A decade ago, cardiovascular imaging was buffeted by a perfect storm of disproportionate growth, unexplained geographic variability, skyrocketing costs, inadequate evidence base, and competition among specialties and modalities. Fortunately, the imaging community and, more broadly, the house of cardiology have appropriately responded to the crisis by fully embracing the concept of value over volume in cardiovascular imaging. As a result, novel initiatives such as appropriate use criteria (first issued in 2005) (1), imaging quality frameworks (promulgated by a series of think tanks in 2005, 2008, and 2015 dedicated to imaging quality [2–4]), subspecialty journals including iJACC and Circulation Cardiovascular Imaging (both launched in 2008) and the European Journal of Cardiovascular Imaging (2011), and close radiology-cardiology collaborations (through such organizations as the Society of Cardiovascular Computed Tomography and the Society for Cardiovascular Magnetic Resonance) have become fully accepted parts of the rich fabric of cardiovascular imaging today. The commitment to value in imaging care is also apparent in the explosion of high-quality evidence generated in the past decade regarding the use of cardiovascular imaging. Indeed, 10 years ago, the idea of a special issue of iJACC devoted to randomized controlled trials would not have been possible. The visual nature of imaging provided clinicians and researchers alike with certainty as to its value and the illusion perhaps that no further evidence was needed. However, the mandate to better justify imaging care overrode the reluctance to investigate what we “know.” Today the reality of imaging research is reflected by the contents of this special issue: a robust collection of methods papers supporting imaging research and placing it in context, topical reviews covering literally dozens of imaging randomized trials, and original research papers.

However, despite this success, there remain many challenges to imaging clinical and translational research. Some of these pertain only to cardiovascular imaging, whereas others are shared more broadly by all diagnostic tests. Although those highlighted here do not constitute a complete list, how we address these questions will define the next decade of cardiovascular imaging research.

First, patients most commonly undergo imaging for elucidation of symptoms prior to receiving diagnoses and often in the absence of established disease. Because many, if not most, patients will not have the disease in question, even fewer will have adverse outcomes associated with that disease. Another common use of imaging, for monitoring stable disease in the absence of symptoms, can also be associated with few adverse outcomes. Thus, even in “intermediate”-risk populations such as those presenting with stable chest pain (5), clinical events will be uncommon, making it exceedingly difficult to demonstrate differences in major outcomes with any precision when comparing competing imaging strategies. This applies to patient-reported quality of life as well; it is often quite high at trial enrollment and therefore harder to affect, especially compared with prior trials enrolling sicker, disease-based
populations. Moreover, many of the health status measures were developed in higher risk patient cohorts, and their precision in imaging populations remains ill defined.

Second, as with all randomized trials, there is a continuum of design goals ranging from traditional demonstration of efficacy using an explanatory approach to assessment of effectiveness using a pragmatic approach. The tension between these 2 poles informs many aspects of trial design, beginning with the imaging itself: when should imaging be performed and analyzed in the community, reflecting real-world care? Or when should imaging research be an “experts only” undertaking with rigorously controlled image acquisition followed by analysis in highly specialized core laboratories capable of providing precision and accuracy in their measurements far beyond the capabilities of most imaging laboratories (6)? The latter would ensure the delivery of a uniform imaging “intervention” akin to tracking pill counts in a pharmaceutical trial, and the results would describe what imaging is capable of in an ideal world. However, this approach is time consuming and expensive and may not be reproducible. There is no single correct approach; no size fits all. Chest pain trials (5,7) have tended toward the pragmatic and generalizable, whereas valve-related studies using core laboratories have contributed mechanistic insights that substantially increased the safety of newly introduced procedures such as transcatheter aortic valve replacement (8). Nevertheless, an important factor in interpreting trial results is the extent to which variability in the quality of image performance and interpretation may have affected the findings or, in the case of highly controlled imaging assessments, whether the results can be replicated in routine care.

