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Outcomes Research Generating Evidence for Best Practice and Policies

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In an era of fundamental concerns about the way that health care is provided to individuals and populations, there is a need for a scientific discipline to bridge the capabilities of the medical profession and the best interests of patients and society. Assumptions about what is achieved by our health-care system should be tested by evidence of what actually results from our efforts. Insights from the experience of patients should provide accountability for the investment in health care. Pledges of equity and fairness should be accompanied by proof that care is provided according to need and not race/ethnicity, sex, or socioeconomic status. The recognition that practical and applied knowledge was needed to guide practice and policy created an opportunity for the emergence of outcomes research. With this article, which provides a context for outcomes research, *Circulation* introduces a series that focuses on key topics in the field.

Outcomes research is defined by its focus on the result of healthcare interventions and policies.^{1,2} Themes of outcomes research are well reflected by *Crossing the Quality Chasm: A New Health System for the 21st Century*, a book from the Institute of Medicine that focuses attention on safety, effectiveness, equity, efficiency, timeliness, and patient-centeredness as key properties of high-quality health systems.³ This taxonomy provides a convenient organization for the survey of outcomes research. Moreover, these areas also provide important targets of study and intervention.

Additional emphasis is on the broad spectrum of patient outcomes in recognition that what seems best for patients and populations based on various sources of knowledge and intermediate or “proxy” outcomes often does not achieve its promise in actual practice and can occasionally produce unintended harmful consequences. The methods are broad and encompass the range of tools capable of resolving uncertainties about the outcomes of medical care.

As an integrated, multidisciplinary field of inquiry, outcomes research spans knowledge generation, translation, and use. The knowledge from outcomes research studies can have direct application to practice or can shape more formative research in the laboratory. It synthesizes aspects of existing disciplines to solve clinical and policy research problems. It

stands at the interface of clinical medicine, clinical epidemiology, health services delivery research, and public health, as well as the more basic biological, mathematical, and social sciences. The research particularly uses the basic sciences of statistics and epidemiology with a clinical, public health, and policy orientation. Moreover, the research commonly draws on the fields of economics, psychology, sociology, anthropology, and the management sciences. Investigators in the field commonly have advanced degrees in one of the core disciplines or have spent additional time acquiring methodological skills.⁴

Improving practice and policy, building upon a strong evidence base, requires attention to science and action. The intent of the research is not only to identify shortfalls in practice but also to develop strategies to improve care and ultimately prevent disease or mitigate its impact. Through an emphasis on accountability, outcomes research seeks to ensure that interventions and policies have their desired effect.

In the last decade, outcomes research in cardiovascular disease has experienced substantial growth. In 1999, the American Heart Association and the American College of Cardiology cosponsored the first Scientific Forum on Quality of Care and Outcomes Research in Cardiovascular Disease and Stroke, which is continuing under the primary auspices of the AHA. In 2005, the National Heart, Lung, and Blood Institute published a report outlining its priorities for outcomes research.⁵ The strategic plan of the institute, published last year, highlights the importance of research that can improve practice and policy.⁶ In 2005, *Circulation* introduced a category for articles in health services research and outcomes research, and the *Journal of the American College of Cardiology* publishes an annual year-in-review article on outcomes research.⁷⁻⁹ Nevertheless, there remains a need for greater investment in this research. Moses and colleagues¹⁰ estimated that although the United States spends an estimated 5.6% of its total health expenditures on biomedical research, <0.1% is allocated to health services research. This year, the new journal *Circulation: Cardiovascular Quality and Outcomes* will launch.

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The following sections describe examples of outcomes research and its promise for influencing practice. The topic areas follow the healthcare system themes noted by the Institute of Medicine, with the caveat of considerable overlap between the areas and a taxonomy that is not intended to create mutually exclusive categories. Moreover, the review is not intended to be exhaustive but rather to provide examples of the spectrum of outcomes research.

