How Can Clinicians Incorporate Research Advances into Practice?

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In 1965, my freshman college chemistry lab partner told me an anecdote about his father, a Michigan country doctor, that left an indelible impression. He contrasted the drudgery of a freshman struggling to master college chemistry with the excitement his father experienced at a medical education meeting. The excitement came from how much his dad had learned. He learned how to be a better doctor. He was going to change his practice, and his patients would be better off because of what he had learned. Although it was not apparent to me as a naive freshman, this anecdote is an example of applied learning—new knowledge and research incorporated into practice. More than 30 years later, the practicing physician has the same opportunity: to improve practice based on new knowledge. Today's practitioner has an array of diagnostic and therapeutic techniques that are quite different from those of my classmate's father. In addition, the material generated by today's global medical research enterprise is extensive and expanding rapidly. We continue to experience the same sense of excitement over opportunities to learn of advances that help our patients. We are also, however, probably more aware today of practices that were adapted, only later to be proved ineffective or even harmful.^{1,2}

The challenges of incorporating research into practice involve several processes. First, the clinician needs to learn of the advance. Second, some judgment should be made about whether a research advance signals the need to make a change in practice. Third, the clinician must change practice, including perhaps learning new skills. Each of these processes is dynamic. One of the joys of practicing internal medicine is the constant interplay of forces old and new—knowledge, judgment, and experience with patients—that constitute everyday decision making and practice.

This article describes the challenges clinicians face learning about medical advances and determining whether an advance is relevant to practice. Examples are provided from recent updates in general internal medicine. A common theme is the importance of consensus in sifting through the scientific literature and in the development of practice changes. Modest changes in therapeutic precision, once proved, tend to be easier to incorporate into practice, whereas more radical changes will require more

evidence and greater consensus. As a consequence, I do not believe in rapidly incorporating new agents into practice if they are only slightly different from existing, effective alternatives.

LEARNING ABOUT RESEARCH ADVANCES

Clinicians have many opportunities to learn about research advances. They are archived in medical journals, whose numbers have expanded dramatically to handle the increased volume of work produced by the medical research establishment. Although journals compete to publish the top, newsworthy advances, the clinician frequently finds it difficult to “find” the truly important advances. Most clinicians, including academicians, spend relatively little time reading traditional medical journals. Most medical journals principally serve an archival purpose and support the needs of the professional organizations that sponsor them. For clinicians, journals are usually not the principal source of news that leads to changes in practice.³

As journals have expanded, so have efforts to translate published research advances for use by clinicians in practice. Annual reviews, yearbooks, or publications of controversies are traditional sources in which experts review, compile, or debate research findings, ostensibly to make them available for practicing physicians. Formal consensus processes have been developed by many diverse organizations,¹ including the federal government (the NIH Consensus Development Conferences), professional societies (the ACP Clinical Efficacy Assessment Project⁴ or CEAP), the AMA's Diagnostic and Treatment and Technology Assessment (DATTA) program, and industry and local groups. All these efforts encourage the standardized, orderly adoption of new medical practices. Various groups seem to compete for the attention of clinicians and policy makers. Consensus groups appear and disappear regularly. Clearly, no single process has adequately solved the sorting problem for the practicing physician.

Newer journals are taking a more critical and telegraphic approach to compiling published research relevant to clinical practice. Journals like the *ACP Journal Club* and *Evidence-Based Medicine* are aligned with traditional publications like the *Annals of Internal Medicine* and *British Medical Journal*. For doctors who wish to improve their practice using published material, the *ACP Journal Club* is helpful. I find that it allows me to review more papers more efficiently. I do not waste time because the editors employ a “quality filter,”⁵ using well-established techniques of clinical epidemiology and critical appraisal.

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Equally important are the editors' attempts to limit what they publish strictly to material that is relevant to clinical practice. Online versions most likely will be even more popular, particularly if they provide more rapid access to proven advances. Ideally, online versions will allow physicians to use clinical research results, published in peer-reviewed journals, to guide changes in their practice. The attraction of abstract journals for busy clinicians is evidenced by the 70,000 subscribers to the paper and electronic versions of *Journal Watch* published by the Massachusetts Medical Society.

CONSENSUS CAN HELP

Even with advances in medical publications, the practicing clinician faces a challenge sorting through the large array of research findings. Traditionally, medical practice changes have emerged through informal networks.⁶ Often a respected local consultant, a popular academician, or a pharmaceutical sales representative, rather than a published research report, is credited with changing community practice standards. This finding suggests that our colleagues, particularly local colleagues, also play an influential role in the incorporation of research advances into medical practice. This phenomenon is reflected in the fact that the standard of practice in malpractice litigation sometimes is determined by local practice standards of physicians of the same specialty.

