

Peer Review

Review of: "The Future of Longevity Medicine: Repairing the Parts or Preserving the Whole? Holmes' Carriage as a Metaphor for Two Fundamentally Different Models of Aging"

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This commentary raises an interesting question — whether "coherence loss" rather than damage accumulation drives terminal decline — but the central metaphor is not new, and several of its empirical claims are either uncited or contradicted by existing literature.

First, Holmes' "one-hoss shay" has already been the standard reference point in this exact debate for over 40 years: Fries and Crapo invoked it explicitly in *Vitality and Aging* (1981) to argue for the "rectangular curve" and compression of morbidity that this manuscript re-derives without citing that source, and Gavrilov and Gavrilova's *reliability theory of aging* (J Theor Biol, 2001) built a formal mathematical treatment of the same "simultaneous vs. sequential component failure" distinction, explicitly using the one-hoss-shay as the idealized non-redundant limiting case. Carey and colleagues (Science, 1998) also discuss and critique the shay as a biologically unrealistic limit given reliability-engineering constraints on redundant biological systems. None of this prior art is cited, and the manuscript would be considerably strengthened — and more honestly positioned — by engaging with it rather than presenting the metaphor as original.

Second, the manuscript's key empirical claim — that traditional/rural populations "sometimes achieve equal or even greater lifespan" than wealthy populations with a short terminal decline — is asserted without a single data citation, and the literature does not support it. Global life-expectancy data (UN, WHO/GBD) show a strong, consistent positive correlation between socioeconomic development and

lifespan, not parity. The "Blue Zones" example the authors cite as evidence (ref [4], Buettner 2008) has itself been substantially discredited: Saul Newman's demographic audit (winner of the 2024 Ig Nobel Prize in Demography) found that supposed longevity hotspots correlate with poor birth/death record-keeping, missing birth certificates, and pension fraud rather than genuine exceptional longevity — several "Blue Zones" shrank by ~90% in life expectancy after basic error correction. Citing Buettner (2008) as support for this claim without acknowledging the subsequent debunking is a citation problem the authors should fix directly.

Third, the in-text citations don't support the sentences they're attached to. References [1]–[3] (Fedichev 2024, Barabási's *Network Science* textbook, Alon's *Systems Biology* textbook) are reused as a blanket citation after nearly every mention of "systemic coherence" throughout the piece, but none of these are empirical sources for the specific claims being made about morbidity compression, rural-vs-wealthy lifespan comparisons, or terminal decline kinetics — two are general-purpose textbooks, and the third is a single conceptual review.

Fourth, even the "compression of morbidity" hypothesis that anchors the whole argument (Fries 1980) is itself contested in the demographic literature, with a substantial body of subsequent work (e.g., Crimmins and colleagues) reporting evidence for *expansion* rather than compression of morbidity in many aging populations — this nuance deserves acknowledgment rather than being treated as settled.

Finally, "systemic coherence" is used throughout as an evocative but operationally undefined construct. If the authors want this to become a genuine research program rather than a metaphor, I'd encourage them to propose concrete, measurable candidates — e.g., composite frailty indices and network-based physiological dysregulation models (Mitnitski/Rockwood/Rutenberg-style frailty networks), multi-organ biological-age-gap ("organ clock") divergence, allostatic load batteries, heart-rate-variability/autonomic coupling metrics, or cross-system entropy/synchrony measures — and to specify how these would be prospectively tracked and validated against actual morbidity-compression endpoints in longitudinal cohorts. Without that, the coherent-vs-fragmented framing remains a compelling narrative device rather than a testable hypothesis.

References

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Declarations

Potential competing interests: No potential competing interests to declare.