Safety

Each year, many lives are lost in hospitals across the nation because of preventable accidents, oversights, miscues, and mistakes. Two women die while undergoing routine cardiac catheterization because oxygen tubing was accidentally connected to a nitrous oxide nozzle. Elsewhere, a missed diagnosis of cardiac tamponade and delays in communicating with an attending physician lead to the tragic death of a young man. The Institute of Medicine estimates that >300 000 such deaths occur each year as a result of lapses in patient safety.¹¹

Not unexpectedly, the topic of safety is attracting more attention with the recognition that errors and mishaps are common in medicine and can have a profound effect on patients. Research on safety issues often focuses on the misuse of medical therapies and oversight in the course of clinical care, placing patients at unnecessary risk for adverse events. Like much of outcomes research, the investigations tend to illuminate gaps in care and areas for potential improvement; the question is not so much what to do but how best to do it, with attention to deficiencies in our current performance and application of knowledge.

Much of the research is focused initially on characterizing opportunities for improved practice by revealing patterns that often are obscured from view. For example, we often assume that the simple act of properly dosing medications is done correctly. However, research now shows that mistakes in dosing account for considerable morbidity and mortality. One such study was performed by Alexander and colleagues¹² regarding excess dosing of antiplatelet and antithrombin agents in the treatment of patients with non-ST-segment elevation acute coronary syndromes. In their cross-sectional, observational study using data from the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines (CRUSADE) registry, the investigators documented dosing errors in the use of unfractionated heparin, low-molecular-weight heparin, and glycoprotein IIb/IIIa inhibitors. The doses for these agents are based on body weight, and adjustment is necessary for each patient.

The rate of excess dosing and its association with adverse events were impressive and revealed a previously unappreciated safety issue. The investigators found that 42% of the patients who were administered antithrombotic agents received at least 1 initial dose that was higher than the recommended range. Excess dosing was associated with a significantly higher risk for major bleeding among those administered low-molecular-weight heparin and glycoprotein IIb/IIIa inhibitors. Moreover, there was a dose response, with the higher excess doses associated with the highest risks of

bleeding. The investigators estimated that perhaps 15% of all major bleeds in these patients may be attributable to excess dosing. In addition, patients who received excess doses were more likely to die during hospitalization and had longer hospital stays.

The research left unanswered the question about how best to remedy this safety issue. To address concerns about unfractionated heparin dosing, simple nomograms have been developed to guide practitioners. Balczak and others¹³ have shown that the use of such a simple intervention is highly effective in improving time to achieve a therapeutic range. However, in a single academic institution, they showed that even with strong institutional emphasis and the integration of the nomogram into the computer order entry system, use of the nomogram did not increase >10%. Physicians preferred to order a standard fixed dose for each patient even after being exposed to educational messages about the problems with this approach. This study illustrates that the identification of a problem is just a first step to improving practice and that even the development of an effective intervention is insufficient if adoption into practice cannot be achieved.

Another example is the important relationship between adherence to clopidogrel and outcomes in patients with drug-eluting stents. Spertus and colleagues¹⁴ revealed that patients who stopped taking clopidogrel within 30 days of the stent placement were 9 times more likely to die during the next 11 months. The recognition that 1 in 7 patients was not taking clopidogrel within 30 days and the apparent consequence led to an AHA advisory.¹⁵ Whether rates have improved is not yet known.

Effectiveness

Effectiveness research is at the core of outcomes research. The basic research questions address the unfortunate gap between what can be achieved through an intervention or policy and what is actually accomplished. Seemingly brilliant interventions may fall short of their promise for many reasons, including whether practices are adopted by clinicians, the way they are applied, the organizational context in which they are provided, the skill of the practitioners administering them, and the characteristics and behaviors of patients who are selected to receive them. Characterizing and addressing these gaps is an important focus for this field. Because of the nature of the inquiry, much of this work is best performed in observational studies, witnessing the experience of patients in actual practice.

The case of spironolactone illustrates the manner by which outcomes research can illuminate the discordance between published literature and practice. Basic biological studies have shown that aldosterone can promote the retention of sodium, the loss of magnesium and potassium, sympathetic activation, parasympathetic inhibition, myocardial and vascular fibrosis, baroreceptor dysfunction, and vascular damage. With the further observation that angiotensin-converting enzyme inhibitors do not fully block the production of aldosterone, a hypothesis emerged that the addition of an aldosterone antagonist might reduce the risk of death among patients with severe heart failure.