One can harness the energy of colleagues to discover the important research advances relevant to developing practice standards. The most popular feature of the annual meetings of the Society of General Internal Medicine (SGIM), American College of Physicians (ACP), and many other professional societies are the updates. For example, for the General Internal Medicine Updates of the 1995 and 1996 ACP annual meetings,^{7,8} my colleagues and I took a systematic approach to "discovering" the seven or eight most important research advances published for the practice of general internal medicine. Initially, we were overwhelmed by the prospect of determining the most important papers for general internal medicine clinicians published in the preceding year. We also did not want to rely on the judgment of just one or two persons to review a year's publications. Thus, we polled colleagues in our division asking them to list the five or more papers or topics in the past year that had the most influence on their practices. We were pleased that a consensus emerged in each of the 2 years we used this approach.^{7,8} As part of our systematic, consensus-building approach, we also shared our findings with editors of the *ACP Journal Club* both years. They agreed with the topics we chose. As part of the update process, we summarized each individual paper on a single page. The information on that page clearly states the implications for changes in practice or lack thereof.

Our presentations of the results have been well received at national and local ACP and SGIM meetings.

Evaluations report that physicians found it valuable to confirm changes they had already made in their practice or to learn of changes they would make. Interestingly, the contents of the updates coincided with material included in ACP updates in the subspecialties of internal medicine, thereby supporting the validity of this method. A better measure of the method's success will be the durability of research advances compiled in this fashion.⁸

PROOF PLUS CONSENSUS

An update satisfies the desire of clinicians to stay current and their need to practice in a way that reflects community standards, which are developed in a collegial fashion. The critical elements of our approach were: the requirement that the research papers be passed through a quality filter and thus meet robust standards of proof, based on clinical, epidemiologic, and critical appraisal principles; the ability of a group of clinicians who read the medical literature to converge on a limited number of developments; and a third step in which *ACP Journal Club* editors "independently" confirmed the importance of the advances.

For me, meeting rigorous standards of clinical proof plus the emergence of consensus among professionals is important in the incorporation of research advances into clinical practice. This approach is conservative but will most likely avoid ill-advised therapeutic adventurism. Also, it presumably will avoid perverse incentives, which arise when clinicians receive what is typically selective information through informal sources such as sales representatives whose goal is to promote their company's product.

RECENT ADVANCES LEADING TO CHANGE

The clinically important advances in general internal medicine presented in 1994–1996 ACP Updates in General Internal Medicine consisted predominantly of changes in the treatment of chronic diseases (Table 1).^{7–9} Most of the information allowed clinicians to make better choices among existing treatments, thereby improving therapeutic precision. For example, a steady stream of evidence of improved long-term outcomes has been used to support more widespread use of angiotensin-converting enzyme (ACE) inhibitors for patients with congestive heart failure or diabetic nephropathy.

The one dramatic change reported in each of 3 years involved the establishment of *Helicobacter pylori* as the common cause of duodenal ulcer. Eradication of *H. pylori* leads to cure. Important clinical details are emerging concerning the value of noninvasive tests and the relative efficacy and side effects of various antibiotic regimens in this disease. Clinicians are increasingly and collectively establishing a standard of practice for treating duodenal ulcer that consists of efforts to eradicate infection with *H. pylori*.

Another theme that practicing clinicians and compilers of updates face is the ongoing, regular appearance of

