

EDITOR'S PAGE



When Evidence Meets the System

The Distance From Proof to Practice

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Some things seem so straightforward that they hardly seem worth testing. For example, a shorter protocol to rule out myocardial infarction should be tested rigorously to determine whether it misses more patients. But who would think to test whether it actually shortens evaluation times? Surely it must.

Yet, what is good in concept does not always translate into what is good in practice.

For everything we do, we ought to ask, in the end: how have we changed the experience for patients? Are they doing better? Is there anything discernible in their favor? That was always the core of outcomes research: the last mile. It does not matter how much we have figured out, how clever we are, or how many trials we have run. What have we actually done for people? Many of us would argue that this is all that ultimately matters.

By the time the 0/1-hour high-sensitivity troponin pathway entered clinical guidelines, it had the evidence that most people had sought: guideline endorsement and extensive validation across algorithms and assays.¹⁻³ More evidence has accumulated since, including prospective comparisons of accelerated pathways and evaluation of a next-generation troponin assay.^{4,5} The pathway promised faster classification of patients with suspected acute coronary syndrome, earlier discharge, and relief for crowded emergency departments.

The MACRO-S-2 (Mersey Acute Coronary Syndrome Rule-Out Study 2) investigators tested that promise in 3,543 patients at 2 busy emergency departments in northwest England. What they found was surprising. The 0/1-hour pathway did not significantly increase discharge within 4 hours, the primary efficiency endpoint: 21.8% vs 19.2%. It was not without benefit. It shortened median emergency department stay by

39 minutes (from 312 to 273 minutes) and increased the proportion of patients discharged by 5 hours, from 32.4% to 41.8%. The pathway also met the prespecified noninferiority criterion for 30-day safety among patients who were discharged, although the number of events limited definitive reassurance. Still, a 2-hour advantage in the protocol became a 39-minute advantage in practice, with no statistically significant difference in who went home by 4 hours.⁶

Why was so much of the theoretical advantage lost? The answer lies in the mechanics. These were branching pathways, not 2 identical clocks. Both allowed some patients to be ruled out from the initial blood sample alone. The first blood draw occurred a median of 47 minutes after arrival, and the result became available to the clinician 81 minutes later. In the 0/1-hour group, the repeat sample had already been drawn before the initial result was available in nearly 4 of 5 patients. In the 0/3-hour group, that occurred in only about 1 of 20 patients. Among patients eligible for rule-out from the initial sample, only 23% in the 0/1-hour group were discharged after that single measurement, compared with 70% in the 0/3-hour group. This asymmetry appears to have made the single-sample branch much harder to use in the faster pathway and likely contributed to the narrowing of its advantage. Pathway breaches, other testing, crowding, and the friction of clinical work narrowed the difference further.⁶

The system did not merely slow the algorithm. It changed how the algorithm worked. The intervention delivered in practice was not quite the intervention described on paper.

This is the quiet lesson beneath much of what we publish. Evidence does not reach the patient untouched. It passes through phlebotomy and a laboratory queue; through result transmission and a

clinician's attention; and through staffing, bed availability, competing demands, and the willingness to send someone home. By the time it arrives, its effect can be amplified, diminished, or transformed.

“The system did not merely slow the algorithm. It changed how the algorithm worked.”

As Wasfy⁷ observes in an Editor's Note, a pathway's effectiveness depends on the setting in which it is deployed. Crisanti et al⁸ make the operational requirements explicit: turnaround time, education, adherence, and quality assurance are not surrounding details. They help determine whether the pathway exists in practice at all. The trial did not test an algorithm. It tested an algorithm inside a hospital, and a pathway performs only as well as the system that carries it.

I learned this lesson directly. Two decades ago, we set out to shorten the time from a patient's arrival with ST-segment elevation myocardial infarction to opening the artery, the door-to-balloon time. The community measured the interval, fed the results back to those involved, standardized the steps, activated teams earlier, and made responsibility visible. Times fell nationally. The real lesson was that primary percutaneous coronary intervention was never an intervention in isolation. Its effectiveness depended on the system around it, and hospitals could get more from it by strengthening that context. Within any given period, patients treated faster had lower risk-adjusted mortality, even though the population-level relationship over time proved more complicated.^{9,10}

MACROS-2 represents one kind of distance from proof to practice: we know what to do, but a system may not yet do it reliably. Closing that operational gap will not come from sensitivity and specificity

alone. It requires asking whether the pathway is producing better results for patients. It requires a laboratory that returns results fast enough, a workflow that makes the next action clear, and a defined owner for each step. These are not footnotes to a pathway's effectiveness. They are among its determinants.

For much of my career, discovery was treated as the scarce achievement and delivery as what followed. That hierarchy no longer holds. The traditional story of innovation ends with publication, regulatory approval, or a guideline recommendation. For the patient, that is often only the midpoint.

So, new evidence deserves not less enthusiasm, but harder questions. Exactly which decision should it change? What system is required to deliver the intervention as tested? And how will we know the patient is actually better off?

Discovery tells us what can work. Delivery determines what does work. The system is not merely the setting around the intervention. It is part of the intervention.

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