To test this hypothesis, the Randomized Aldactone Evaluation Study (RALES) randomized 1663 patients with severe heart failure and left ventricular ejection fraction $\leq 35\%$ to spironolactone or placebo.¹⁶ The study excluded patients with many comorbid conditions, including serum creatinine concentration >2.5 mg/dL (221 $\mu\text{mol/L}$) and a serum potassium concentration >5.0 mmol/L. The trial was so favorable for spironolactone that it was terminated early. At that point, spironolactone was associated with a 30% reduction in the risk of death over a mean follow-up period of 24 months. This high-profile 1999 *New England Journal of Medicine* publication was heralded as having important implications for the treatment of patients with heart failure, and guidelines quickly incorporated spironolactone as a Class I recommendation.¹⁷

Outcomes research also played a role in extending the trial data and investigating the translation of this new knowledge into practice. Several studies had shown that patients enrolled in trials represent only a subset of patients seen in practice, often because of restrictive inclusion criteria.^{18–20} Because trials cannot be performed in all relevant populations and because real-world conditions vary from those in trials, observational studies can be used to generate further knowledge that may in some cases support the extension of a treatment beyond the trial data and in other cases raise concerns about its use. For example, studies of β -blockade after an acute myocardial infarction (AMI) have supported its use in patients with diabetes and chronic pulmonary disease.^{21,22} The experience with spironolactone, however, raised concerns.

Spironolactone should have had dramatic effects on patients with heart failure, but in practice, there were problems. Aldosterone antagonists are known to increase the risk of hyperkalemia, particularly in patients with renal dysfunction, who were excluded from the trial for that reason. Renal dysfunction is common in patients with heart failure, making many ineligible for the drug. In fact, Masoudi et al²⁰ showed that only 25% of Medicare beneficiaries met the enrollment criteria for RALES.

There is also the question of the adoption of medications as new knowledge is translated into practice. Masoudi and colleagues²⁰ showed that the publication of RALES was associated with an increase in the use of spironolactone (from 3% to 21%), but many patients who would have been excluded from the trial were treated, including 14% of those with a creatinine level >2.5 mg/dL. Ko and coinvestigators²³ showed similar results in a Canadian study. These studies showed both slow and inappropriate adoption. The adverse consequences of this pattern were suggested by Juurlink and colleagues.²⁴ Using data from Ontario, they demonstrated that after the publication of RALES there was no evidence of a decrease in mortality after heart failure admissions and an abrupt increase in hyperkalemia-associated morbidity and mortality. After these disappointing studies, evidence is still lacking about how best to apply the lessons of RALES into practice so that patients benefit and harm is avoided.

The experience with spironolactone is not unique, and the delays in clinician adoption of guideline recommendations are common, as illustrated well by studies illuminating the

underuse of efficacious therapies for patients with an AMI.^{25–30} Other studies have documented marked heterogeneity in the use of guideline-based therapies.³¹ The factors associated with rapid and appropriate adoption tend to be a combination of organizational context and themes, as well as specific tools to facilitate practice.^{32,33} Outcomes research helps reveal these gaps in treatment through the development and reporting of quality measures and ultimately supports the recently documented improvements in practice.^{34,35}

Interventions to translate knowledge into practice also require rigorous evaluation; the expectation that an intervention will have an effect is insufficient. Work in this area may involve either trials or quasi-experimental designs. An example of recent promising work is the trial by Heidenreich and colleagues,³⁶ which seeks to rigorously test an intervention to inform doctors about guideline recommendations that are embedded within an echocardiography report to assist decision making at the point of care.

Missed opportunities in practice also may result from a lack of recognition of a diagnosis. In another example of cardiovascular outcomes research focusing on patient safety, Masoudi and colleagues³⁷ investigated the misinterpretation of emergency department ECGs in patients with an AMI in a retrospective cohort study of 1684 consecutive patients presenting to 5 emergency departments. Overall, 12% of the patients had a high-risk ECG abnormality that was not detected by the emergency department physician. Those with undetected high-risk findings had a higher risk of in-hospital mortality. This study contributes a foundation on which to base interventions to improve the interpretation of ECGs in the emergency department.

