

## LETTERS—CONCISE RESEARCH REPORTS

## Letter About: Use of Mortality as an Endpoint in Noninferiority Trials May Lead to Ethically Problematic Conclusions



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A balance between prospective benefits versus the accepted loss in efficacy that one considers “noninferior” requires thoughtful consideration in noninferiority trials. Is it hard to imagine how our metaphorical ethical scale will ever be balanced when the heavy weight of participants’ deaths lies on one end of it.

Dear Sir/Madam,

I read with great interest the outstanding work by Andrew M. Hersh and colleagues. Their study illustrates very clearly the ethical dangers of using mortality as an endpoint in noninferiority trials.<sup>1</sup>

Their results remind us that some participants in these studies, when randomized to the new treatment, may have died because they did not receive the “alternative treatment,” which already had proven value. One of the ethical principles outlined by the Belmont Report, the principle of Beneficence, is probably violated in those situations.<sup>2</sup>

Another essential principle, Respect for Autonomy, is probably violated as well. It seems unlikely that lay people understand the nuances of noninferiority design. In fact, many participants in noninferiority trials are not given adequate information and may erroneously believe that they are enrolling in a superiority clinical trial.<sup>3</sup>

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**Compliance with Ethical Standards:**

**Conflict of Interest:** The author declares that he does not have a conflict of interest.

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