Table 1. Clinically Important Advances in General Internal Medicine, 1994–1996*

1. Heart disease
Thrombolysis is most effective when used early for acute myocardial infarction; differences in agents are not as great as differences related to timing; emergent percutaneous transluminal coronary angioplasty (PTCA) also is effective.
PTCA and coronary artery bypass graft (CABG) are similar in efficacy in selected patients with angina, but PTCA is associated with faster recovery while CABG results are more durable.
Angiotensin-converting enzyme (ACE) inhibitors have life-prolonging efficacy in the management of congestive heart failure.
There is more convincing evidence that cholesterol lowering with statin drugs prevents progression of arteriosclerotic vascular disease.
Estrogen with or without progestin can be recommended as safe and generally favorable for cardiovascular risk reduction.
2. Hypertension
Antihypertensive therapy is safe and effective for systolic hypertension in elderly patients.
The results are variable regarding differences in the efficacy and safety of antihypertensive agents; lower-dose thiazide treatment generally is effective and safer than higher doses.
3. Thromboembolic diseases
Clinical signs and ultrasound will diagnose or rule out most cases of suspected deep venous thrombosis (DVT).
Warfarin dose is the most important factor determining bleeding complications.
After DVT or pulmonary embolus, 6 weeks of warfarin treatment is insufficient duration compared with 6 months.
Increasing evidence supports the efficacy of low molecular weight heparin, which can be administered at home as an effective substitute for in-hospital treatment with heparin in selected cases.
4. Duodenal ulcer
<i>Helicobacter pylori</i> is the most common cause of duodenal ulcer disease.
Eradication of <i>H. pylori</i> leads to cure.
So-called triple antibiotic therapy can lead to 90% eradication rate.
5. Viral diseases
There is additional evidence that influenza vaccine is effective in elderly plus new evidence that vaccinated working-age adults will miss fewer days of work when epidemic influenza occurs.
Famciclovir reduces the duration of postherpetic neuralgia in persons over age 50.
Acyclovir reduces shedding in genital herpes virus infection.
Interferon α has beneficial effects for some persons with chronic progressive hepatitis C.
6. Prevention
There is new evidence favoring influenza vaccine in the elderly, fecal occult blood screening tests for colonic carcinoma, and screening sigmoidoscopy and colonoscopy for colonic carcinoma in special groups.

Table 1. Continued

Ordinary activity as tolerated is more effective than forced bedrest for acute low back pain.
There is new information about the magnitude of smoking-related mortality and the J-shaped relationship between alcohol consumption and mortality from long-term follow-up studies.
7. Asthma
Long-acting inhaled corticosteroids are the cornerstone of treatment for asthma.
A long-acting β agonist, salmeterol, is useful for persons not responding to inhaled steroids.
8. Diabetes
In Type I diabetes, ACE inhibitors and more intensive insulin therapy have favorable effects on long-term outcomes.
Metformin is useful as monotherapy or as an adjunct to glyburide in non-insulin-dependent diabetes.

*Sources: Larson and McGee,⁷ Larson and Sheffield,⁸ and Goldman.⁹

new chemotherapeutic agents, chemically related to drugs already in use, but offering possible advantages in terms of slightly greater efficacy, ease of administration, or more favorable side-effect profiles. Examples that usually do not merit inclusion in annual updates of clinically significant advances are new nonsteroidal anti-inflammatory drugs (NSAIDs) for arthritis or the latest addition to the growing number of cephalosporin antibiotics. These so-called advances are really not “news” given their predictable appearance. They are also not very important for physicians to incorporate into practice as they rarely have a major effect on patients’ well-being. By contrast, a recent example cited in the ACP Updates is a demonstration that famciclovir reduces the duration of postherpetic neuralgia in patients over age 50 with *Herpes zoster*. In this case, even though famciclovir is quite similar to acyclovir, the finding was new and indicated a change in how to treat a relatively common problem.

Two topics that did not appear in the updates but were associated with practice changes reported by our colleagues were the growing use of selective serotonin reuptake inhibitor (SSRI) drugs for depression and the safety and efficacy of daily doses of aminoglycosides. In the case of SSRI drugs, a practice change was occurring, but a convincing randomized trial comparing SSRIs with traditional antidepressants was not available. The aminoglycoside dosage change certainly could have been included as an advance that should be incorporated into everyday practice.

GUIDING PRINCIPLES

How does the clinician incorporate research advances into clinical practice? Well done *randomized trials* of *biologically plausible* treatments along with a rising tide of *consensus* invariably lead to practice changes. Beyond

these self-evident observations, there are some principles that I follow.

Research designed to improve the *therapeutic precision* with which we use existing agents is usually easier to incorporate into practice. Recent examples are the increasing use of ACE inhibitors, progressive improvements in the way we use warfarin and heparin, and the increased appreciation that inhaled corticosteroids should be the cornerstone of the treatment for asthma.

By contrast, prudent clinicians should learn to be wary of drugs that are marketed as improved variations of existing drugs, especially when their utility has only been demonstrated for carefully selected patients in relatively short-term efficacy studies. This skepticism is particularly important when existing, generally effective drugs are already available to patients and there is little need for a new version. In the 1970s, a new drug, zomepirc, was widely promoted as an improved NSAID. It was marketed heavily to physicians and arthritis self-help groups. Arthritis patients came to their doctors asking for treatment. The doctors who quickly incorporated this drug into practice eventually discovered a high prevalence of renal toxicity only evident through postmarketing surveillance. Eventually even patients who tolerated the drug had to be given an alternative NSAID when the drug was withdrawn, as its potentially lethal side effects became apparent. Ticynafen, a thiazide-like diuretic, enjoyed brief popularity particularly because of its uricosuric effects, but rapid adapters were disappointed when the drug was withdrawn in 1980 because patients developed acute renal failure and allergic hepatitis.

