From the Page to the Patient: A Critical Analysis of the Policy Issues Associated with Translating Evidence into Evidence-Based Practice

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Abstract

Although most people today assume that evidence-based medicine has had a significant effect on improving certain aspects of health care quality, it is also clear that evidence-based medicine has yet to reach its full potential and still has quite a bit of room to grow. Unfortunately, the principle that served as the foundation of evidence-based medicine has not lived up to its original promise. In this paper, I examine guideline implementation programs with the intention of identifying the underlying characteristics that contribute to their success and exploring ways in which these values can be adapted in the future. First, I briefly discuss the historical context of evidence-based medicine, its original intention, and how that perception has changed over time. This discussion presents the three-step process of practicing evidence-based medicine: developing systematic reviews; creating clinical practice guidelines; and implementing those guidelines in clinical practice. It addresses the barriers impeding the process and shows how guideline implementation programs dismantle those obstacles.

Second, the paper delineates the treatment gap between best practice defined by research evidence and actual clinical practice and it illustrates the gap by looking specifically at beta-blocker use in the secondary prevention of myocardial infarction. The analysis shows that guideline implementation programs targeted to increase the use of beta-blockers in myocardial infarction patients appear to be related to more evidence-based practice and, through that improved practice, on better health outcomes.

The literature suggests that general data feedback, clinical care coordinators, and clinical education are associated with successful guideline implementation programs. Programs designed to reach multiple hospitals benefit from simultaneous use of a wide variety of implementation supports. Smaller programs, on the other hand, benefit from goal-directed designs focusing on a few key components tailored to their particular needs. The paper concludes with implications for research, ongoing program development, future policymaking, and the success of evidence-based medicine in general.

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Introduction

Evidence-based medicine first began entering the consciousness of the medical community in the early 1990s, and with it came the promise that this approach would elevate the quality of health care delivered to patients. From its inception, evidence-based medicine was designed to improve patient outcomes by helping physicians integrate the best available medical evidence into their clinical decision-making.[1, 2] In one of the most cited definitions, Sackett et al. described evidence-based medicine as "the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients".[3] Initially this concept met with a great deal of resistance from the medical community: it was viewed by many to be a threat to physician autonomy and a recipe for "cookbook medicine".

Recently researchers have started using the term "evidence-based practice" instead of "evidence-based medicine." Evidence-based practice is defined as the "integration of best research evidence with clinical expertise and patient values".[4] Although many people use the two terms interchangeably, evidence-based practice explicitly takes into consideration the patient's and physician's shared responsibility for decision-making, and evidence-based practice does not carry the same taint of being "cookbook medicine" as did evidence-based medicine. To avoid any confusion, this paper will primarily use evidence-based practice to refer to the translation of research into practice, and will only refer to evidence-based medicine when discussing the history of its terminology. In the past 15 years the perception of evidence-based practice has changed considerably and many clinicians have now come to embrace the idea evidence from clinical research can and should be a major component in clinical decision-making.[1]

Although most people today assume that evidence-based practice has had a significant effect on improving certain aspects of health care quality, it is also clear that evidence-based practice has yet to reach its full potential and still has quite a bit of room to grow. Unfortunately, the principle that served as the foundation of evidence-based practice has not lived up to its

original promise.[2] On the one hand, evidence-based practice has been instrumental in changing the way medical research is conducted, assembled, and analyzed. In the past decade alone, significant advancements in the organization of medical research can be seen in the forms of systematic reviews and clinical practice guidelines (CPGs), and evidence-based practice is institutionalized in infrastructures of various types, including the all-volunteer, public private hybrid Cochrane Collaboration and the Evidence Based Practice Centers sponsored by the Agency for Healthcare Research and Quality (AHRQ), signifying the place of evidence-based practice on the public agenda..

On the other hand, the effect evidence-based medicine has had on how medicine is practiced in the everyday clinical setting has not been nearly as profound.[5] The ability of research evidence, assembled in the form of systematic reviews and CPGs, to inform clinical decision-making has proven to be more difficult than early proponents hoped.[5] The literature on translation of research into practice (commonly known in health services research circles as "TRIP") continues to uncover substantial gaps between the best practices supported by research evidence and the way medicine is practiced in the real-world setting.[1, 5, 6] Clearly, we must remain focused on fulfilling the original intentions of evidence-based practice and maximizing its influence on health care outcomes if evidence-based medicine is to live up to its promise.

CPGs, or any other evidence-based practice tool for that matter, are not designed to be applied in every patient. As stated before, evidence is not the only element of decision-making, and not all patients can be expected fit the criteria specified by guideline recommendations. Therefore, even with a strong evidence base, CPGs will have some limitations to their use. Although CPGs can be treated as standard of care, their role in relieving or stimulating liability concerns is a contested one. In light of these considerations, the goal should be to maximize the use of CPGs, not to universalize them.

The goal of this paper is to elucidate some of the reasons why evidence-based practice has failed to realize its full potential by investigating how guideline implementation programs can be more effective at translating evidence into improvement in patient care. This paper will use programs that seek to implement widely agreed-upon guidelines for prescribing beta-blockers in patients with a history of myocardial infarction (MI) as an example of the challenges facing those who wish to institutionalize evidence-based practice. The evidence for post-MI beta blocker use is strong and non-controversial, and the intervention – providing a prescription most often at the time of discharge from the hospital – is not difficult. Yet prescribing beta blockers to appropriate patient candidates is still not the norm. If such an uncontroversial and relatively easy manifestation of evidence-based medicine is not routine, more difficult implementations will face even greater challenges. I will use the example of post-MI prescription of beta-blockers to identify the specific program components that are indicative of successful guideline implementation, and suggest ways that factors associated with success can be adapted to apply to other settings for the ultimate purpose of improving the effectiveness of evidence-based practice.

Subject Relevance

The study of successful guideline implementation programs is important for several key reasons. The first and perhaps most important public health contribution is the degree to which improving guideline implementation and extending the reach of evidence-based practice can improve health care quality on a population level. Second, guideline implementation programs have yet to be developed or studied to the same degree as have the methods associated with developing systematic reviews or CPGs and yet, without an understanding of best methods of implementing these tools of evidence-based practice, the tools themselves have limited utility. Finally, an understanding of guideline implementation is important because the provider

community must be able to "build implementation in" to its plans for translating research into practice and policy change if the translation is to succeed.

It is important to recognize that evidence-based practice cannot be the answer to all clinical problems. Research evidence is only one of several factors taken into consideration when delivering care. Clinicians must also take into account the values of their patients, the constraints of their health care system, and their own expertise when making clinical decisions for their patients. Apart from the importance of other factors, the evidence base is limited. Few clinical practices in medicine are supported by strong empirical evidence. The British Medical Journal of Clinical Evidence, for example, concluded that only 15% of clinical practice is supported by "strong" evidence.[7] Ethical, financial, and practical limits mean that strong evidence can never be expected to support all clinical situations.

Even in situations where research evidence is applicable patients often do not receive evidence-based care.[5] McGlynn, Asch, Adams et al. found, in a noted study, that only 59% of patients received recommended care.[8] Studies continue to demonstrate that scientific evidence is not being used to its full potential, with treatment gaps – discrepancy between what the evidence suggests and what real-world practice is -- common.[1, 5, 6] Despite all the attention devoted to the advancement of evidence-based medicine in recent years, the health care system is still having difficulty translating evidence into clinical practice.

Quality of care can be improved by the incorporation of the best available evidence into practice. Persistent treatment gaps suggest that not nearly enough resources have been devoted to seeing that the evidence is translated into practice. Guideline implementation programs help physicians incorporate guidelines into their real-world practice environments. Further, the development of systematic reviews and CPGs absorbs considerable time, money, and energy. When these tools are not used, the resources poured into their creation may be wasted. The emphasis on guideline implementation is relatively new, but critical analyses of what succeeds and fails in guideline implementation is appropriate. Critical analyses of the

effectiveness of evidence-based practice also have particular relevance for future policy change.

Background and rationale

Systematic reviews and CPGs have emerged as the primary tools to deliver evidence-based medicine.[2, 5] Systematic reviews are "concise summaries of the best available evidence that address sharply defined clinical questions".[9] They assess the strength of the available literature and help practitioners identify the evidence that is most relevant to the treatment of their patients. Over 2 million articles are published each year and systematic reviews are one of the resources available to help clinicians manage the overwhelming amount of new research.[10] It is rare that a single study is robust enough to provide clinically meaningful knowledge with any kind of certainty. Systematic reviews are advantageous because, by pooling the results of many different studies, they help determine if consistencies exist among the literature.[5] They also help decrease biases and improve the reliability of the results by compiling raw data.[10, 11]

Recently, the science of developing systematic reviews has also become an increasingly important area of study, as epidemiologists have searched for ways to improve current research methods.[5] Programs such as the Evidence-based Working Group and the Cochrane Collaboration have been instrumental in improving the development of systematic reviews. The Evidence-based Working Group has created user guides to aid in the critical appraisal, grading, and interpretation of primary studies.[11] The Cochrane Collaboration has been instrumental in the preparation, maintenance, and dissemination of systematic reviews.[11, 12] These initiatives represent a remarkable advance in the process of assembling, evaluating, and interpreting medical research. The underlying hope supporting the time and energy spent by the members of these groups is that improving the quality of evidence will lead directly to improvements in the quality of care.

