



ARTICLE

FROM SURROGATES TO OUTCOMES

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THE PREMISE

Medicine's moral purpose is to improve lives, not numbers. Yet modern clinical science has inverted that priority. Increasingly, we evaluate interventions not by their impact on survival, function, or well-being, but by their influence on surrogate markers—biochemical or radiographic signals presumed to represent those outcomes. Surrogates are seductive: easy to measure, fast to change, and statistically cooperative. They make research cheaper, quicker, and more publishable.

But surrogates are not outcomes. They are hypotheses about causality—claims that one measurable variable stands reliably in for a human experience. When those claims fail, the consequences are measured not in p-values, but in lives.

THE DISTORTION

The overreliance on surrogates distorts every stage of clinical inquiry:

- **Design distortion.** Trials substitute short-term biomarkers (e.g., cholesterol, viral load, tumor size) for patient-centered endpoints (e.g., mortality, mobility, quality of life). Success becomes a matter of laboratory change, not lived benefit.
- **Commercial expediency.** Surrogates accelerate regulatory approval, enabling drugs and devices to reach market before their true impact is known. Negative downstream findings rarely retract early triumphs.
- **Scientific myopia.** Mechanisms that improve surrogates can harm outcomes. Lowering blood sugar may worsen mortality; shrinking tumors may extend suffering without prolonging life.
- **Statistical convenience.** Continuous laboratory values yield high statistical power, disguising trivial effects as breakthroughs.

When the measurement becomes the mission, medicine loses its moral center.

THE CONSEQUENCE

This surrogate obsession erodes both credibility and care:

- **Clinical misdirection.** Physicians act on numbers that look better but patients who do not feel better. Treatments calibrated to markers rather than meaning distort clinical judgment.
- **Regulatory failure.** Agencies approve interventions with incomplete evidence of benefit, shifting risk onto the public.
- **Economic waste.** Billions are spent optimizing variables that never mattered to patients, while research addressing outcomes of dignity—pain, independence, comfort—remains underfunded.
- **Ethical regression.** When efficacy is defined by convenience, compassion becomes collateral damage.

The system thus sustains itself on a statistical mirage, confusing motion with progress.

THE WAY FORWARD

Restoring moral coherence to measurement demands a return to purpose:

- **Define outcomes before surrogates.** Let patient value—not laboratory feasibility—determine what counts as success.
- **Validate surrogates empirically.** Demand longitudinal evidence that a change in the marker reliably predicts a change in outcome across contexts.
- **Design hybrid endpoints.** Combine mechanistic precision with patient-centered meaning—biological insight anchored to functional relevance.
- **Strengthen regulatory ethics.** Require post-approval outcome trials for surrogate-based approvals, with transparent public disclosure.

- **Reframe success.** An effective therapy is one that restores capacity, not merely normalizes data. The metric must again serve the mission.

Medicine's greatest test is not whether it can change numbers, but whether it can change lives. Surrogates may signal progress, but outcomes define it.

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