

## Regarding Empiricism and Rationalism in Medicine and 2 Medical Worldviews

**To the Editor:** I am pleased that our work on medical reversal<sup>1</sup> and my recent commentary<sup>2</sup> describing 2 schools of clinical reasoning have drawn attention and generated discussion from many, including leaders in academic medicine.<sup>3</sup>

In response, I wanted to make 2 points. First, when it comes to untested practices with strong preclinical rationale and improved surrogate end points, I only oppose their widespread use when there are no ongoing studies examining patient-centered end points. If such practices are currently being tested in randomized controlled trials (RCTs) powered for hard outcomes, then the use of the practice on a provisional basis in the general population is appropriate based on a shared decision-making process between physicians and patients, fully acknowledging the limited evidence base. This is the philosophical footing for the US Food and Drug Administration's accelerated approval program.

The one major caveat I would add is that community use is warranted as long as that use does not hinder the ongoing enrollment of clinical trials meant to assess that practice. One example is intracavitary catheter-based breast brachytherapy. The first such device was approved through the US Food and Drug Administration's 510(k) mechanism in 2002, with very limited safety (and even more limited efficacy) data. In the years since, the device's use has skyrocketed, and RCTs testing the device's impact on hard outcomes has been hindered by most patients being treated off protocol. One editorialist noted that if only a fraction of the patients who received breast brachytherapy in the community "had been treated on the trial instead of off protocol, the study would have closed...and we would already have the results."<sup>4</sup> As

long as new practices are being tested in RCTs that have met recruitment goals, provisional approval based on surrogates is not unreasonable.

The second point concerns the argument<sup>3,5</sup> that some medical practices are like parachutes: their benefit is so clear, randomized trials are unnecessary. In general, I agree that there are such cases in medicine, but while proponents are quick to think that their particular practice is a parachute, the truth is that very few are.<sup>6</sup> Empirical evidence supports this claim. Pereira et al<sup>7</sup> examined 85,002 forest plots from more than 3000 Cochrane reviews and specifically focused on practices with very large treatment effects (those with nominally significant results and a magnitude of benefit with an odds ratio  $\geq 5$ ). These interventions with very large effects were less likely to examine mortality and more likely to have small sample sizes than other studies, and 98% of these effects became smaller in subsequent studies or meta-analysis. Only one intervention (extracorporeal oxygenation for severe respiratory failure in newborns) had a large effect on mortality in the entire Cochrane Database of Systematic Reviews.

There will always be a place for the thoughtful deliberation of physicians in medicine; however, I continue to believe that given the pressures of the modern marketplace and university promotions, most decisions should be firmly grounded in RCTs powered for hard end points.

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The views and opinions of Dr Prasad do not necessarily reflect those of the National Institutes of Health or the National Cancer Institute.

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## Two Medical Worldviews

**To the Editor:** I read with interest the articles and editorial in the October 2013 issue of *Mayo Clinic Proceedings* on empiricism and rationalism in medicine,<sup>1-3</sup> a subject that has captured my attention for virtually my whole career. I agree with the editorial authors, Drs Lanier and Rajkumar,<sup>1</sup> that these approaches are complementary and must both be utilized in the diagnosis and treatment of the individual patient.

I started my career as a basic scientist. Much time and effort is expended in graduate programs teaching students how to distinguish strong from weak evidence and how to recognize erroneous conclusions; we spent a lot of time tearing apart bad papers. After going to medical school and starting my residency training, I was taken aback to find that evidence accepted as conclusive in medicine often would not pass muster in basic science. Of course, this is the nature of the beast; we are not all genetically identical white mice or bacteria living in controlled environments.

Medical research cannot be held to the same standard as basic science, but we must remain aware of the (relative) weakness of the evidence we rely on in applying "evidence-based" principles. There must always be a place for rational decision making based on experience and the situation of the individual patient. Survival curves for 2 different therapies that appear nearly identical