The second evidence-based medicine implementation tool, and the logical extension of the systematic review, is the CPG. The Institute of Medicine defines a clinical practice guideline as a "systematically developed statement to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances".[13] The process of creating CPGs begins with evidence gathering in the form of systematic reviews; the next step is that of using the review, enhanced by "grading" of the literature and modulated with expert clinical judgment, to make recommendations about clinical practice. Theoretically, CPGs, when used properly, will improve quality, reduce inappropriate variation in care, and serve as valuable education tools for physicians and patients.[14] Guideline implementation programs are intended to make it easier for clinicians to deploy the resulting tool – the CPG – in real world settings of care and apply this research evidence in their everyday practice.

Systematic reviews and CPGs are the foundations of evidence-based medicine, but they are only part of story. CPGs are not meant to be a one-size-fits-all dictate. They are meant to serve as recommendations that clinicians and patients can factor into their decision-making Only recently have concerted efforts to assist practitioners with adapting evidence found in systematic reviews and CPGs become more common. These efforts have led to the development of several guideline implementation programs focused on making sure that scientific evidence actually reaches the patient. Improving the translation of the best research evidence into clinical practice is paramount in the struggle to improve quality of care.

Paper Outline

In this paper, I examine guideline implementation programs with the intention of identifying the underlying characteristics that contribute to their success and exploring ways in which these values can be adapted in the future. First, I discuss the historical context of evidence-based medicine, its original intention, and how that perception has changed over time. I examine the three-step process of evidence-based practice: developing systematic reviews;

creating CPGs; and implementing those guidelines in clinical practice. I discuss the barriers that impede each step of the process and show how guideline implementation programs help dismantle those obstacles.

Second, this paper sheds light on the treatment gap between best practice defined by research evidence and actual clinical practice. I illustrate the gap with a case study of beta-blocker use in the secondary prevention of myocardial infarction. In particular, I investigate whether guideline implementation programs targeted toward increased prescribing of beta-blockers following myocardial infarction in appropriate patients on prescribing and, via the provider's changed prescribing behavior, on health outcomes.

Third, I more fully describe the methods and results of this study and conclude by addressing some of the implications of these results for future research on guideline implementation, for ongoing program development, future policymaking, and the success of evidence-based medicine in general.

Evidence-Based Medicine: A Historical Perspective

History

Before diving headfirst into the study of guideline implementation programs, it is important to take a step back and look at evidence-based medicine from a historical perspective. Understanding the historical context of evidence-based medicine and how it has evolved over time is essential for three reasons. First, the history of evidence-based medicine provides a wealth of background knowledge that illuminates the current process of generating, assembling, and analyzing evidence. Second, when conducting policy analysis, the historical context is often a critical, determinative variable in the analysis; policies are often understood as the result of path dependence, or the dependence of current policy arrangements on choices made – and not made – earlier.[15] Third, implementing meaningful policy change in the future depends on an understanding of policy origins and context, just as analysis of current policy

must resort to its history. Understanding the original intention of evidence-based medicine, its effect on the field of medicine, and how it has changed over time is the only way to ensure that we do not repeat mistakes of the past.

The term "evidence-based medicine" first appeared in the medical literature in the early 1990s but one can trace its roots back to the early work of Florence Nightingale and Ernest Codman.[16-18] In the mid-19th century, Florence Nightingale pioneered the systems approach to health care research and purposefully gathered, analyzed, and used evidence to determine the best treatment strategies for patients. She routinely monitored the progress of her hospitalized patients and kept extensive records of their health outcomes. Her constant data collection enabled her quickly to identify ineffective or harmful treatments and use that information to improve the processes of care.[17]

At the start of the 20th century Ernest Codman added to the ideas originated by Nightingale. He believed that physicians should regulate themselves by monitoring the clinical outcomes of all their patients, analyzing treatment failures, and making the necessary changes to improve their clinical practice. He was also an advocate for making these records of patient outcomes available to the public to serve as a motivation for what we would now call quality improvement. The common thread between Nightingale and Codman is that they both appreciated the role of research evidence in changing the processes of care. They also recognized that scientific inquiry into a treatment's effectiveness was just as important as the treatment itself. [18]

After World War II, the field of medicine experienced a surge in therapeutic options due in large part to the acceptance of germ theory, the discovery of antibiotics, and the development of new treatment procedures.[1, 19] Optimism within the medical community grew as physicians were able to provide a greater variety of treatment options to their patients. Physicians began to move from simply managing a patent's condition to actually being able to treat it.[19] This transition to more active medicine occurred at a time when the field of medicine had no system

set in place to study the effectiveness or potential harms of their new treatments.[19] The increase in therapeutic options proved to be a double-edged sword for the health care system. On the one hand, it afforded physicians the opportunity to offer their patients treatment options heretofore unavailable. On the other hand, medicine developed in comparatively unchecked ways, in an environment where many new, and potentially harmful, treatments could be widely disseminated to patients without proof of their effectiveness.

In the 1960s, randomized control trials began increasing in popularity as medical researchers sought to provide evidence of efficacy for the new treatments they were providing and reduce the occurrence of treatment disasters.[16] Practitioners and researchers at that time were reminded of the value of scientific inquiry and realized that without proper investigation, many of the new diagnostic and therapeutic procedures could be causing their patients more harm than good.[1] The renewed interest in scientific inquiry led to a surge in the amount of clinical research being conducted, particularly randomized control trials. During the 1970s, many of the randomized control trials were primarily focused on assessing the effectiveness of new technological advancements.[16] It would take both time and evidence of compromised health care quality before the focus of research would shift to the exploration of health outcomes.

One of the first studies to reveal questionable effectiveness and appropriateness amidst rising cost was the small area variation work of Wennberg and Grittelsohn first published in 1982.[20] Their study of the surgeons in New England revealed widespread geographic variation in the rates of clinical practice. Although variation by itself is not a threat to health care quality, the clinical practice discrepancies found by Wennberg and Gittelsohn are significant because they could not be explained by population differences, they often resulted in more expensive health care, and yet did not give rise to significantly better health outcomes.[20] The most troubling implication of their findings was that the variation in clinical practice was not associated with factors such as need for care, but instead it had more to do with factors such as geography, socioeconomic status, local practice preferences, ethnicity, and gender.[21] Not only did they find

that this variation was unnecessary and unwarranted, but it often compromised health care quality, cost, and safety of the patients involved.

Subsequent studies revealed that inappropriate clinical variation was not specific to the New England region. In fact, Wennberg's and Gittelsohn's results proved to be indicative of a much larger problem.[20] Unwarranted variation has been demonstrated in a variety of clinical practices and throughout the United States.[22-24] Evidence-based medicine, in theory, should help eliminate inappropriate variation and promote higher standards of practice in clinical medicine. This is not to say that evidence should eliminate all clinical variation; it is, instead, to say that variation must be based on the needs and values of patients rather than random, unjustified factors such as local practice precedents.

Wennberg's and Grittelsohn's revelation that decision-making strategies might be compromising health care quality helped usher in the modern movement of evidence-based medicine. It advocated for the idea that the dissemination and implementation of strong medical evidence on a broad scale could be an effective means of improving the quality of health care delivered to patients.[25] Evidence-based medicine has sought to improve health care quality by shifting the basis of clinical decision-making from a model based solely on factors unique to the patient and physician to one with a stronger scientific foundation that aims to integrate individual expertise with external evidence.[2, 3] Wennberg and Grittelsohn suggested that incorporating medical literature into clinical decision-making would create uniformity in some aspects of care without eradicating either clinical judgment or the need to tailor care to individual patient needs.

Dramatically rising health care costs and growing evidence of inappropriate care are some of the reasons why randomized control trials begin evaluating health related outcomes.[16] The medical research community began evaluating patient outcomes in an effort to understand the effect of unjustified variations in medical practice on health care quality and cost.[21] As a means of helping physicians manage the growing volume of randomized control trials, systematic review articles became a staple in medical literature.[16] But as more studies were

conducted, physicians found the process of incorporating research evidence into clinical practice increasingly difficult.[5] Systematic reviews made it easier for clinicians to find the highest quality research in an orderly, transparent manner and then apply that knowledge to their clinical decisions.

