

# ARTICLE

## MECHANISM MATTERS

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## THE PREMISE

Medicine is built upon two great traditions: *empiricism* – the disciplined observation of outcomes – and *mechanism* – the understanding of why those outcomes occur. Over the past half-century, the former has eclipsed the latter. Evidence-based medicine, once intended to harmonize observation and mechanism, has devolved into a hierarchy that prizes numerical association over biological coherence. Clinical truth has become something to be *measured*, not *explained*.

But medicine cannot be sustained on inference alone. Without mechanism, evidence is brittle—vulnerable to misinterpretation, inapplicable across contexts, and blind to unseen harm. Mechanism is not a luxury of theory; it is the moral geometry that keeps empiricism honest.

## THE DISTORTION

The modern research ecosystem has devalued mechanism through several intertwined forces:

- **The cult of the outcome.** Journals and funders reward large datasets and statistically significant results, not careful mechanistic reasoning. Trials report that an intervention works but rarely how.
- **The fragmentation of knowledge.** Disciplinary silos isolate molecular biologists from clinicians, and data scientists from physiologists. The connective tissue of explanation is lost in translation.
- **Algorithmic opacity.** Machine learning models generate correlations too complex to interpret, producing predictions without comprehension.
- **Commercial acceleration.** Pharmaceutical pipelines built on surrogate biomarkers or high-throughput screens bypass mechanism to reduce time-to-market. The result is reproducible efficacy without conceptual integrity.

When mechanism is ignored, error becomes undetectable. We can no longer distinguish a genuine causal chain from a statistical coincidence.

## THE CONSEQUENCE

The absence of mechanistic grounding leads to three major failures:

- **Clinical fragility.** Interventions derived from weak causal reasoning fail under slightly different conditions because no one knows what drives their effect.
- **Ethical opacity.** Without understanding how a therapy works, informed consent becomes hollow; we are asking patients to trust a black box.
- **Scientific amnesia.** Lacking mechanistic continuity, knowledge becomes disposable. Each new dataset overwrites the last rather than extending it.

At scale, this erodes the moral legitimacy of biomedicine. A discipline that heals without understanding risks becoming one that harms without noticing.

## THE WAY FORWARD

Re-centering mechanism requires both intellectual and structural reform:

- **Reinstate mechanism as a criterion of proof.** Require that empirical claims describe plausible biological or behavioral pathways.
- **Reunite data and biology.** Incentivize cross-disciplinary research that integrates statistical findings with mechanistic modeling and experimental validation.
- **Use AI as microscope, not oracle.** Machine learning should generate mechanistic hypotheses, not replace them.
- **Reform journals and funding.** Reward causal explanation and replication across mechanistic axes, not just outcome heterogeneity.
- **Educate for causality.** Training in medicine should emphasize how systems behave—not just how signals correlate.

Mechanism is the conscience of empiricism. Without it, data tell us what happens; with it, they tell us *why*, and therefore *what to do next*.

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