Patient adherence, another major impediment to the effectiveness of therapies, is an additional focal point for outcomes research. No matter how efficacious a medication, its effect depends largely on the patient's willingness and ability to take it. The consequence of nonadherence puts the issue in context. Spertus and colleagues¹⁴ demonstrated the relationship between premature discontinuation of thienopyridine therapy and the occurrence of adverse events for patients receiving drug-eluting stents. Ho and colleagues,³⁸ in a retrospective cohort study of 3998 patients with diabetes and ischemic heart disease, evaluated the use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, β -blockers, and statin medications on the basis of filled prescriptions. Approximately 20% of the patients were non-adherent, and those who did not fill prescriptions had a higher risk of mortality. In the Prospective Registry Evaluating Myocardial Infarction: Event and Recovery (PREMIER) study, Ho et al³⁹ reported that discontinuation of medications after hospitalization for an AMI is common and associated with an almost 4-fold increased risk of mortality in the subsequent year. Morgan and others⁴⁰ showed that difficulty taking medications in patients with heart failure is associated with worse health status, an association that was mediated in part by depressive symptoms. Rasmussen and colleagues,⁴¹ in a population-based study of 31 455 survivors of an AMI, found that among those treated with statins, lower adherence was associated with a higher mortality. Importantly, low adherence to calcium channel blockers, which are not ex-

pected to have a mortality effect, was not associated with a worse outcome. The findings in this study did not represent the result of an intrinsic characteristic of the patients (the "healthy adherer") but rather was related to the lack of taking a specific beneficial medication. From these studies, it is clear that opportunities to improve outcomes are being lost because of gaps in treatment based on patient adherence issues.

A future frontier is the development of strategies to improve adherence, including approaches that will involve patients in decisions and ensure that they understand the balance of risks and benefits. Weymiller and colleagues⁴² have shown that the use of a decision aid for patients deciding about the use of statins enhanced decision making from the patient perspective and increased adherence.

Effectiveness represents the final translation of medical knowledge into practice and benefit, a critically important step toward achieving the highest yield from our research. Investigations into effectiveness also reveal associations that may not have been predicted from extrapolating basic scientific observations, studies of more restricted populations under experimental circumstances, or investigations from the most experienced centers.

Equity

A health system should be built on fairness, an assumption that defies historic events and patterns that reflected discriminatory practices. Patients should have the opportunity to be treated according to their health needs, although it is not always so. The US government is committed to eliminating disparities, yet inequities remain. Such a goal should be guided not by rhetoric or polemic but by science. In this effort, outcomes research has a considerable role.

Outcomes research often is focused on whether nonclinical factors such as race, sex, and socioeconomic status influence the care and clinical outcomes of patients. The research can determine the underlying nature of the relationships and reveal opportunities for intervention. In addition, it can distinguish between differences in care that do not have consequence for patients and differences that contribute to disparities in outcomes.⁴³ The work is timely because many studies and documents, including an Institute of Medicine report, provide evidence of racial differences in healthcare use and outcomes.⁴⁴

An example of the contributions of outcomes research to this topic is seen in studies that explore the relationship between hospitals at which patients seek care and national racial differences in outcomes. Skinner et al,⁴⁵ using a national database, reported that risk-adjusted mortality after AMI is significantly higher in US hospitals that disproportionately serve black patients. In an article based on the Cooperative Cardiovascular Project, Barnato and colleagues⁴⁶ also reported that black patients more commonly received treatment at hospitals with higher mortality rates, and this pattern might explain some racial disparities. Bradley and others⁴⁷ reported that black patients had greater delays in the use of primary angioplasty treatment but that much of the racial difference was explained by the hospital effect. These studies do not obviate the burden on blacks, but they provide important insight into how the excess mortality is mediated.

The research does not assume that patient-level discrimination accounts for all differences.

Much attention has focused on the higher procedure rates in white compared with black patients. This simple observation does not provide insight into the reasons behind this occurrence or the consequences of this pattern. Chen and colleagues^{47a} approached the issue by investigating the role of physician race on racial patterns in the use of procedures for patients hospitalized with an AMI. Using a national retrospective database, they found, as expected, that black patients had lower rates of cardiac catheterization than their white counterparts. However, this pattern persisted whether the attending physician was white or black. Also interesting was that the adjusted mortality of black patients was lower than or similar to that of white patients over 3 years of follow-up. The findings bring into question the role of patient-level discrimination (although they do not exclude institutional discrimination) and the outcomes question of whether black patients are disadvantaged by this practice pattern, signaling the need for more work in the area and the rejection of simple explanations for the patterns and assumptions about their consequences.