CPGs soon developed out of the same need that had called for systematic reviews.[26] Medical professional organizations and other institutions began making concise clinical recommendations based on evidence compiled from systematic reviews. These CPGs were developed to provide clinicians with management strategies rooted in evidence but capable of adaptation to patient values and clinical expertise.

Current state of evidence-based medicine

In recent years, the medical community has changed the way it thinks about the role of evidence in clinical medicine.[1] Evidence-based medicine is no longer regarded as the panacea for the entire health care system or feared as a destroyer of individual physician autonomy and judgment. Instead, it is viewed as one of many tools used in the decision-making process.[1] The focus has slowly shifted from evidence-based medicine to evidence-based practice. Evidence base practice is defined as "the integration of the best research evidence with clinical expertise and patient values". Evidence-based practice differs from evidence-based medicine because it is rooted in the principle of shared decision making and stresses the importance of both patients and physicians in health care decision-making.

Over the years the evidence-based approach has won over much of the medical community.[26] In the process, evidence-based practice has also shaped the way many physicians approach clinical medicine. Although the widespread acceptance of evidence-based practice has been a relatively recent movement, the idea that clinical practice should be rooted in scientific evidence has been several years – or even a century, to give Nightingale and Codman their due -- in the making.[1, 16] In the process of adopting this new way of thinking, the

medical community also changed its ideas about what it considers high quality health care and the best way to achieve it in clinical practice.[1]

In the past 15 years, many organization and programs have been developed in an effort to help implement evidence-based medicine. The Cochrane Collaboration is an international not-for-profit organization whose goal is to improve informed decision-making by preparing, maintaining, and ensuring the accessibility of systematic reviews.[12] Efforts such as the quality of reports of meta-analysis (QUOROM) statement have also attempted to standardize the presentation of evidence by providing explicit instructions to physicians and researchers on how to report systematic reviews and meta-analyses.[26, 27]

The Agency for Healthcare Research and Quality (AHRQ), the Department of Health and Human Services entity charged with vigilance for the nation's health care quality, and the American Medical Association (AMA) created the National Guideline Clearinghouse to help the medical community to manage the growing number of clinical guidelines being produced. The National Guideline Clearinghouse provides executive summaries and the full guidelines for a very large number of conditions and combinations of conditions. The Clearinghouse's mission is to further the dissemination and implementation of CPGs.

In 1997 AHRQ, then known as the Agency for Health Care Policy and Research, commissioned the development of 12 evidence-based practice centers (EPC). The purpose of the EPCs is to "promote evidence-based practice in everyday care". The 12 EPCs set out to improve the quality, effectiveness, and appropriateness of health care by providing evidence reports for topics relevant to clinical medicine.[28]

Each of these examples demonstrates what some have referred to as the current "trend to evidence".[26] As the medical community has become more comfortable with the approaches of evidence-based medicine, many have expended effort to help put the approach into action. The next step in the goal of implementing evidence-based practice is to analyze the effectiveness of

our current efforts to implement guidelines and to identify the areas where there is room for improvement.

Evidence-Based Medicine: The Process and the Barriers

Generating systematic reviews

The development of systematic reviews is a multi-step process posing difficulties at each step.[29] Systematic reviews' first steps are framing a focused clinical question (driven by intellectual as well as practical needs, since an overwhelming literature can be managed only by limiting and targeting the clinical question on which the literature is brought to bear), and identifying the appropriate literature to review.[29] The next steps are reviewing the literature (itself a significant task), assessing the quality of the literature using a validated grading system, and generating a comprehensive summary of the literature.[29] The final step is the interpretation of findings and discussion of the clinical meaning of the systematic review results.[29]

At each step of the process, potential barriers impede the creation of good systematic review. One of the main review challenges is the many questions that could potentially provide valuable clinical information but cannot be answered because of a lack of evidence. Deciding which literature databases to use and determining which combination of medical subject headings (MeSH) will capture an acceptably high proportion of relevant articles is also problematic. Finding appropriately rigorous and yet usable tools for grading the quality of the evidence is another barrier to the development of good systematic reviews. Lohr and her colleagues conducted an analysis of the grading systems most commonly used to assess the quality of research articles and found that out of 121 grading systems they evaluated, only 19 met the scientific standards necessary to analyze the quality of evidence effectively.[26] Finally, the actual process of the review is never as straightforward or linear as these clear steps suggest. Systematic reviews are challenging.

Generating clinical practice guidelines

Generating a guideline means formulating and limiting the clinical question at the heat of the guideline, analyzing the pertinent evidence (most often meaning conducting a systematic review), using a combination of evidence, clinical experience, and expert consensus to make evidence-based recommendations about clinical practice, and then making those recommendations public. Various organizations and institutions have begun developing CPGs to suit their specific needs and unique patient populations. The proliferation of guidelines is evident in the hundreds of guidelines (many medical professional associations, academies, and colleges post over 100 guidelines each) maintained by the National Guideline Clearinghouse.[30]

One of the problems with creating guidelines is that they are only as good as the evidence on which they are based. Guidelines based on limited data or poor quality studies do the evidence-based medicine movement a disservice. In addition, CPGs should take into account real-world factors such as cost-effectiveness and clinical significance. For example, some populations are underrepresented in the primary studies and, as a result, physicians may be hesitant to use guidelines in their treatment of members of these populations. CPGs that cannot be made relevant to clinicians' needs are much less likely to be used..

Evidence-based practice: putting guidelines into practice

CPGs do not have the force of law; they must be adopted voluntarily. Thus guideline implementation programs are designed to support the tailoring, and embracing, of guidelines at the level of the individual health system. Guideline implementation programs can be developed by any group with a vested interest in trying to use evidence-based medicine to improve care, from large organizations such as insurance companies and patient advocacy groups to smaller health care systems like community hospitals or private practices. The goal of these programs is to adapt the recommendations of CPGs to suit different health care systems and different patient populations.

The barriers to guideline implementation can be divided into two broad classes of physician factors and system factors. Physician factors include physician awareness and willingness to adopt guidelines.[31] Before guidelines are implemented, health care professional must be aware of the recommendations and must be willing to implement them, even – or especially – when they require a change in practice. System factors include environmental or organizational factors such as financial and structural limits, time constraints, and the desires of the patients. If guideline implementation programs are to be successful they must overcome the barriers posed by both sets of factors.[31, 32]

Example: Beta-Blocker Use in the Secondary Prevention of Myocardial Infarction

Why myocardial infarction?

Myocardial infarction (MI), commonly known as a heart attack, is defined as a reduction of blood supply to the heart that results from a blockage of one or more of the coronary arteries and ultimately leads to damage to or death of heart tissue.[33] While myocardial infarction is classified as a disease on its own, it is also part of a broader umbrella condition known as coronary heart disease (CHD). Coronary heart disease is a spectrum of diseases that result in compromised blood flow to the heart. In its mildest form CHD is asymptomatic, but in its most severe form patients may experience a myocardial infarction or death.

Myocardial infarction is a disease that lends itself easily to the study of guideline development and implementation for several important reasons. First, it carries a high burden of disease. Myocardial infarction is a major health concern in United States because it is a significant cause of morbidity and mortality.[34] Currently 15.7 million people in the United States have been diagnosed with CHD.[35] In this year alone an estimated 1.2 million people will have a myocardial infarction.[35] Of these, 700,000 are expected to be new infarctions and 500,000 will be recurrent myocardial infarctions.[34]

Coronary heart disease is the leading cause of death in the United States and accounts for approximately 654,000 deaths each year. Each year approximately 38% of all the people who experience an MI will die from it, for an approximate total of 221,000 MI deaths each year.[35] Having the evidence that a significant number of these deaths could be prevented by implementing guidelines makes guideline implementation an important public health concern.

The second reason to use this example is that MI management has a well-established and evidence-based standard of care. The appropriate treatment of patients with myocardial infarction has been the target of CPGs for years. Both the American Heart Association (AHA) and the American College of Cardiology (ACC) have been leaders in the creation of guidelines for MI management, having released joint guidelines on the management of MI since 1999. As a testament to the general acceptance of these guidelines, the Joint Commission and Centers for Medicaid and Medicare Services (CMS) have adopted many of the recommendations as quality indicators. [36]

In the joint AHA /ACC guidelines issued for the secondary prevention of myocardial infarction, the highest recommendation (Class 1) was given to the recommendation that physicians start post-MI patients on beta-blockers and to continue their use indefinitely in "all patients who have had myocardial infarction, acute coronary syndrome, or left ventricular dysfunction with or without heart failure symptoms, unless contraindicated".[37]

The third reason why myocardial infarction is such a suitable topic for the study of guideline implementation programs is the strong evidence that a treatment gap exists.[34, 38, 39] The recommendation to start and continue beta-blockers is clear, simple, and supported by high quality evidence. Following the guideline will result in better outcomes for post-MI patients. Why should a gap between the recommendation and actual practice persist? Understanding the gap, and successful strategies for closing the gap, should produce findings that can be applied to other guideline implementation efforts.

