

EDITORIAL

Translating Clinical Guidelines Into Care Delivery Innovation: The Importance of Rigorous Methods for Generating Evidence

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Translating novel science and clinical guidelines into practice is a vital step toward improving the health of populations. This is particularly true for outpatient management and transitional care after hospital discharge, where social determinants of health and logistical complexities can obstruct patients from receiving the therapies they need.

See Article by Ho et al.

In the delivery of cardiovascular care, numerous apparent gaps exist. Many patients with atrial fibrillation are not on appropriate anticoagulation,¹ many heart failure readmissions appear preventable,² and many patients with a history of atherosclerotic cardiovascular disease are not on appropriate statin therapy.³ These gaps raise the possibility that innovations in care delivery could be associated with major improvements in quality. The impact of such interventions can be large, similar to the treatment effects of novel drugs and devices. In fact, one recent innovation, a remote lipid management program for patients at high atherosclerotic cardiovascular disease risk, achieved a 45% overall decrease in low-density lipoprotein through an algorithmic, navigator-led program.⁴ Given these observed quality gaps, it is critical to study the way we deliver care with the same rigor that we study other biomedical innovations.

However, evaluating differences in outcomes associated with innovations in care delivery is complex. Single-center results may not be widely generalizable to other patient populations or health care systems. Furthermore, results of nonrandomized observational analyses may be plagued by confounding and treatment selection bias. For example, patients who receive an intervention could differ from those who do not in ways that are hard to measure or adjust for. One striking example was the “hot-spotting” program created by the Camden Coalition of Healthcare Providers, designed to improve the quality of care and reduce spending for patients with very high utilization of healthcare services.⁵ The program identified medically and socially complex patients and provided them with a wide range of comprehensive face-to-face services. The program reached national prominence as a model for care delivery, and versions of it were adopted around the United States. However, when the model was tested in a randomized controlled trial of 800 patients, there was no significant difference in the study’s primary end point of 180-day readmissions. The authors noted that had the study focused solely on a single-arm comparison of the intervention group before and after program enrollment, they would have been misled by a 38% decline in readmissions. Such an apparent decline could have simply reflected regression to the mean. The true effect of the program, in this case, no effect, was only

Key Words: Editorials ■ care delivery ■ implementation science ■ innovation ■ pragmatic trials

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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evident after being subjected to randomization with a control group. Adding to the complexity of these methodological issues, however, is that similar interventions have been effective in other single-center randomized trials of high-risk patients.⁶ Accordingly, even randomized trials in different settings can yield discrepant results, underscoring the limited external validity of small trials.

Given the critical importance of understanding how to deliver better care and the difficulties interpreting smaller or observational analyses, large randomized controlled trials that involve multiple sites have a critical role. These types of trials, however, are logistically challenging and expensive.

As such, when large, multicenter studies of health care delivery interventions are attempted, the trialists should be warmly praised. In this issue of the *Journal of the American Heart Association (JAHA)*, Ho and colleagues implemented a multicenter trial aimed at improving P2Y12 medication adherence after percutaneous coronary intervention (PCI).⁷ Prior analyses have demonstrated that a significant percentage of patients delay filling their P2Y12 medication on hospital discharge, and many others discontinue their P2Y12 agent prematurely. Given the strong evidence for the benefit of a course of a P2Y12 inhibitor after PCI, developing approaches to increase medication adherence *should* improve patient outcomes.

Despite implementing a multifaceted program that included patient education, delivery of the medication to the bedside, reminder calls, and patient outreach, the intervention produced mixed results. Patients were less likely to delay filling their P2Y12 medication at discharge and were more likely to be adherent at 1 year. However, those in the intervention group had higher rates of 1-year major adverse cardiovascular events, driven primarily by repeated. In addition, there were logistical challenges implementing the intervention, including institutional review board delays, staffing difficulties, and delays in rolling out the intervention at study sites. These reported challenges highlight how difficult large, multicenter pragmatic trials are to implement.

Using a stepped-wedge approach, this trial demonstrates that a pragmatic intervention – designed to facilitate broad adoption – can reduce P2Y12 prescription filling delays and improve overall adherence over a 1-year period. Although the increased rate of repeated is difficult to interpret, it is reassuring (and in line with P2Y12 clinical trial data) that subsequent myocardial infarction, stroke, and death were reduced in the intervention arm. Accordingly, despite conflicting clinical outcomes, this study is an important addition to the science of improving P2Y12 adherence after PCI.

To improve the quality of pragmatic implementation trials in cardiology, it is important to reflect on prior

work to determine themes that may be helpful in designing future interventions.