Equity issues also cut across socioeconomic status, and outcomes research can highlight the multiple factors that in combination can produce gradients in outcomes by socioeconomic strata. For example, many studies show that patients with lower socioeconomic status have a greater mortality risk after an AMI.^{48–54} Bernheim and others⁵⁵ recently showed that the relationship was largely explained by differences in baseline clinical status on admission. Similarly, Alter and others⁴⁹ reported that past events and vascular risk factors accounted for much of the mortality benefit by income strata. The findings of these studies suggest that efforts to eliminate disparities might best be focused on factors preceding hospitalization, with a particular emphasis on risk factors.

Outcomes research also can provide insight into the effect of policy remedies. The prospect of full insurance for all patients has fostered the hope that problems related to financial barriers to care can be eliminated. However, Rahimi and colleagues⁵⁶ showed that financial barriers to health care and medications, which can occur among the insured and even in those with higher incomes, is a powerful independent predictor of adverse outcomes after an AMI. This study reveals that efforts to provide full insurance to the population should not obscure the deleterious effects of underinsurance.

Differences in care by socioeconomic status have been attributed to the incentives within our fee-for-service system. Alter and colleagues⁵⁰ addressed this hypothesis in a careful examination of these patterns in the Canadian universal coverage and access system. They found socioeconomic status to be strongly associated with coronary angiography and waiting times, suggesting that forces beyond the absence of universal coverage account for the influence of socioeconomic status and treatment patterns. Universal access is a desirable goal, but this study indicates that it should not be expected to eliminate all differences in treatments.

The effort to eliminate disparities will benefit from research that generates evidence about the underlying causes of differences in care and their effect on outcomes. The research

needs to investigate access, quality of care, effectiveness of care, and barriers to proper treatment and response. As interventions develop, this research also needs to be able to assess its effect.

Efficiency

Escalating healthcare costs are leading to concerns about the sustainability of the current system and its effect on the economy. The total spending on health care, about \$2.1 trillion in 2006, is expected to reach \$4.1 trillion by 2016, representing about 20% of the gross domestic product.⁵⁷ The extent of healthcare spending and its continuing growth raise important questions about waste in the system, inefficiencies, perverse incentives, moral hazards, conflicts of interest, and the effects that new clinical strategies and healthcare policies to constrain costs are having on patients.

Outcomes research may be best known for prominent studies that have questioned the relationship between health care use and outcomes. John Wennberg conducted seminal studies in that area, revealing marked geographic variation in practice that often is driven as much by the supply of services as the demand for them. In a 1973 article in *Science*, Wennberg and Gittelsohn² described marked variation in use, facilities, and expenditures across 13 hospital service areas in Vermont. In another example of their classic work, Wennberg and colleagues⁵⁸ compared hospital use and mortality among Medicare beneficiaries in Boston and New Haven, finding that rates of discharge, readmission, length of stay, and reimbursement were 47%, 29%, 15%, and 79% higher, respectively, in Boston, where the per capita availability of beds was higher. The difference was accounted for by high-variation medical conditions for which there is little consensus regarding criteria for hospitalization. For the low-variation conditions, the rates were similar. Interestingly, the mortality rates were similar in the 2 locations. A follow-up study reported that readmission rates were 64% higher in Boston even though mortality rates were similar.⁵⁹

Research making use of variations in care has provided insight into the use and effectiveness of cardiac procedures. In a study conducted in 1995, Guadagnoli and colleagues⁶⁰ found that coronary angiography was performed after AMI much more commonly in Texas compared with New York (45% versus 30%). However, over a 2-year period, patients from New York had a lower adjusted mortality rate, lower frequency of angina, and lower functional limitations. These results question the incremental benefit of the higher procedure rate.

In another pair of classic and elegant articles, Fisher and colleagues^{61,62} examined whether regions with higher expenditures achieved better outcomes. One study, which focused on healthcare expenditures for patients in the last 6 months of life, reported that patients in higher-spending regions received 60% more care even though their health status was similar. The higher spending was a result of more frequent physician visits, more testing, more procedures, and more use of specialists and hospitals. In the second study, 5-year AMI mortality rates reported in higher-spending regions were significantly higher, with no significant differences in satis-

faction. This type of inquiry forms a basis for efforts to eliminate wasteful variation in practice.