Why Beta-blockers?

Of all of the guideline recommendations available for the treatment of myocardial infarction, the underuse of beta-blockers is one of the clearest cases of unwarranted failure to use the evidence. Since the late 1980s medical research has supported the long-term use of beta-blockers after myocardial infarction in order to reduce mortality and reinfarction.[6, 40] It is thought that beta-blockers decrease the workload of the heart by slowing the velocity of contracting and allowing the coronary vessels more time to fill.[34] From the first publication of the evidence 20 years ago to the present, the evidence has supported the use of beta-blockers for the secondary prevention of myocardial infarction.[41]

Initial studies found that use of beta-blockers in post-myocardial infarction (post-MI) patients reduced mortality by 19-48% and decreased rates of reinfarction by as much as 28% [34, 38] Phillips et al. found that if beta-blockers were prescribed to all first-MI survivors without contraindications for the next 20 years, 72,000 CHD deaths and 62,000 cases of MI would be prevented. They also found savings of $18 million dollars and gains of 44,7000 life-years.[41]

In addition to its health and cost benefits, beta-blocker use is a good case for testing the power of guideline implementation programs because it is an easy outcome to measure. Other very important quality indicators are much more difficult to measure. Beta-blocker prescriptions' comparative ease of measurement make them among the "low-hanging fruit" of quality improvement research, but this does not make studies of their use any less important. Indeed, to the degree that compliance with the beta-blocker recommendation is not only easy to do, but easy to measure, finding a treatment gap in this case should suggest the size of the challenge to practice evidence-based medicine.

The treatment gap

Despite evidence from countless systematic reviews and multiple evidence-based guidelines, beta-blockers are substantially underused in post-MI patients.[38, 39] The gap between

best evidence and every day practice first began gaining public attention in the mid-1990s.[34] It has been estimated that as many as 80% of patients who have a myocardial infarction should be prescribed long-term regimen of beta-blockers yet only 40% actually receive beta-blockers in the clinical setting.[38]

From the patient-centered perspective, the most important consequence of poor adherence to guidelines is the unnecessary mortality and morbidity. In an attempt to quantify the gap between best practice, defined by research, and everyday practice, Sim and Cummings conducted a sophisticated analysis of hospital discharge data to determine the number not prevented (NNP) by beta-blocker under-use.[6] The NNP is a numerical representation of the numbers of deaths that would have been prevented if patients had received the recommended therapy, which in this case was beta-blocker prescription after MI. Their calculations uncovered approximately 2995 U.S. patients annually who died in their first year post-MI and whose deaths would otherwise have been prevented had beta-blockers been prescribed. The ability to quantify the treatment gap is useful because it can so starkly illustrate the consequences of poor adherence to guidelines.[6]

Bradford, Chen, and Krumholz examined economic effects of beta-blocker underuse and found three types of cost arising from poor adherence to guidelines.[34] Underuse of beta-blockers is costly to the health care system because of the resulting unnecessary morbidity and mortality; it is also costly because underuse leads to more use of health care resources following the failure to engage in secondary prevention. Finally, they argued, beta-blocker underuse raised health care costs because post-MI patients who did not receive beta blockers were more likely to use other, more expensive, but less effective treatments. Their framework helpfully organizes the costs to the health care system of treatment gaps.[34]

Methods

Selecting Studies

Before selecting the program evaluation articles that would be analyzed in this paper, I first had to design a comprehensive search strategy. My search strategy included picking the literature database, selecting a combination of search terms, and choosing the inclusion and exclusion criteria for accepting or rejecting articles. Time constraints, limited resources, and a desire to focus on U.S. studies of guideline implementation led to my choosing PubMed, the National Library of Medicine's massive biomedical literature archive.

The most difficult part of finding the literature was selecting the appropriate search terms. PubMed can be searched with any key words, but the Medical Subject Headings (MeSH) system is the most sophisticated and detailed structure of search terms. The size and complexity of MeSH, however, and the fact that different MeSH terms may be assigned to substantially similar articles by different human coders, make identifying the best combination of search terms an uncertain task. To complicate matters further, many MeSH terms can seem redundant and overlapping. For example, articles that deal with beta-blockers may be coded as "adrenergic beta-antagonist", "anti-hypertensive agents", or "anti-arrhythmic agents" depending on coder judgment about the direction of the article.

This search was additionally challenging because its focus was unlike that of other systematic reviews. The goal of this study was not to do a systematic review of all the evidence supporting beta-blocker use in myocardial infarction patients. Instead, the focus of my search was to identify the studies that have evaluated the health systems' attempts to create and sustain successful programs to assure these beta-blockers are prescribed.

After consulting with experts in the field of library sciences, my advisors and I decided on which specific combination of MeSH terms would be the most effective at capturing all of the appropriate studies. The MeSH terms used included ("Adrenergic beta-Antagonists"[MAJR] OR "beta blockers"[tw]) AND ("Myocardial Infarction/drug therapy"[MAJR] OR "Myocardial

Infarction/prevention and control"[MAJR]). Even with this precise combination of MeSH terms, the initial search still yielded 1083 articles. To get to the real focus of the search – evaluations of guideline implementation programs – I added the string "quality improvement OR quality assurance OR program evaluation" to the search algorithm. This additional string helped narrow the search to 79 articles. From these 79 articles, five fit the predetermined inclusion and exclusion criteria. I found the additional 10 articles by searching the "related articles" list of the first five retrieved articles.

I also selected criteria for including or rejecting articles before conducting the literature search. All of the articles included in this analysis resulted from studies of randomized control trials or before-and-after analyses. I made this decision because it was important that all the articles include a comparison between the intervention – some technique or effort to improve guideline adherence -- and those who were not exposed to the intervention. In the randomized control trials, the intervention group had to have been compared to a control group receiving no intervention. In the before-after studies, beta-blocker prescription rates had to be measured both before and after the intervention (and, ideally, other control variables that might explain changed rates also needed to be measured). Some studies included a combination of these two study designs, often featuring groups of patients divided into control and intervention groups, with primary outcomes – beta-blocker prescription rates -- measured before and after implementation of a guideline adoption effort. Studies comparing one intervention to another without a reference control group were excluded from this analysis.

I also limited the search to studies written in English and conducted on human participants. Each of the guideline implementation programs evaluated in these studies had to be targeted to patients with myocardial infarction. The outcome of interest had to include some measure of beta-blocker use or prescription on hospital discharge. It was important that the articles specifically investigate beta-blocker prescriptions on hospital discharge because including other types of beta-blocker use might have complicated the results. For example, if

outcomes such as beta-blocker prescription on admission, or use overall, were included, we would be unable to attribute real change to improved guideline adherence.

It was also important that each published study was conducted in the United States. As mentioned above, since many of the policy issues associated with guideline implementation are unique to the United States health care system, I wanted the articles included in this study to reflect how guideline implementation works within the United States. Finally, all included studies had to have been published within the last 10 years (from May 15th 1997 to May 15, 2007). The health care system is continuously evolving and a great deal can change in 10 years. This analysis needed to reflect recent and current practice. Guideline implementation programs are also a relatively new phenomenon, so seeking literature from the last decade gave a good likelihood of capturing most of what has been done.

The completed search yielded a total of 15 articles meeting all the inclusion and exclusion criteria, and I use all 15 articles in the following analysis. Although it is unlikely that all possible eligible articles were found with this search strategy, I believe that an acceptable percentage of these studies are analyzed here. The search strategy was comprehensive enough to generate a representative sample of program evaluation studies to evaluate and draw meaningful conclusions. A brief description of the final 15 articles analyzed in this study can be found in Table 2.

Selecting variables

After selecting the articles to be included, I had to design a set of variables to select the list of variables that would direct the coding of the resulting body of literature. The variables needed to provide clear ways of distinguishing the main components of each guideline implementation program and of cataloging apparently important sources of program success. I chose coding variables based on studies that have investigated the hospital characteristics associated with high guideline adherence. Bradley, Herrin, and Mattera et al. published two

extensive surveys of various hospitals throughout the United States that identified hospital characteristics most highly correlated with beta-blocker prescription rates after acute myocardial infarction.[36, 42] The studies were conducted between 1996 and 1999 and the authors primarily looked at patient characteristics and hospital characteristics. Patient characteristics included factors such as the basic demographic information (age, gender, race and insurance status), clinical information, and laboratory values. Each of these characteristics were gathered from the medical records of hospitalized patients as part of the National Registry for Myocardial Infarction (NRMI). Hospital characteristics included geographic region, ownership type (government vs. for-profit vs. nonprofit), quality improvement interventions, average MI volume, and the baseline rate of beta-blocker use.[36, 42]

Since the present study is focused primarily on the qualities of guideline implementation programs that are indicative of success, I extrapolated from the Bradley, Herrin, Matera et al. studies all the program characteristics that might lead to successful guideline implementation. Of all the patient and hospital characteristics they studied, only the variables that could possibly be components of a guideline implementation program were included. For example, the authors found that hospitals with clinical pathways, multidisciplinary teams, and general data feedback had higher rates of beta-blocker prescriptions than did hospitals without these features. Because it is possible for clinical pathways and multiple disciplinary teams to be components of a guideline implementation program, they were included in the list of variables.