In general, there is little reason to quickly adopt new therapies when existing treatments offer a variety of reasonably safe, effective treatments. Face-to-face comparison studies of similar treatments are relatively uncommon, as clinically important differences tend to be difficult to demonstrate in these settings. Typically, new treatments involving drugs chemically related to existing drugs are compared with no treatment—not with the closely related or parent drug.

In contrast, incorporating truly major changes in therapy into practice will typically require more time and more proof. The ongoing story of *H. pylori* emerged over the past 10 years, although evidence pointing to a bacteriologic agent like *H. pylori* as a possible cause of peptic ulcer disease was evident at least 50 years ago, or is at least evident through the retrospectroscope. For me, long-term follow-up information is important in studies of chronic disease management. In the *H. pylori* instance, a short article describing a simple, 7-year follow-up study of some of the first patients with duodenal ulcer treated with antibiotics demonstrated that short-term bacteriologic eradication or failure to eradicate correlated with long-term remissions and cure or relapses.¹⁰ Successful antibiotic treatment of relapses also led to cure. For *H. pylori*, the nature of the change in practice is instructive. A relatively brief but complex antibiotic treatment had to

compete with type 2 histamine (H_2) blockers, a treatment that had gained widespread worldwide acceptance over the past 20 years. H_2 blockers are generally well tolerated, but most patients require them for long periods. Experienced clinicians had to be convinced of both short-term and long-term efficacy. We also had to develop a new understanding of an old disease and a major change in the way we “teach” patients to care for this heretofore chronic disease.

TREATING THE INDIVIDUAL PATIENT

Another problem frequently facing clinicians is the question of whether a treatment is likely to work in an individual patient. Traditionally, clinicians have relied on previous learning, published papers and texts, accumulated clinical experience and observations, and advice from colleagues and consultants. However, we often use treatments that are old but unproved, or established and proved, but novel. In most instances, treatments are applied to patients who don't meet criteria for inclusion in a randomized controlled trial. One method a clinician can consider for improving therapeutic precision is an *n*-of-1 clinical trial,^{11,12} particularly when efficacy is truly in doubt and when treatment, if effective, will be continued long term. In this situation, the clinician solves the question of incorporating a research advance or treatment of uncertain value by performing effectiveness research on a single patient, using techniques developed for rigorous assessment of efficacy in cohorts of patients. These techniques include randomized allocation of treatment, blinding of patient and caregiver to treatment allocation, and predetermined measures of effectiveness. The techniques are time-consuming. They require a willing and interested patient and clinician and typically an interested pharmacist. Thus, *n*-of-1 trials face an uncertain future.

Results of *n*-of-1 trials do demonstrate an important principle: both new and well-established symptomatic treatments need to be assessed for their value in the single patient who receives them in everyday practice. A recent trial of *n*-of-1 trials compared with standard practice demonstrated that doctors tend to be optimistic, believing that treatments we offer to individual patients will and do help¹³; the patients in the “control” group were prescribed more symptomatic medications than the patients in the group in which therapeutic choice was based on results of *n*-of-1 trials. A simple rule I follow: if symptomatic treatments aren't producing the desired effect, there is usually no reason to continue them.

CONCLUSIONS

Research advances present clinicians with opportunities to provide better patient care. Clinicians are challenged, however, by the vastness of the medical research enterprise to find truly important and durable advances. Efforts to distill published research into advances most

applicable to clinical practice are more likely to be successful when they employ a critical appraisal quality filter. Another selection mechanism is needed to limit published material to research relevant to clinical practice.

Practice patterns are usually determined in a collegial fashion. Efforts to select important research advances can harness the collective wisdom of colleagues and arrive at general consensus regarding the most important advances in the past year for a field like general internal medicine. These advances typically involve modest changes in the treatment of chronic diseases. Research that improves the therapeutic precision with which we deliver established treatments is usually easy to incorporate into practice. Major changes in therapeutics tend to emerge over 5 to 10 years. New agents that promise only modest improvement over existing, effective agents do not need to be adopted rapidly by most clinicians. Major changes, by contrast, may require clinicians to develop a new understanding of an otherwise familiar disease, as exemplified by the recent discovery that *H. pylori* is the most common cause of duodenal ulcer.

In spite of the increased use of randomized clinical trials to demonstrate efficacy, effectiveness in individual patients may remain uncertain. Clinicians may use single-patient trials to test efficacy in selected patients. For treatment designed to promote symptomatic relief, clinicians need to ascertain that treatment is actually producing the desired effect. Ineffective treatments should be stopped.

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