LEARNING FROM PAST IMPLEMENTATION CHALLENGES

Complex problems that require multiple levels of interventions and are dependent on many external factors pose a challenge for implementation science. A prime example that has been studied repeatedly without significant success are interventions targeting heart failure readmissions. Despite incredibly varied, innovative, and intensive interventions, few (if any) have demonstrated success when tested in randomized controlled trials.^{8–13} Most recently, Asch and colleagues provided patients with digital scales, electronic pill bottles, and lottery-based financial incentives for adherence.⁸ Each patient's longitudinal clinician was sent weight information via the electronic health record, and patients were called by study staff if they were not adherent to daily weights or did not open their diuretic pill bottles for an extended period. Despite the innovative design and use of behavioral economics, outcomes were identical between the intervention and control arms of the study. Although a recent randomized controlled trial in Poland demonstrated a benefit of a multimodal telemedicine approach to preventing heart failure readmissions,¹⁴ it may lack generalizability to the US healthcare system and heart failure population with heart failure, especially considering the numerous similar studies in the United States that have produced negative results. Preventing readmissions after an acute heart failure exacerbation requires a multitude of interventions and is likely dependent on many external factors (eg, home environment and access to healthy food), which are more difficult to modify in a clinical intervention.

Clinical scenarios that require significant patient and provider “buy-in” pose an additional barrier to success. For instance, appropriate anticoagulation in atrial fibrillation is one such arena that has been frequently targeted in implementation research. Despite a host of innovative approaches aimed at improving guideline-recommended anticoagulation prescribing, these interventions have largely failed.^{15–18} In the SUPPORT-AF II (Supporting Use of Anticoagulants Through Provider Profiling of Oral Anticoagulant Therapy for Atrial Fibrillation) trial, clinicians were sent clear graphics highlighting their anticoagulation percentage relative to peers as well as information about the calculated 5-year stroke risk (estimated via the CHA₂DS₂-VASC score) for patients on their panel who have atrial fibrillation but were not on anticoagulation.¹⁸ In addition, clinicians were offered academic detailing to learn more about the appropriate use of anticoagulation in atrial fibrillation. Despite these efforts, there was no

increase in anticoagulation in the intervention group. When physicians were surveyed as to the reasons anticoagulation was not instituted, clinical gestalt (whether justifiable or not) and patient preference were the primary justifications for not initiating anticoagulation. In contrast, a study aimed at improving anticoagulation uptake in middle-income countries through education efforts targeting both patients and clinicians yielded a significant increase in anticoagulation uptake.¹⁹ From this and other work, we can infer that interventions requiring significant “buy-in” to alter strongly held baseline beliefs may face implementation challenges.

LEARNING FROM PAST IMPLEMENTATION SUCCESSES

Focused interventions with clear metrics of success may be optimal for testing innovative models of care delivery. Two such areas where novel implementation strategies have demonstrated improved outcomes include hypertension and dyslipidemia. Both conditions have clear targets and clear methods to achieve guideline-based goals. With clear, objective targets, the management challenge is medication titration and frequent follow-up. For these disease states, creating algorithmized pathways and training nonphysicians to institute and monitor progress have yielded impressive results.^{4,20,21} Accordingly, testing interventions in clinical conditions for which there is broad management agreement may yield important information.²² As past successes have demonstrated, creating programs that unload (rather than burden) the primary longitudinal clinician may further increase the chance of success.

Finally, interventions that harness insights from behavioral science to improve care delivery may prove beneficial. Specifically, certain types of intervention strategies, commonly known as “nudges,” are designed to influence behavior without restricting choice.²³ For instance, when researchers instituted a default opt-out decision pathway for referral to cardiac rehabilitation, they noted a 47% increase in rehabilitation referrals.²⁴ This type of strategy has also been implemented in other clinical areas with promising results.²³ Intentionally designing and optimizing health technology to facilitate appropriate clinical decisions without burdening the clinician can incorporate these insights from behavioral science to improve care delivery.²⁵

THE NECESSARY PATH FORWARD FOR TRIALS IN CARDIOLOGY CARE DELIVERY INNOVATION

Both the importance and the difficulty of determining optimal approaches for improving care delivery cannot

be overstated. As we work to close existing gaps in clinical care and as new technologies emerge, methods to widely implement evidence-based medical practices must evolve. As part of this important work, Ho and colleagues implemented a multilayered program to improve P2Y12 adherence. Although their intervention produced mixed results, it nevertheless stands as an important model for implementation science. As a large, multicenter, step-wedged randomized controlled trial, this work reinforces the importance – and the difficulty – of subjecting care delivery innovation to rigorous testing methods. The logistical challenges that these trialists encountered (namely, institutional review board delays, staffing difficulties, and site drop out) are likely to be a challenge for other investigators designing large, multicenter trials of care delivery. Anticipating these difficulties or exploring creative collaborations with established clinical trials groups around the country to streamline trial implementation may decrease the barriers to successful implementation research. Future endeavors should look to this work and others in this important field as guideposts for innovating, testing, and implementing novel approaches with the goal of improving care delivery.

ARTICLE INFORMATION

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Disclosures

Dr Wasfy is supported by a grant from the American Heart Association (18 CDA 34110215) and has received past consulting fees from Pfizer. Dr Berman has no disclosures to report.

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