If a characteristic was negatively associated with beta-blocker use, I excluded it from my list of variables. For instance, the hospital survey found that physician-specific data feedback that targeted guideline non-adherent clinicians was negatively correlated with later compliance to beta-blocker guidelines; I did not include data feedback as a variable in the present study. It is important to note the difference between general data feedback and physician specific data feedback. General data feedback was feedback that did not single out specific clinicians but rather provided information about state or hospital guideline adherence rates. General feedback

has a positive correlation with program success and was therefore included in this list of variables. Physician-specific feedback only provided feedback information to clinicians who fell below a predetermined acceptable level of guideline adherence. This component was not associated with program success and was not included in this list of variables.

As another example, Bradley, Herrin, and Matera et al. found that New England hospitals had higher rates of beta-blocker prescriptions. Geographic location, however, is not amenable to change, so I did not include it as a variable. Rather than where they are located, we need to know what it is about New England hospitals that makes them more guideline-adherent, and ask whether those features can be exported to hospitals in other regions. The final list of variables used to code each study can be found in the Appendix. I evaluated each study to see how many of the variables were present in their programs, and whether the variables appeared to make a significant difference to guideline adherence. I then grouped the studies according to what combinations of variables provided the context for successful interventions.

Critical Appraisal

Assessing the internal and external validity of these studies must be critically examined in order to have a solid understanding of the results. Internal validity is a measure of how well as study measure what it intends to measure. The best way to assess internal validity is to evaluate the potential for selection, measurement, and confounding bias. External validity is a measure of how meaningful a study's results are to those not involved in the study. External validity is best assessed by evaluating the generalizability of the results.

Selection bias

Selection bias is a systematic error in the way participants are selected. When selection bias is not taken into consideration, study groups may end up being different from each other in ways other than the variable in question. If this occurs, the final results may be biased and it can

be difficult to interpret the findings. The randomization of participants into different study groups is one technique often used to reduce the potential for selection bias; however, in this analysis only 3 studies used this method to recruit their participants.

Another way to evaluate the potential for selection bias is to compare the two groups on a series of basic characteristics to see if there are similarities. Whether or not a study uses the randomization, most studies will display group comparisons in a table format commonly known as a Table 1. This is done as a way to show that the two groups being studied are alike in every way other than the variable in question. Out of the 15 articles analyzed, a total of 11 provided a table that compared the two groups in terms of characteristics such as age, sex, and medical history.

For the studies that included a Table 1, the study groups were found to be statistically similar on most characteristics indicating a decreased potential for selection bias. Although the studies that did not randomize their participants or provide a Table 1 do increase the potential for selection bias, its effect on the final results seems to be minimal. Because most of the studies included in this analysis had Table 1 comparisons that demonstrated similar study groups, it seems unlikely that selection bias would be affecting the results in any major way.

Measurement bias

Measurement bias occurs when there is a difference in the measurement or detection of a study's intended primary outcome. One way to reduce the potential for measurement bias is to blind or mask those in charge of making the observations so that they are not aware of which groups to which participants are assigned. This makes it less likely that outcome measurements will be differ depending on the study group. Unfortunately guideline implementation program evaluation studies there is no way to effectively blind people to the invention.

Another way to reduce measurement bias is creating a priori definitions of the primary outcome before the study begins to ensure that outcome is measured equally in both groups. All

of the studies included in this analysis used pre-determined definitions of the primary outcome, which in this case was beta-blocker prescription. Most studies relied on medical records to ensure that the outcome was measured the same way. This likely helped reduce the potential for measurement bias. In terms of making sure that this

Confounding bias

Confounding bias is when another unknown variable distorts the association between the mean exposure and primary outcome. The same methods that are used to decrease selection bias are used to reduce the potential for selection bias are also used to decrease confounding bias. Randomization is the best way to account for all unknown variables and is one of the best methods of reducing confounding bias. Since very articles randomized their participants, confounding bias remains a concern when evaluating this quality of these studies. Unlike selection bias, there are an unlimited number of variables that could be contributing to confounding bias. When considering the internal validity of these studies, confounding bias is perhaps the biggest problem.

Generalizability

Generalizability is the extent to which findings from a particular study can be applied to the general population. Generalizability becomes a problem when the sample population is not representative of the larger target population. In the evaluation of guideline implementation programs, generalizability is particularly problematic because programs are often created for specific health care systems and are difficult to apply elsewhere.

The two biggest threats to generalizability are randomization and volunteer bias. Sometimes in RCTs, the randomization process can control for so many variables that the sample population no longer resembles people in the general population. Thi was not a particular problem in this analysis because so few of the studies included used randomization.

When patients volunteer to participate in studies, subjects may have characteristics that are unlike the general population and therefore not capable of being readily applied. Volunteer participants may be more health conscious, more compliant, or different in other ways that do not make them representative of the general population. Volunteer bias is not an issue in this analysis because these studies used medical records as opposed to recruited participants.

Recruitment into the study was determined primarily by the a priori MI definition and inclusion criteria determined by each individual study. The clinical definition for MI varied slight for different studies. The range of criteria for MI included ICD-9 codes, cardiac biomarkers cutoffs, and medical record discharge diagnoses. While these definitions are likely to recruit slightly different types of MI patients, all of these criteria are used in the real world and therefore generalizable to the general MI population.

While it can be argued that generalizability is not an issue in this analysis because not many studies used randomization or volunteered participants, application of these results should be done with caution. Because the types of guideline implementation programs vary so much, it is probably better to apply the results of these studies to programs of similar scope and size.

Findings

The literature search described above yielded 15 articles for analysis. The studies and their main features are presented in Table 1. The articles fell into one of three types of studies. The before-and-after design was used in 11 out of the15 articles and was the most common type. There was only one randomized control trial. The three remaining articles had some combination of randomized control trial and before-after study design.

Overall, the studies demonstrated that guideline implementation programs are successful at increasing the percentage of post-MI patients who receive beta-blocker prescription. All but one of the studies included in this analysis demonstrated some

improvement in guideline adherence after an implementation intervention. Six studies demonstrated a statistically significant increase in beta-blocker prescriptions after program implementation. An additional eight studies demonstrated an increase in guideline implementation whose significance was either not significant or whose significance could not be determined. One study found a statistically insignificant decrease in beta-blocker use.

The types of programs described by the studies in this analysis ranged from small, focused, hospital-based programs to large-scale interventions that involved hospitals in multiple states. Over half of the studies included in this analysis described state-wide interventions or interventions covering a region within a state. Four of the state studies examined hospital-based programs; three were multi-state programs.

In addition to differing in their scope, the guideline implementation programs also differed in their overall components. The most common component was general data-feedback which was present in over 70% of the implementation programs. General data feedback about hospital performance was either made available to individual physicians or public disseminated in routine meetings. The other common components of the guideline implementation programs included standing order sets, educational programs, and computerized decision support systems. The least common components of successful programs were the use of multidisciplinary teams and rewards or recognitions for guideline-adherent physicians. A detailed list of each variable and their prevalence among the overall and successful guideline implementation programs can be see in Table 3.

Certain variables seemed to be more common than were others in successful programs. All but one of the statistically significant studies demonstrated some form of data feedback. In some programs, such as the one described by Berthiaume, Davis, and Tiara, data feedback about national, statewide, peer-group averages was distributed to all physician in the form of quarterly reports.[39, 43-45] LaBresh et al. and Zhang et al. described rapid-cycle data feedback that could be accessed by physicians at any time.[46, 47]

Clinical education is another component correlated with success and was present in four out of the six programs with statistically significant improvements. (*Table 3*) Clinical education for most programs involved providing health care providers with information about the most recent clinical practice guidelines and to which patients those guideline apply. Some clinical education was delivered face-to-face [44, 48, 49], while others were delivered in the form of a newsletter [39, 43]. Neither face-to-face or newsletter seemed to be equally effective at predicting program success.

Clinical pathways and clinical care coordinators were also more common among programs with statistically significant improvement. Unlike general data feedback and education components, there was little variation in the way clinical pathways and care coordinators were implemented in the guideline implementation programs. Clinical pathways were presented through either the computer system or in paper form depending on whether how the hospital placed its medication orders. In each of program care coordinators were in charge of following guideline appropriate patients and issuing reminders to their physicians.