Third, the linkage between the performance of a diagnostic test and a measurement of a clinical outcome is indirect in almost all cases, as imaging findings must first translate into changes in diagnosis, then changes in treatment, followed by treatment effectiveness to have an impact on outcomes. Coupled with the low event rates in imaging populations, this indirect path to clinical impact provides the rationale for the appropriate use of intermediate outcomes as endpoints and may require consideration of these nontraditional outcomes for successful research. The range of potential intermediate endpoints is broad (9). However, the indirect connection between imaging and events can have implications beyond the choice of endpoints and analysis plans, including the question of whether a trial should specify in detail how imaging findings will be acted on during the course of the study or leave the response to the local care team to decide how, or even if, they need to be incorporated into care. Many trials have taken a pragmatic approach, allowing local clinicians to decide how to incorporate imaging results, whereas others have been more prescriptive. This choice can dramatically affect treatment decisions and trial results; subgroup exploratory analyses examining only centers familiar with the novel imaging strategy under study and expert in implementing changes in care can provide insight into real-world implementation of imaging-guided practices that result in effective patient care (10).

Fourth, although most randomized trials of drugs and devices ask questions related to efficacy (i.e., does this therapeutic intervention improve clinical outcomes in this disease setting?), most imaging trials ask questions related to the relative benefit of 1 imaging strategy versus another. These types of questions lend themselves well to comparative effectiveness trials, and most of the trials reviewed in this special issue compare imaging modalities. However, comparative effectiveness designs generally sidestep the question of whether imaging is indicated in the first place, making it difficult to assess when testing is not indicated or should be deferred. To date, although the outcomes in most imaging trials would support such an approach, few studies have addressed such questions. As a variation on this question, other trials have studied conditional testing: the use of a second test or analysis only if the results of the first are positive, such as was performed in the CRESCENT (Computed Tomography Versus Exercise Testing in Suspected Coronary Artery Disease) trial, in which computed tomographic angiography was performed only in patients with positive calcium scores (11).

Fifth, although guidelines and standards documents necessarily lag behind evidence generation, the incorporation of imaging data into guidelines can be slow. The 2012 American College of Cardiology and American Heart Association guidelines for stable ischemic heart disease have not yet been updated on the basis of the completed, multiple large randomized trials in this patient population published 2 years ago; even the U.K. National Institute for Health and Care Excellence, in its guidelines for chest pain updated in late 2016, based its decision to recommend computed tomographic angiography as the test of choice for those with typical angina and no history of heart disease largely on cost-effectiveness rather than on the now robust evidence base, including clinical outcomes, with different diagnostic strategies (12). Implementation in the community can lag further
behind, dependent not only on dissemination of trial results but also on reimbursement changes and, at times, imperfect cardiology-radiology collaborations.

Finally, to continue the strong progress achieved in the past decade, imaging research will require ongoing access to research funding. The crisis confronting imaging in the early to mid-2000s provided a strong motivation to funding agencies to explore the validity of an imaging outcome research paradigm, first through a workshop (13) and then through funding of several randomized trials, including PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) (14) and ROMICAT (Rule Out Myocardial Infarction/Ischemia Using Computer Assisted Tomography) (15). This sense of urgency has dissipated and momentum slowed by a sobering recognition of the difficulties involved in performing imaging outcomes randomized trials. To date, industry has not provided funding sufficient for large trials, nor have payers engaged extensively (with the notable exception of the Michigan Advanced Cardiovascular Imaging Consortium coronary computed tomographic angiography observational registry) (16), despite calls for enhanced quality. There is much that remains to be learned, but without ongoing research funding and engagement, what should be the celebration of our initial successes could instead be heralding the premature withering of future investigation.

The U.S. health care delivery system is in the midst of a profound redesign intended to hold physicians and providers more accountable for quality of care and patient health. Thus, the volume-to-value transitions of the past decade in cardiovascular imaging are prescient. Robust imaging evidence, including outcomes-based randomized controlled trials, continues to be needed to support this aim. Over the past decade, we have learned a great deal about what constitutes patient-centered imaging in cardiovascular medicine, but also much about how to perform imaging outcomes research. Together, these advances, summarized in the papers in this special issue, will provide a strong foundation for imagers and imaging clinical scientists into the future.

ADDRESS FOR CORRESPONDENCE: Dr. Jagat Narula, Icahn School of Medicine at Mount Sinai, One Gustave Levy Place, New York, New York 10029. E-mail: narula@mountsinai.org.

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