## When Medicine Reverses Itself: Avoiding Practice Pitfalls

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An article in *American Family Physician* summarizing the top 20 research studies of 2011 reported on a number of practical, patient-oriented findings.[1] One striking feature of this article is the inclusion of several studies that challenge traditional medical opinion. In the 1990s, for example, high-carbohydrate, low-fat diets were all the rage; now the Mediterranean diet is shown to have better results in managing and preventing disease. Other studies show that using tight control in patients with diabetes mellitus has produced fewer benefits than previously thought, and long-term treatment with bisphosphonates does not reduce the risk of femoral neck fracture.

These examples highlight just a few of the time-honored treatment recommendations we have had to rethink in the past few decades. In a reversal that is now well-accepted, the U.S. Preventive Services Task Force recently recommended against hormone therapy as a preventive measure against chronic disease in postmenopausal women.[2] Yet 20 years ago, a gynecology textbook advised physicians that hormone therapy was the "main treatment" for climacteric symptoms and to prevent long-term adverse effects, such as osteoporosis, cardiovascular disease, and urogenital atrophy.[3] Although there is now greater public awareness of the potential risks of hormone therapy, which except for limited use in managing symptoms generally outweigh the benefits, there was a time when as many as 90 million prescriptions were filled for this treatment every year.[4] More recently, physicians have learned that the long-claimed reduction in post–myocardial infarction mortality associated with beta blockers may, in fact, have been overstated. This conflicts with efforts to improve physician compliance with guidelines that recommend indefinite post–myocardial infarction beta blockade.[5,6] To cite yet another more recent example, physicians have also learned that in many contexts, computed tomography is not only unnecessary and costly, but potentially harmful.[7-9]

How is it that we have seen such dramatic modifications, if not retractions, of important practice recommendations? How can we trust that we will not make the same mistakes in the future?

Clinical recommendations may be more vulnerable to reversal when research conditions favor bias and error. For example, declining effect size when studies are replicated has been attributed to both publication bias and unconscious errors in data interpretation.[10,11] Other flaws in scientific studies include the following:

- Poor design and small size.[10] Recommendations for hormone therapy, for example, were based on observational studies and were later challenged by prospective trials.
- Focus on disease-oriented evidence.[12] Disease-oriented evidence, which concentrates on surrogate markers such as blood levels, imaging findings, and results of other tests, is often conflicting and inconsistent. Studies that measure patient-oriented outcomes, which address morbidity, mortality, and quality of life, often follow (and contradict) disease-oriented outcomes. In the case of hormone therapy, high-density lipoprotein levels were improved, but patient-oriented cardiovascular outcomes were not affected.
- Application of findings to nonstudy populations. The use of erythropoietin for anemia in patients on dialysis was expanded to treat anemia across a broad spectrum of patients without benefit. In some cases, this treatment caused serious harm.[13] Recommendations of tight control in type 1 diabetes were applied to some groups of patients with type 2 diabetes (e.g., patients with renal disease, older persons) without demonstrated benefit.[14]

• Unidentified harms. Subsequent to recommendations, follow-up studies raise questions about adverse effects of medications, such as the potentially deleterious cardiovascular effects of calcium supplementation.[15] Studies can also raise questions about harms associated with technology (such as radiation exposure from computed tomography) and testing (such as the harms of interventions initiated based on prostate-specific antigen testing exceeding the benefits of this testing).[16]

• Economic factors. Economic conflicts of interest encourage harmful or unproven technologies and treatments (e.g., pharmaceutical companies that pressured physicians to expand use of erythropoietin)[17]; public pressure creates demand (e.g., increased prostate-specific antigen screening in response to widespread fear of prostate cancer) and high-profile media coverage of medical "breakthroughs" may be unwarranted or premature.

Where do these observations leave us? Fortunately, primary care physicians are well-adapted to medical uncertainty. To minimize the dizzying impact of changing recommendations, physicians should focus on patient-oriented evidence, and not be distracted by disease-oriented evidence.[1] Physicians should become familiar with the basic principles of good research, and avoid drawing premature conclusions from observational studies or studies with design flaws.[18] Physicians should also recognize the pharmaceutical industry's influence on research studies and practice recommendations.[19]

Adherence to current standards of care and shared decision making should be coupled with a well-reasoned reticence in responding to new findings.[18] Clinical experience matters, and the insight a family physician acquires from knowing patients (and often, their families) is another invaluable tool. Treatments with a strong track record should be considered proportionately more trustworthy when a new study confirms that treatment's benefit.[10] Educating our patients, applying evidence judiciously, and avoiding undue influences will help us avoid the pitfalls of the ever-changing practice of medicine.

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