Discussion

The goal of this analysis of the guideline implementation literature was to evaluate whether guideline implementation programs have been effective at increasing guideline adherence, and if so, what specific components are responsible for their success. Not only does this paper shed light on the components that make guideline implementation programs successful, it also reveals which programs appear to be successful at which kind of adherence improvement.

Overall the results of this analysis demonstrate that guideline implementation programs can be effective at increasing the rate at which physicians write beta-blocker prescriptions for post-MI patients. Out of the 15 articles included in this study, six programs demonstrated statically significant improvements in guideline use. Although many factors no doubt contribute

to program success, some trends are particularly notable. The studies that demonstrated the strongest success tended to be large multi-state programs with large sample sizes – making significance easier to demonstrate -- and certain program components – that may be genuine indicators of what works.

The factors most strongly correlated with success were the use of general data feedback and clinician educational programs. These components were the most common variables among the statistically significant guideline implementation programs, yet, it is difficult to determine if these components are the reason for success; institutions who are disposed to form multidisciplinary teams and provide clinician education might, with all things being the same, be more likely to use guidelines, multidisciplinary teams and educational programs were also common in programs that were less successful. It does, however, seem reasonable to suggest that both team formation and education would be good strategies for guideline adoption.

What do the results mean?

This analysis suggests that certain variables are associated with success in all programs but some variables work better in certain types of programs, and not in others. In general, most programs seem to benefit from the presence of clinical care coordinators. The clinical care coordinator is someone who tracks all of the patients within the health care system and identifies the patients to whom the guideline applies. He or she also makes sure that those patients receive recommended care and that their physicians are aware of the guidelines. The presence of clinical care coordinators does not assure that every patient will receive evidence-based care. Instead, they prevent guideline-appropriate patients from slipping through the cracks by reminding physicians of the patients to whom the guideline applies, and giving them the discretion to decide whether the guideline is appropriate to that patient. Although the clinical care coordinator is only present in about a third of all the evaluated programs, they are present

in half the programs with significant levels of success. Clinical care coordinators may facilitate the deployment of guideline recommendations to the right patient at the right time.

Clinical educational initiatives also seem to be indicative of success in most guideline implementation programs. Four out of the six statistically significant studies had some sort of clinical education initiative. Even if the guideline implementation programs are not capable of providing a wide variety of components, education initiatives have been shown to be one of the strongest influences on guideline adherence.[50] This study and other interventions like it seem to suggest that making sure clinicians are aware of existing guidelines, even without the supplemental program components, may be enough to improve guideline adherence.

Although statistical significance is often the primary way of measuring program success, we must not lose sight of the importance of clinical significance, particularly as small program evaluations may lack statistical power to show the statistical significance even of meaningful change. Most of these programs appear to have demonstrated quality improvements even without associated statistical significance. Determining what makes a result clinically significant can depend on factors such as the magnitude of the result, the burden of the disease in question, and the cost-effectiveness of the intervention. Ultimately, clinical signficance has to be determined by the providers who are delivering the care.

Different types of programs

This analysis has also shed light on the variety of implementation programs and the components that might be most important to them. One structural factor distinguishing different types of guideline implementation programs is the scope of the intended change. This study found three distinct programs differing according to the number of people they are targeted to reach. The smallest scope of intervention included in this study is the hospital-based programs. The largest interventions were simultaneous multi-state programs. In between hospital based

and multi-state interventions were state-wide programs implemented throughout the entire states or portions of states.

Aside from differing in the number of people the programs reach, the scope of an intervention may also be an indicator of its effectiveness. In this analysis, the large-scale interventions were more likely to be statistically significant than the smaller hospital-based programs at least partly for structural and size reasons. All three of the multi-state interventions had statistically significant results.[47, 51, 52] Of the four small hospital-based interventions, only one showed statistical significance.[53] Of the eight state-wide interventions, only two demonstrated statistical significance.[43, 44] A more detailed description of these the studies and there results can be found in the evidence table, Table 1.

This example of varying significance may be a simple artifact of larger Ns of cases, since all studies with Ns of 3000 or more were significant. Studies with larger sample sizes are more likely to have statistically significant findings. It is also possible that broad, multistate guideline implementation efforts may represent intense desire for change at high levels. Simply undertaking to arrange a multistate intervention is itself a demonstration of the commitment to improve guideline adherence. In order to truly understand what is causing this phenomenon, a meta-analysis of program evaluation studies will need to be conducted. The increased statistical power offered by meta-analysis can help determine is the success of larger programs is a real association.

One of the advantages to implementing smaller interventions, on the other hand, invokes what can be thought of as a physician factor: that is, small interventions can be tailored closely to fit local patient populations and care delivery circumstances, and the literature suggests that physicians are much more likely to welcome guidelines the development or adaptation of which they feel they have influenced.[50] By design, guidelines are meant to be tailored and adapted as needed to fit different clinician and patient populations. Smaller interventions can address the specific concerns of health care systems in a way that larger programs may not. The

disadvantage of smaller interventions, as noted above, is that smallness can make success difficult to measure

Another physician factor, physician education, seems to be an important component for any guideline implementation program. It seems to have greater significance for smaller programs. One of the strongest predictors of guideline adherence is awareness that the guideline exists.[50] The first step in implementing guidelines is making sure that the clinicians and patients to whom the guidelines apply are aware of the recommendations. Education components are especially important for smaller interventions because these programs often have limited access to resources for quality improvement and guideline implementation. Education is one of the less expensive program components, and it seems to be indicative of success.

Structural variables such as health care coordinators and multidisciplinary teams, although shown to be effective when included in guideline implementation programs, typically require considerable resources, including hiring staff and enforcing changes in the delivery of care. Unlike these more expensive components, education initiatives can be effective at increasing guideline awareness and guideline adherence at relatively low cost.

Another structural distinction between different types of programs is determined by the number of components included in an intervention. Because so many variables can be included in a program, the development of a new guideline implementation program often raises concerns about which components to include. Different components have different advantages, and it can be difficult to decide on narrow rather than broad approaches to change.

This analysis suggests that the goal-specific approach to picking program components is particularly beneficial for hospital-based or small statewide programs, probably for "physician factor" reasons. The only hospital-based intervention with statistically significant results chose to focus completely on providing a comprehensive clinical pathway[53], and this local adaptation is the kind of physician-led effort that the literature says is necessary for physician acceptance of

guideline recommendations. If a hospital has many other components already in place but only lacks one potentially beneficial variable, it is better to add the missing component than to try broader change, potentially exhausting resources and diffusing energy.

In contrast, larger multi-state interventions seem to work better if they are broad multifactorial programs. Because larger statewide programs and multi-state programs usually have infrastructure and resources, they can afford to invest in a wide variety of components. By their very nature, state-wide programs and multi-state programs are dealing with a variety of health care systems; this diversity of systems may mean that a broad program, with many features, has a better chance of hitting the target of better adherence in different contexts. For example, within the same statewide program, one hospital may already be meeting most guidelines and providing many of the components important to guideline implementation; such a system may need comparatively few new elements in order to achieve further success. In the same statewide program, small community hospitals with limited resources may have difficulty establishing guideline adherence. Programs capable of delivering many different components can address both kinds of system needs.

What is contributing to the results?

It is possible that the relationship between the scope of an intervention and its effectiveness has more to do with the sample size of the study. The articles evaluating multi-state interventions tended to have larger number of participants, whereas hospital-based and state-wide interventions tended to have smaller sample sizes. The likelihood that a study will demonstrate statistical significance is fundamentally determined by the sample size and statistical power of that study. This means that the effectiveness of multi-state interventions might not have had anything to do with the scope of the intervention, although, as noted, the sheer effort required to create a large intervention itself demonstrates commitment to success. Another sucees factor, probably interacting between physician and structural considerations, is

the baseline adherence rate at the time of the intervention. Clearly, floor and ceiling effects are at work: programs with baseline adherence rates of less than 80% were more likely to have statistically significant results because they had more room in which to move. Ceiling effects need to be kept in mind when evaluating the potential for further change of already high-performing systems.

The importance of patient outcomes

Identifying the best candidates to improve patient outcomes is the point of this analysis. If guideline implementation programs are not effective at improving patient outcomes then there is really no point in applying them. In the case of beta-blockers and MI, the patient outcomes of interest are mortality and morbidities such as repeat MIs or heart failure. Even though studies have suggested that guideline implementation programs can increase beta-blocker use and the medical literature has demonstrated that beta-blockers are effective at reducing morbidity and mortality in MI patients, we need studies that demonstrate the vital connections between guideline adherence and better outcomes for patients.

It is possible that a guideline implementation program that is successful at improving quality indicators such as beta-blocker prescriptions may only have a modest effect on health care outcomes such as mortality or repeat MI. It is important that program evaluation studies evaluate patient outcomes in addition to quality indicators. In the larger scheme of health care, it is not enough to know that guideline implementation are improving guideline adherence, but that those programs are improving health care in general.