A series of articles by Tu and colleagues⁶³ made a similar point with a comparison between the United States and Canada. They described markedly higher angiography and revascularization procedure rates after an AMI for patients hospitalized in the United States without evidence of differences in mortality at 1 year. Interestingly, the pattern in Canada is similar to that of New England, suggesting that it is not merely a matter of a different healthcare delivery system.⁶⁴ A comparison of heart failure patients also showed higher procedure rates in the United States but similar mortality rates at 1 year of follow-up.⁶⁵ Mark and colleagues,⁶⁶ using data from the Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO) trial, found that the Canadian patients, who had undergone far fewer procedures, had more cardiac symptoms and worse functional status 1 year after AMI. These investigations suggest that the incremental contributions of these procedures may be reflected in quality of life but not mortality. A benefit cannot be excluded in studies that focus only on mortality.

Studies making use of comparisons within and across countries also have shown that although medicine may be built on a common body of knowledge, its application is quite variable. The practice pattern differences seen in these studies were not the result of differences in patients. In many cases, trials of these strategies could not be conducted because practitioners were certain of the benefit of their approach, even though it may have been at odds with the approach in another region.

To address differences in usage, some organizations are developing appropriateness criteria,⁶⁷ which often are based largely on expert consensus. With little evidence to support which of many common discretionary strategies for specific patients are most likely to promote better patient outcomes, the area of appropriateness criteria is in great need of further study.

Fiscal pressures are leading to policies and practices that are designed to restrain expenditures and limit variation. Outcomes research is poised to provide insights into how these approaches, often implemented with little scrutiny, affect patients. This research ideally includes the perspectives of economists, methodologists from various fields, and clinicians. For example, an increasing focus on length of stay as a surrogate of cost led to directed strategies to shorten hospitalization, resulting in marked national changes in practice. Strong incentives guided these actions because hospitals were most often paid a fixed amount for each hospitalization. Such efforts were instituted without any systematic evaluation of patients and without acknowledgment that such policies might affect patients. Even now there is little understanding of how this change affected patient outcomes, readmission rates, admission to skilled nursing facilities, or overall cost. In an examination of trends in the care of Medicare patients hospitalized with heart failure, Kosiborod and colleagues⁶⁸ reported marked reductions in length of stay with concomitant increases in readmission rates and discharges to skilled nursing facilities. The impact of overall

cost was not investigated, but it is certainly possible that the efforts to reduce lengths of stay did not improve efficiency.

The question remains whether, once found, innovative strategies to improve patient outcomes and reduce cost are appropriately adopted. Outcomes research also should address the gap between the research to reduce costs and outcomes and the policies that exist to facilitate their adoption. Trials that demonstrate the value of practice change leading to more efficient care can fail to be translated into policy. Many studies have demonstrated that disease management programs can reduce the risk of readmission for patients with heart failure,⁶⁹ improving outcomes for patients and decreasing the costs for the healthcare system. However, centers that showed remarkable results in disease management rarely continued the service after the trial concluded.⁷⁰ In addition, Medicare reforms implemented a model of heart failure management that differed from the studies without discussion of the scientific literature.

Finally, ways in which physicians and institutions may be influenced that may not be in the best interest of patients and society require further examination. The intermingling of marketing, science, and payments to physicians and institutions can produce inefficient practice patterns that lead to wasted resources. These influences, such as payments to physicians, are unfortunately not transparent. Ross and colleagues⁷¹ revealed that even states with mandated disclosure of payments to physicians failed to provide access, and there is little information on the effect of these relationships. Studies are needed to explore conflicts of interest and their impact on patient care and outcomes.

Timeliness

Timeliness in this context often refers to access issues within the healthcare system. If patients encounter obstacles to care, they are denied the opportunity to benefit from care. In a society in which millions are uninsured and underinsured, barriers to access can profoundly affect patient outcomes. Efforts in this topic overlap considerably with work to understand and promote equity within the healthcare system.

Timeliness can also refer to system responsiveness. Much of medical education focuses on what should be done for patients with the assumption that the implementation is a straightforward process; our experience and the findings of outcomes research contrast with that view. Studies can clearly indicate what should be done for patients, but studies of practice reveal variability. Outcomes research can focus on how best to improve care, with an emphasis on complementary strategies about “how” to translate the “what” that occurs in practice.

