Resilience as a metric: Why midlife interventions matter more than ever

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Dr Rebecca Crews and Heather Makar from Renue By Science advocate for changing health policy to prioritize proactive resilience maintenance over reactive disease treatment, especially during midlife. They emphasize the benefits of NAD+ biology as a measurable intervention framework

Health policy is balanced at an inflection point. By 2050, the global population aged 60 and older will reach 2.1 billion, while birth rates decline across developed nations. Simultaneously, chronic diseases now affect younger cohorts at unprecedented rates. Type 2 diabetes among thirty-somethings has increased 70% between 1990 and 1998, with reason to believe that percentage is even greater today, while cognitive decline markers appear decades before clinical diagnosis.

These converging trends demand a fundamental shift from late-stage disease treatment to proactive maintenance of functional resilience, particularly during midlife (ages 35–55) when biological decline accelerates beneath the surface of apparent health. Resilience, encompassing functional independence, cognitive sharpness, mitochondrial capacity, and metabolic adaptability, must become the primary target for public health policy.

Unlike traditional health metrics that measure disease presence, resilience indicators predict future functional capacity and respond to early intervention, delineating a measurable pathway from reactive healthcare to true health preservation.

The hidden onset: Why midlife matters

Most age-related decline begins decades before symptoms emerge. Mitochondrial dysfunction, cellular energy depletion, DNA damage accumulation, and metabolic inflexibility develop silently during midlife, creating the foundation for later pathology.

The metabolic system shows the clearest early warning signs. Insulin resistance develops gradually from the late twenties onward, accompanied by visceral fat accumulation and declining NAD+ levels. These changes occur while individuals feel normal and pass routine medical screenings, yet cellular dysfunction steadily accumulates.

Neurological decline follows similar patterns. Brain imaging studies reveal structural changes associated with dementia beginning 15-20 years before symptom onset. Early markers include reduced synaptic plasticity, low-grade neuroinflammation, and subtle cognitive fatigue that individuals attribute to normal aging or stress.

The musculoskeletal system demonstrates equivalent vulnerability. Mitochondrial biogenesis in skeletal muscle peaks in the late twenties, followed by a gradual VO2 max decline and early sarcopenia development. By age 40, most individuals have lost 3-8% of muscle mass, establishing the trajectory toward frailty.

For women, reproductive health provides particularly clear evidence of this phenomenon. Declining NAD+ levels directly impact oocyte quality and reproductive aging, with fertility beginning to decline in the early thirties through mechanisms that parallel broader cellular aging processes.

Central to all these changes is NAD+ (nicotinamide adenine dinucleotide), a coenzyme essential for cellular energy metabolism, DNA repair, and stress response. Research by Imai, Guarente, and others has established NAD+ as a fundamental driver of aging biology, making it an ideal biomarker for midlife intervention strategies.

NAD+ as the linchpin of midlife resilience

NAD+ enables sirtuin activation – protein enzymes necessary for longevity that regulate metabolism, DNA repair, and stress responses. It supports mitochondrial energy metabolism and coordinates inflammation regulation, all core components of functional resilience.

NAD+ levels drop approximately 50% between ages 40 and 60 across multiple tissues, directly correlating with diminished mitochondrial function, immune senescence, and slower cellular repair cycles. As NAD+ availability decreases, cells struggle to maintain basic functions, leading to the gradual damage accumulation recognized as aging.

Recent clinical research demonstrates that NAD+ precursors, including nicotinamide mononucleotide (NMN), nicotinamide riboside (NR), and emerging compounds like trigonelline, can effectively restore cellular energy levels in various tissue types. Clinical trials show that NMN and NR supplementation improves physical performance in older adults, protects muscle mass, enhances cognitive function in neurodegenerative conditions, and supports metabolic health across age groups. If there is a greater focus on NAD+ maintenance during midlife, researchers believe that those benefits will carry forward, protecting function and independence for older adults.

NAD+ levels can now be measured precisely through both lab blood tests and home intracellular assays, enabling personalized interventions based on individual biological status rather than chronological age assumptions.

Building a longevity-first public health model

Current health systems excel at acute care and late-stage disease management but fail at preventing functional decline. Current data shows that 90% of the nation's $4.5 trillion in annual healthcare expenditures stem from chronic and mental health conditions, with

86% of total healthcare costs attributable to chronic disease alone. Screening protocols focus on disease detection rather than resilience preservation, missing the window when interventions could have maximum impact.

A longevity-first public health model would implement 'Midlife Resilience Screening' as standard healthcare practice, including NAD+ testing to evaluate cellular energy status, mitochondrial function markers to assess cellular efficiency, cognitive performance evaluations to establish baselines, and metabolic flexibility measurements to identify early dysfunction. Each of these metrics would be tied to protocols designed to optimize function through an active dialogue between patient and practitioner.

Educational campaigns about evidence- based lifestyle and supplementation interventions would enable individuals to receive actionable data about their biological age and specific recommendations for maintaining resilience before pathology develops.

When healthcare systems implement coordinated chronic disease management, results include 6% fewer hospitalizations, 29% fewer emergency department visits, and reduced costs of $10.3 per patient per month. German health insurance data comparing 10,000 diabetes patients receiving coordinated care versus usual care showed 50% fewer deaths, 25% fewer disease complications, and 11% lower costs over four years.

Personalized longevity implementation

The future of health policy lies in personalized midlife planning based on biological rather than chronological age. Just as cancer treatment has evolved toward genetic profiling and targeted therapy, longevity interventions must be customized to individual cellular status and risk factors, factoring in innate biology with personal lifestyle preferences.

Tools like intracellular NAD+ testing and biomarker assessment provide precise measurements of cellular energy status, enabling targeted interventions that address individual deficiencies rather than applying broad population-based recommendations.

Midlife becomes a stage where informed interventions can dramatically alter aging trajectories. The integration of continuous biomarker monitoring with Artificial Intelligence will further enhance this approach, creating feedback loops that enable real-time optimization based on individual responses.

Measuring what matters

The scientific foundation for resilience- based health policy exists today. NAD+ biology provides a concrete, measurable framework for intervention, while emerging technologies make personalized implementation practical at scale.

Access to resilience testing and midlife longevity protocols represents not just sound health policy but economic necessity. Managing ever-increasing chronic disease burdens with shrinking workforces is unsustainable. By measuring and maintaining midlife

resilience, we can preserve not just individual health but the foundation of productive, independent societies.

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