Cost effectiveness

We should consider cost effectiveness when we evaluate the implementation of any CPG program. Although most people today assume that evidence-based medicine has had a significant effect on improving certain aspects of health care quality, it is also clear that

evidence-based medicine has yet to reach its full potential and still has quite a bit of room to grow. Cost-effectiveness requires more attention in studies of guideline adherence than it usually receives. Programs not only have to be effective at improving patient outcomes, but they are usually expected to do so in economically sustainable ways.

One of the common misconceptions about cost effectiveness is that improving the quality of health care will, ipso facto, reduce health care cost. Just because inefficient health care often wastes money, however, it does not mean improving that health care system will necessarily save money. In fact, the opposite is often true. Improving health care on systems levels may well require significant resources. Hiring new staff, implementing systems changes, and maintaining those efforts not only requires a great deal of effort but also a large amount of money.

I think that money, or the fear that money will have to be spent, has been one of the greatest obstacles to the translation of evidence into clinical practice. Systemic reviews and guidelines are available for areas of medicine with strong scientific evidence, but developing the tools needed to support these recommendations may require money that is often not available (small hospitals and private practices, for example, may lack the resources to adopt Health Information Technology, as so many guidelines recommend).

Instead of a focusing strictly on saving money, health care systems should look at guideline implementation programs and other evidence-based medicine tools as an opportunity to spend money more efficiently. Instead of devoting resources to efforts that do not have evidence of effectiveness, it makes more sense to find out what is working and spend energy doing that. Studies like the present work are important because they help determine whether resources are being used well, and suggest how they can be used better. If we see that certain guideline implementation program are more effective than others, this will help health care systems, especially those under tight fiscal constraints, spend their resources in the most effective manner.

Should programs be optional or required?

In the hustle and bustle of an inpatient course or outpatient clinic, failure to implement guidelines in appropriate patients may have more to do with time constraints and momentary forgetfulness than blatant disregard for the medical literature. As a result, many of the components that are common among guideline implementation programs have been set in place to address these obstacles. The question is whether program components such as clinical pathways and reminder forms should be optional or required.

While components of guideline implementation programs like reminder forms and data feedback are helpful, they are often not adapted in a way that matches with the evidence that spawned them. If the evidence is strong enough to warrant guideline recommendation, it is likely also strong to warrant making these tools a vital part of that health care system. Instead of making reminder forms available in such a way that clinicians have to remember to use them, why not make these reminder forms the default system?

Most optional guideline implementation programs leave much to the discretion of the practitioner. The way most such programs are designed, even helpful tools, by being "optional," may not be readily available to clinicians. The downside to a completely optional program is that practitioners must make a conscious effort to seek out these programs in order to use them. In contrast, programs with "required" components are incorporated into the existing health care system as the defaults.

When most programs are implemented, their features are not often fully integrated into the existing system of care. Although research evidence will never apply to all patients, in areas of medicine where there is strong clinical practice guideline those recommendations will likely apply to most of them. Therefore, it makes sense to make guideline implementation programs and their components the standard within the health care system, rather than an addendum that practitioners must seek out. For example, beta-blockers are recommended for about 80% of

post-MI patients.[38] Given the strength of the evidence, post-MI beta-blocker use should become the default standard of care.

Should we move on to larger results generated by national programs?

The results from this analysis suggest that larger programs tend to be more successful at improving guideline adherence than are smaller programs. If this is the case, is it safe to say that a national program will have the greatest efficacy? In this case, a national effort to make post-MI beta-blocker prescriptions for all appropriate patients may be a very effective strategy to change the standard of care. Theoretically, even small health care systems should be able to adopt this strategy, particularly if those small systems know that adoption meets a national standard.

Limitations

Even though the topic of post-MI beta-blocker use has been extensively studied when compared to other guideline recommendations, the number of studies is still limited, and the small number of program evaluation studies means that interpretation of results can be difficult. Surely, continued study of what makes guideline implementation most successful is warranted.

Future studies

This analysis has the potential to improve the development of future guideline implementation programs and influence how these programs are evaluated. In the future, studies must be conducted with enough statistical power to detect a statistically significant effect of different interventions. Many of the studies looking at the effectiveness of guideline implementation programs are analyzing pilot studies with few subjects.

If the goal of these programs is to improve the translation of guidelines into clinical practice, effectiveness studies should be conduced in populations that reflect the health care

systems that need the programs. Many of the evaluation studies are conducted in health care systems with guideline adherence rates that were already well above the national average. While it may be argued that even hospitals with high beta-blocker prescription rates need incentive to improve their rates, the issue of selecting appropriate study populations still needs to be considered.

Not only does the baseline rate of guideline adherence affect the ability demonstrate statistically significant improvement, results from studies done in hospitals with high guideline adherence rates may be difficult to replicate in settings with lower adherence rates at the outset. Further, initiating change may require different strategies than does sustaining the change one has initiated. Finally, change for one patient population may not achieve the same kind of change in systems with different populations. Future studies need to give considerable attention to the context in which change is desired.

Conclusion: Looking Forward

As health care systems attempt to find the most effective way to improve guideline adherence, patient adherence should also be explored. Evidence-based practice requires that physicians provide care supported by best evidence, but patients must also be receptive to that care and adhere accordingly. This involves finding ways to increase health literacy and improve access to treatments. Although these are complicated issues they are worth thinking about because many of these components can be incorporated in guideline implementation programs. Some of the programs analyzed in this study had components that also included patient education devoted to improving patient compliance with beta-blocker use. They measured patient response by recording how many of the beta-blocker prescriptions had been filled by patients. Although patient adherence to therapy is a separate issue from physician adherence to guideline recommendations, they work hand in hand in the translation of evidence into clinical practice. Both are necessary if any health care benefits are going to be seen.

Appendix. Variables Indicative of a Successful Implementation Program

- Physician/Opinion Leaders
  - 0 = No Opinion Leader
  - 1 = Unofficial Leader (present but not part of intervention)
  - 2 = Official Leader (present and part of intervention)
- Standing Order Sets
  - 0 = Not Available
  - 1 = Available but optional
  - 2 = Available and mandatory
- Data Feedback
  - 0 = Not collected
  - 1 = Collected but not discussed
  - 2 = Collected and discussed in regular meetings
  - 3 = Collected and made public for hospital staff
- Clinical Pathways
  - 0 = Not Available
  - 1 = Available but optional
  - 2 = Available and mandatory
- Organizational Support For Quality Improvement (Health care system that provides adequate resources for projects, support from administration, physicians and nurses)
  - 0 = No organizational support
  - 1 = Minimal organizational support
  - 2 = Adequate organizational support
- Educational Programs
  - 0 = No
  - 1 = Yes, Optional
  - 2 = Yes, Mandatory with intervention
- Multidisciplinary Quality Teams
  - 0 = No
  - 1 = Yes
- Care Coordinators (person in charge making sure all eligible patients are following recommended care)
  - 0 = No
  - 1 = Yes
- Computer Support Systems
  - 0 = No
  - 1 = Yes
- Reminder Forms
  - 0 = No
  - 1 = Yes
- Recognition and Rewards For Successful Efforts
  - 0 = No Recognition
  - 1 = Private Recognition
  - 2 = Public Recognition