With respect to timeliness, this concept may be best illustrated by focusing on time to reperfusion for patients with ST-segment elevation myocardial infarction.⁷² Studies have demonstrated that rapid treatment of patients with ST-segment elevation myocardial infarction is essential, with mortality rates increasing as delays accrue.⁷³ Moreover, there is considerable variation across the country, with relatively few patients being treated within guideline recommendations.⁷⁴

Using a mixed-methods approach that combines qualitative and quantitative research, Bradley and coworkers^{75–77} investigated the factors that allowed certain institutions to excel in their timeliness. Eight themes were common among the top performers: commitment to an explicit goal to improve door-to-balloon time motivated by internal and external pressures, senior management support, innovative protocols, flexibility in refining standardized protocols, uncompromising individual clinical leaders, collaborative teams, data feedback to monitor progress and to identify problems and successes, and an organizational culture that fostered resilience to challenges or setbacks in improvement efforts. A national survey revealed 6 strategies that were significantly associated with a faster door-to-balloon time, including emergency medicine physician activation of the catheterization laboratory, a single call system to a central page operator to activate the laboratory, emergency department activation of the catheterization laboratory while the patient is en route to the hospital, the expectation that staff arrive in the catheterization laboratory within 20 minutes of being paged (versus >30 minutes), having an attending cardiologist on site at all times, and use of real-time data feedback by emergency department and catheterization laboratory staff.

This research illustrates the possibility of linking scholarship with adoption of knowledge. In an effort to leverage the publication of the article about effective strategies, Door-to-Balloon (D2B): An Alliance for Quality was launched by the American College of Cardiology, along with 38 partners, including the AHA; National Heart, Lung, and Blood Institute; and American College of Emergency Physicians.^{77a} This effort, which enrolled >1000 hospitals, seeks to improve the timeliness of primary percutaneous coronary intervention through the adoption of many of the evidence-based strategies.

Patient-Centeredness

Patients care about more than survival and events or intermediate or proxy outcomes like premature ventricular beats, blood pressure levels, coronary artery calibers, coronary calcium, or inflammatory marker levels. Patients care about how they feel and what they can do. They care about the burden of illness and the impact of adverse effects of medications and complications from procedures on the way they live. Thus, decision making must necessarily incorporate the transfer of information about the broad range of outcomes encountered by patients.

Outcomes research is particularly concerned with the outcomes that matter most to patients. Most medical decisions involve tradeoffs between the potential benefits of the intervention and adverse effects. In some cases, there may be tradeoffs between the quality and quantity of life. Patients and their clinicians need information about the full range of outcomes associated with interventions to make decisions. Many studies rely on intermediate outcomes, often for the sake of efficiency with regard to study design. Thus, it is more convenient to determine whether a drug reduces a risk factor than to investigate its effect on quality and quantity of life. Through inquiry into how an intervention affects people's lives, outcomes research seeks to complete the evalua-

tion and provide patients and their clinicians the information they need to decide among options. Outcomes research also seeks to characterize the trajectories of illness and recovery to define key determinants and points of intervention.⁷⁸

Central milestones in this research were the publication of the Seattle Angina Questionnaire by Spertus et al,⁷⁹ the Kansas City Cardiomyopathy Questionnaire by Green and colleagues,⁸⁰ and the Minnesota Living with Heart Failure Questionnaire by Rector and Cohn.⁸¹ These instruments provide the means for valid collection of information about disease-specific health status. They represent a true advance in taking a patient's history, tracking temporal changes in the burden of disease, and assessing the impact of an intervention from the patient's vantage point. These instruments complement more generic health status instruments and provide specificity about the impact of particular conditions or symptoms; they have transformed the experiences of patients into quantitative, valid, and reproducible data. They are finding use in studies such as the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial,⁸² which hinge on the health status benefit of the intervention.

There are many examples of studies using these tools that provide a broad view of the patient experience. Conard and others⁸³ showed that patients with heart failure who perceived difficulties in affording medical care had worse health status with more functional limitations. Sedrakyan and colleagues⁸⁴ found no differences in the health status of patients undergoing aortic valve replacement with tissue or mechanical implants. Vaccarino and others,⁸⁵ examining sex differences in outcomes after coronary artery bypass graft surgery, reported lower functional gains among women.

