 NMN meta-analysis found no significant increase in overall adverse events, serious adverse events, withdrawals or liver-enzyme abnormalities across the available randomized trials.

That should not be interpreted as proof of long-term safety. Most studies have lasted weeks or months rather than years, while people interested in longevity may contemplate taking these compounds indefinitely.

There are also theoretical questions worth continuing to investigate. NAD metabolism is involved in many fundamental cellular processes, including pathways relevant to cancer biology. This does not establish that NMN or NR causes cancer, and current human evidence does not demonstrate such a risk. But the complexity of NAD biology is another reason that “more NAD+ must be better” should not be treated as an established principle.

Cost is a more immediate consideration. If supplementation reliably changes a biomarker but meaningful health benefits remain uncertain, consumers need to decide how much that biochemical effect itself is worth to them.

What We Still Don't Know

The largest unanswered question is surprisingly straightforward: **who, if anyone, meaningfully benefits from raising NAD+?**

Effects may differ between younger healthy adults, older people, people with metabolic dysfunction and those with diseases associated with altered NAD metabolism. It is entirely possible that averaging these populations together obscures benefits confined to particular biological contexts.

We also need longer trials. Ageing develops over decades, whereas most supplementation studies last months. Trials need clinically meaningful prespecified outcomes rather than large collections of exploratory biomarkers, and promising findings need independent replication.

Finally, NMN, NR and intravenous NAD+ should not be treated as interchangeable simply because they ultimately relate to the same metabolic pathway. They are different interventions with different pharmacology and very different evidence bases.

The Practical Takeaway

The science behind NAD+ is real. The anti-ageing claim is not yet established.

NMN and NR can increase NAD-related biomarkers in humans, and that makes them scientifically interesting compounds rather than empty wellness products. But after multiple randomized trials, we still do not have convincing evidence that raising NAD+ produces broad improvements in metabolic health, cognition, physical function or other outcomes that would demonstrate slower human ageing. There is no evidence that these supplements extend human lifespan.

That distinction changes how I would think about using them.

For a healthy person considering NMN or NR specifically to slow ageing, **the evidence is not currently strong enough for me to recommend routine supplementation for that purpose.** Someone may reasonably choose to take one after understanding the uncertainty, particularly given the relatively reassuring short-term safety data, but they should regard it as an experiment based on promising biology—not as a proven longevity intervention.

This does not mean NMN or NR have been shown not to work. Particular populations, doses or outcomes may ultimately prove beneficial, and some human trials already contain signals worth pursuing. What it does mean is that the central commercial proposition—boost NAD⁺ and thereby slow human ageing—has moved ahead of the clinical evidence.

Intravenous NAD⁺ is harder to justify. Despite appearing more intensive and medical, its evidence base for anti-ageing and general wellness is substantially weaker than that for oral NMN or NR. On current evidence, I would not regard IV NAD⁺ as an evidence-based longevity treatment.

There is an important lesson here. We often assume that identifying something that changes with ageing, and then reversing that change, means we have treated ageing itself. Biology is rarely that simple.

We have shown that we can raise NAD⁺. We have not yet shown that doing so makes humans age more slowly.

For now, that is where the signal ends.

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