Reply to Dr. Buffington

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To the Editor:

I welcome this opportunity to respond to Dr. Buffington’s letter and to emphasize the important fact that, “some patients are ‘responders’ and benefit from the treatment while others (the majority, perhaps, are not).” As I pointed out, the US Food and Drug Administration and the National Institutes of Health have explicit policies to minimize the risk that subgroups’ benefits from a treatment may be overlooked if data analysis is limited to outcomes pooled across all groups. These and other prestigious organizations now leading the way toward individualized therapies are certainly not quasiscientific.

I further wish to challenge Dr. Buffington’s condemnation as “not ethical” my call for individualized treatment when he points out that, “treatment costs money and... almost always involves risk of harm.” I agree that treatments have risks and costs as well as benefits. I personally supported evidence-based pain medicine, have evaluated “medicine worth paying for,” and presented risks of pain therapies alongside their benefits. But even Archie Cochrane, the father of contemporary evidence-based medicine, emphasized that group statistics cannot do justice to the typically heterogeneous populations that seek medical treatment. Cochrane conveyed this insight in elegant graphs and declared, “the considerable problems, conscious and unconscious, to provide the physicians with a simple rule to tell them what it all mean.” He further declared, “the concept of ‘normal limits’ defined as lying within plus or minus two standard deviations from the mean. Theoretically there is nothing to support this idea.” The worldwide collaboration named after him involves consumers in its editorial process for systematic reviews and meta-analyses. In a Cochrane Collaboration monograph, one such lay representative wrote, “whether randomized controlled trials and systematic reviews of effectiveness have focused on testing narrowly defined interventions and broadly defined populations with the aim of informing policy decisions, personal decision making would benefit from trials testing a broad choice of interventions in a narrowly defined population... The ultimate in personally relevant trials are ‘n of 1’ trials.”

I agree with Dr. Buffington when he calls for an “objective and reliable way to identify the subset of patients that could benefit.” Sharing this concern, pain physicians including myself have described approaches ranging from behavioral or genetic profiling to “n of 1” trials. Individual clinical outcomes, however, cannot generally be predicted with perfect precision. Patients with refractory neuropathic, infectious disease, epilepsy, or other serious illnesses are normally offered complex treatments not used for routine initial care of the same conditions. Such treatments are reimbursed in full knowing that their benefits cannot be guaranteed a priori in every case. Failure to do the same for patients with pain deprives them of their right to treatment. Pain, especially persistent pain, can impair quality of life at least as much as other major conditions. Just as it is risky to generalize observations from a single patient to make treatment decisions for a broad population, the opposite is also true, particularly because the evidentiary basis for much of pain practice is still emerging. That is why I wrote and now reiterate, “No one would argue for the merit of a treatment not ever observed to benefit anyone more than placebo, nor deny the need to improve the quality and quantity of evidence for many pain therapies, particularly invasive ones.” Yet when certain individuals clearly respond to a specific treatment more than to a placebo, although group mean response statistics are equivalent for the treatment and placebo, the latter cannot justify refusal to pay for therapeutic trials to identify responders whose quality of life will improve with that treatment.”

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REFERENCES


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