For times when more nuanced information than that provided by closed-ended questions is required, qualitative research can elicit information on which future assessments and interventions can be based. The use of qualitative methods also can provide insights that are unanticipated and direct the researcher to focus on listening to subjects and being open to learning about their experiences.

An underlying premise of outcomes research is that optimal decision making requires a shared decision-making framework in which the patient is an active participant. Decisions should respect each patient's values, preferences, and goals. This construct also acknowledges that many patients want to be involved in decisions regarding their care.

Chaudhry and colleagues⁸⁶ provide an example of shared decision making in recommending how physicians should assist patients in decisions about isolated systolic hypertension. They adopt the shared decision-making model by outlining the clinician's responsibility to assess the patient's blood pressure, advise about options, agree on a strategy, and assist the patient by reviewing the plan and arranging follow-up. In advising the patient, the clinician needs information about the benefits, risks, and consequences of different strategies, along with knowledge of the degree of uncertainty associated with these estimates.

Ultimately, the challenge for outcomes research is to take the perspective of a patient and promote an understanding of the patient experience. The research should elevate the goal

of promoting the full range of patient outcomes into view as we characterize current patterns of outcomes and health system performance and assess the effect of interventions. The farther we get from the patient experience, the less sure we are about whether we are achieving the desired effect of clinical decision making and the healthcare system.

Future Directions and Challenges

The questions for outcomes research expand as challenges to the healthcare system increase, including the aging population, growing knowledge base, broad range of vested interests, increasing sophistication of patients, and the pressures to demonstrate the value of health care to patients and society. In addition, the revolution in health information technology continues to make available greater amounts of data, with the concomitant opportunities and hazards. The emerging technology, software, and data enable analyses on a scale and in a time frame that could not have been imagined even decades ago. Yet, these data raise questions about the appropriateness of the types of analyses that are conducted and the truthfulness of the inferences that derive from them. Scientists need to make the distinction between analyses intended to test hypotheses and those pursued for exploration of potential relationships. Moreover, the need for replication of findings will also grow in importance.

The abundance of data makes the use of sound scientific principles more important than ever before. The availability of data and access to software facilitate access to these types of investigations but also highlight the continuing need to train scholars in the principles of research. The translation of data into useful information, filtering out the noise and strengthening the signal, is a principal goal. This work can monitor and promote safety, effectiveness, equity, efficiency, timeliness, and patient-centeredness at the patient and system levels—for patients and their clinicians and for policy makers and their public.

We could be entering an era in which we conduct virtually real-time research with expansive and responsive surveillance systems with the ability to evaluate rapidly the adoption and effects of innovations in care. In an environment where surveys are inexpensive and patients' experiences with illness and the healthcare system are easily tracked, we can understand how to improve services and address deficiencies. We can tailor approaches and quickly distinguish responders from nonresponders with greater nuance and increased confidence. We can follow physiological, psychological, and symptom parameters over time in ways that were previously cumbersome and inexact. Through these efforts, we can promote the best interests of those whom the health system seeks to serve. In addition, technology can facilitate the integration of a dynamic decision support model, placing research back into practice in the service of clinical decisions at the bedside. In all these aspects, outcomes research can illuminate the results of care, promote improvements, facilitate feedback, and collect more data in the ongoing delivery of care.

Conclusions

What is outcomes research? It is relevant, practical, and applied scholarship that interfaces with efforts to improve

care in the service of promoting the best interests of patients and society. It seeks to make visible what was formerly obscured regarding patterns of care and their effect on patients. The research fundamentally seeks gaps in the quality of care and supports constructive remedies. It can be the voice of patients with its focus on patient experience. The research can assist in the responsible allocation of resources and the elimination of waste. The evaluation of policies can reveal what is truly being achieved by the system and when unintended consequences conspire to undermine policies and strategies implemented with the best of intentions, as well as those of questionable intent. With the growing complexity, cost, capability, and consequences of healthcare interventions, outcomes research is poised to provide scholarship that can support efforts to improve medical practice and healthcare policies.

Disclosures

None.

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KEY WORDS: health policy ■ outcomes research ■ quality of care