Table 1. Evidence Table

Study	Study Design	No. of patients	Scope of intervention (Location)	Definition of MI	Length of Study	Demographics (Age/Sex)	Outcome Results (control vs. intervention) RCT (before to after) before-after	P-value
Bailey, 2007	RCT	853	Hospital-level (Barnes Jewish Hospital)	Troponin > 1.4 ng/mL	4 months	Age: ▪ <55 y - 22.7% ▪ 55-66 y - 29.1% ▪ >67 y - 48.2% Sex: 40% Women	91.8% vs. 95.9%	P = 0.08
Berthiaume, 2007	Before-after	25,801	Statewide (Hawaii)	2 diagnoses of MI, CAD or documented CABG	4 years	Age: ▪ <40 y - 2% ▪ 40-64 y - 56.8% ▪ >65 y - 41.2% Sex: 33.6% Women	36% to 47%	**P < 0.001**
Biviano, 2004	Before-after	292	Hospital-level (NY Presbyterian)	ED patients w/ trop.> 2.0 ng/ml	1 year	Age: mean age = 68 y Sex: 65.5% Women	89% vs. 94%	P = 0.45
Butler, 2006	Before-after	576	Hospital-level (Vanderbilt Hospital)	ICD-9 code for MI	2 years	Unknown	88% to 95%	P = 0.07
Fonarow, 2001	Before-after	558	Hospital-level (UCLA)	Medical record diagnosis of MI	4 years	Age: mean age = 70 y Sex: 42% Women	12% to 61%	**P < 0.01**
Hilbert, 2000	Before-after	400	Statewide (TX)	Medical record diagnosis of MI	3 months	Unknown	57.5% to 74.3%	Unknown
LaBresh, 2004	Before-after	1,738	Statewide (MA)	Not specified	1 year	Unknown	85% to 84%	P > 0.05
Lappe, 2004	Before-after	57,465	Statewide (UT)	Medical record diagnosis of MI	6 years	Age: mean age = 66 y Sex: 42.3% Women	53% to 91%	**P < 0.001**
Marciniak, 1998	Before-after	12,339	Multi-state (AL,CT, IA, WI)	Medicare pts discharged w/ MI	4 years	Age: mean age = 75 y Sex: 48% Women	31.8% to 49.7%	**P < 0.001**
Mehta, 2002	Combo	1,649	Statewide (MI)	Discharge ICD-9 code for MI	1 year	Age: mean age = 73 y Sex: 47.9% Women	70.3% to 86.4% (control) 87.3% to 92.9% (intervent.)	P = 0.27*
Mehta, 2004	Before-After	1,022	Statewide (MI)	Medical record diagnosis of MI	1 year	Age: mean age = 67 y Sex: 43.3 % Women	78.4% to 90.4%	P = 0.075
Rammuno, 1998	Before-After	350	Multi-state (ME,NH,VT)	Discharge diagnosis of MI	3 years	Unknown	69.1% to 82%	**P < 0.01**
Sauaia, 2000	Combo	1,367	Statewide (CO)	Discharge diagnosis of MI	2 years	Age: mean age = 74 y Sex: 43% Women	65% to 88% (control) 48% to 73% (intervent.)	P = 0.47*
Zhang, 2005	Before-After	11,394	Multi-state (CA, LA, FL)	Discharge diagnosis of MI	1 year	Age: mean age = 70 y Sex: 40% Women	62.4% to 83.5%	**P < 0.001**
Zuckerman, 2004	Before-After	2284	Statewide (PA)	Medicaid patients with a medical record diagnosis of MI	1 year	Age: ▪ <50 y – 11% ▪ 50-69 y – 40% ▪ >70 y – 49% Sex: 63.8% women	46.3% to 49.6% (7 day analysis) 61% to 64.7% (30 day analysis)	P = 0.13 P = 0.12

* the p value refers to comparison of the follow-up values (after implementation) between the control and intervention groups
The unit of analysis for all of the above studies is the patient. All randomizations were at the level of the patient.

Table 2. Brief Study Description

Study	Brief Description
Bailey, 2007	A randomized prospective study conducted between 02/01 and 05/01 in St. Louis, MO at Washington University. It was a hospital level intervention done within one university-teaching hospital. The intervention included a computer support system that flags eligible patients and a care coordinator contacted physicians (by phone or face-to-face) about eligible patients who were not receiving evidence-based health care.
Berthiaume, 2007	A retrospective observational analysis (before-after study) conducted between 2000 and 2004 in Hawaii. It was a statewide intervention conducted on patients enrolled in Hawaii Medical Service Association (HMSA), an independent licenser of BCBS. All patients were diagnosed with CAD or CABG/PTCA. The intervention included education for physicians via newsletter, medication reports, and CME credit; flowsheets/pathway, case manager, pay-for-performance, and general data feedback reports.
Biviano, 2004	This is a before-after hospital-level study conducted between 2000 and 2001 in NY Presbyterian Hospital. All patients presented with troponin > 2.0 ng/mL within 24 hours. The preprotocol group was comprised of patients evaluated before the intervention. The protocol group was divided into control (where the intervention was used) and the intervention group (where the intervention was not used. The intervention included educational sessions for house staff physicians, clinical pathways, and clinical care coordinators.
Butler, 2006	A before-after study conducted between 7/01 and 6/02 at Vanderbilt University. The intervention included a computer system that flags patients with AMI before they are discharged to give them a reminder about standard AMI care. Use of the program increased from 7% to 52% throughout the intervention.
Fonarow, 2001	A before-after study conducted between 1992-1995 in a university/teaching hospital. Participants had documented CAD (256 pre-CHAMP and 302 post-CHAMP). The intervention for the Cardiac Hospital Atherosclerosis Management Program (CHAMP) and included a treatment algorithm (clinical pathway to make sure that beta-blocker therapy was started on all patients with AMI or UA
Hilbert, 2000	A before-after trial conducted between 1999 and 2000 throughout Texas. Baseline measures were collected using self-chart audit and followed at 3 months, 6 months, and 12 months. This was a multifaceted interactive statewide intervention with Texas Health Care Partnership (HCP). Each hospital looked at 50 charts and each physician practice looked at 30 charts. The comprehensive intervention included an education program, consensus development about quality improvement process, and development of patient education tools. Data feedback was also provided.
LaBresh, 2004	A before-after study was conducted between 07/00 to 06/01in 24 Massachusetts hospital. From. It was a state level intervention. There were 1738 patient with CAD and AMI. The intervention for the Get With The Guidelines program included physician leaders, hospital teams, reminder screens, data collection with real time feedback, printed order sets, discharge forms and web-based management.
Lappe, 2004	A before-after study conducted between 1996 and 2002 and based in Utah. It was a state-based intervention in the 10 largest hospitals in Utah associated with Intermountain Health Care – a non-profit health care system. The "discharge medication program" was a multi-hospital integrated system that included an institution-wide database with monthly feedback meetings, extensive education campaigns, patient discharge forms, care coordinators (d/c planning nurse), computerized system to track discharge medications.
Marciniak, 1998	A before-after study conducted between 1992 and 1995 in various states (Alabama, Connecticut, Iowa, Wisconsin). All participants were Medicaid patients diagnosed with AMI on discharge. The Cooperative Cardiovascular Project included education efforts, PRO physicians leaders, and data feedback presented by PROs, telephone, mailings. They also offered recommendations for standing orders and clinical pathways.
Mehta, 2002	This is a before-after/control study of the Southeast Michigan. Between July 1998 and July 1999. The intervention included AMI standard orders sets, clinical pathways, pocket guides for AMI, patient information, discharge forms, chart stickers, hospital performance charts, standard orders, and educational support.
Mehta, 2004	This is a before-after study conducted from 01/01 to 03/02 conducted in Flint and Saginaw Michigan expansion. The intervention included AMI standard orders sets, clinical pathways, pocket guides for AMI, patient information, discharge forms, chart stickers, hospital performance charts, standard orders, and educational support.
Rammuno, 1998	A before-after study conducted between 1994 and 1997 in various states in northern New England. Cooperative Care Project. All participants had confirmed AMI diagnosis at hospital discharge (217 participants in the before group and 133 in the after group). The Cooperative Cardiovascular Project included data feedback mailed to physicians with hospital-specific, state-wide, and peer group data. It also included new action plans for improvement.

Table 2. cont.

Study	Brief Description
Sauaia, 2000	A randomized control trial conducted in Colorado. Included 18 hospitals (10 rural and 8 urban) that were randomized to the Coopertaive Cardiovascular intervention or standard written feedback. All participants were diagnosed with AMI when discharged from the hospital. The intervention included on-site presentation by a physician leader that provided feedback about individual physician performance in comparison to state and national averages. Hospitals were also encouraged to organize multidisciplinary quality teams and include them in the groups.
Zhang, 2005	A before-after study conducted between 01/01 and 06/02 in multiple sites throughout the nation (Southern California, New Orleans, and South Florida). It was conducted in hospitals owned by the Tenet Healthcare Corporation. There were 11,394 patients included in the study who were diagnosed with AMI and discharged from the hospital. The intervention included a rapid cycle computer data feedback, process improvement teams (senior management, director, case management team, quality department and clinicians), case managers, and internal reporting website.
Zuckerman, 2004	This is a before-after study conducted in Pennsylvania. Done between 11/98 and 11/99. It was done state-wide with physicians of the Pennsylvania Medical Society. The intervention included identifying physicians with less than 80% beta-blocker prescription rates and providing them with educational material (by mail for CME credit) and Medicaid patient feedback. This study evaluated patients at 7 days and 30 days post-MI.

Table 3. Program Components

	Percentage of all of studies	Percentage of successful programs
Physician/Opinion Larders	4/15 (27%)	1/6 (17%)
Standing Order Sets	7/15 (47%)	3/6 (50%)
Gen. Data Feedback	11/15 (73%)	5/6 (83%)
Clinical Pathways	6/15 (40%)	3/6 (50%)
Organizational Support	6/15 (40%)	1/6 (17%)
Education Programs	7/15 (47%)	4/6 (67%)
Multidisciplinary Teams	3/15 (20%)	1/6 (17%)
Care Coordinators	6/15 (40%)	3/6 (50%)
Computer Support	7/15 (47%)	2/6 (33%)
Reminder Forms	4/15 (27%)	0/6 (0%)
Recognition/Rewards	1/15 (7%)	1/6 (17%)
Discharge Form	4/15 (27%)	1/6 (17%)

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