

The Interpretation section of the abstract in an article by Nicole Le Saux and associates¹ reads as follows: “Our results did not support the hypothesis that placebo was noninferior to amoxicillin (i.e., that the 14-day cure rates among children with clinically diagnosed acute otitis media would not be substantially worse in the placebo group than the treatment group).”

There seem to be several possible interpretations of what the authors might mean. Which is correct?

- Placebo is superior to amoxicillin.
- Placebo is equivalent to amoxicillin.
- Placebo is inferior to amoxicillin.
- Placebo is equivalent but not quite so.
- Our data are equivocal and more study is needed.

I not infrequently have difficulty divining the true meaning of sentences that contain double negatives.

Z. Kondziewski

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Reference

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Competing interests: None declared.

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[Three of the authors respond:]

Barry Pless asks why a noninferiority trial was chosen over an equivalence trial for our study of the treatment of otitis media.¹ There are subtle but important differences between these types of trials in terms of both sample size requirements and interpretation. We were not aiming to demonstrate statistically significant superiority of amoxicillin over placebo, as this has already been well established. Our objective was to show that waiting to treat (which we simulated by using placebo) would not be substantially worse (within a 10% clinically acceptable difference in failure rates compared with amoxicillin) than giving amoxicillin to children present-

ing with acute otitis media. In recent terminology, this is known as a noninferiority trial. By contrast, an equivalence trial seeks to demonstrate that the outcomes of 2 interventions are not substantially different, without prespecifying which intervention will lead to better results. Hence, for our question, a noninferiority trial was appropriate.

In response to Mathieu Lemaire, we found the article by Gomberg-Maitland and associates² off the mark. The context of the Lemaire quotation was a 3-arm study (placebo, active control and experimental treatment), which was not the design of our study. Similarly, Lemaire's last remark (following the citation from Chen and colleagues³) is in reference to noninferiority trials with active control, which was not part of the design of our trial.

Brian Blakley brings up an important clinical point. Within the clinical definition for acute otitis media one has to meet the “time” criterion of abrupt onset of signs and symptoms of middle ear inflammation and middle ear effusion. This presentation is distinct from otitis media with effusion, which is a subacute or chronic problem, does not display inflammation and does not usually require antimicrobial therapy. We agree that potential overdiagnosis of acute otitis media is a common problem and must be addressed for each child. Even among children with clinically diagnosed acute otitis media, however, many (80% in this trial) will experience resolution of the problem without specific antimicrobial therapy.

Both Pless and Kondziewski found the double negatives in our interpretation baffling. We plead guilty to this charge, but note that equivalence and noninferiority trials are notoriously difficult to report. In our trial, for all children aged 6 months to 5 years, placebo was statistically inferior to amoxicillin. The CONSORT Group is presently working on a CONSORT extension for noninferiority trials.

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Guidelines for treating acute otitis media

In a recent commentary, R.A.M.J. Damoiseaux¹ misquotes the guideline for the treatment of otitis media that has been endorsed by the Guidelines Advisory Committee (GAC) of the Ontario Ministry of Health and Long-Term Care and the Ontario Medical Association.

The article states that the GAC “advises using antibiotics to treat any symptomatic episode of acute otitis media.” In fact, the GAC-endorsed guideline² also recommends watchful waiting, among other options. Furthermore, the GAC “guideline note” on this subject points to the degree to which clinicians underestimate the natural history of this condition and the marginal impact of antibiotics on outcomes.³

Dave Davis

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3. Otitis media: antibiotic therapy. Guideline notes. Toronto: Guidelines Advisory Committee.

tee; updated 2005 Mar 31. Available: <http://gacguidelines.ca/article.pl?sid=02/07/03/2017236> (accessed 2005 Apr 28).

Competing interests: None declared.

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[The author responds:]

It is not a matter of misquoting, but it may be selective quoting. Dave Davis is correct that the GAC “guideline note”¹ mentions the overuse of antibiotics for acute otitis media. But the recommendations themselves² advise that symptomatic patients be treated with antibiotics; only for asymptomatic patients can antibiotics be deferred. My plea³ was to be even more restrictive.

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HRT and antidepressants

Roger McIntyre and associates¹ discuss reciprocal relationships between hormone replacement therapy (HRT) and antidepressant treatment. Although some women experience significant mood changes related to changes in estrogen levels at menopause, I believe there is another obvious explanation for the increase in prescriptions for selective serotonin reuptake inhibitors (SSRIs) after publication of the Women’s Health Initiative (WHI) trial.²

Hot flashes occur in 65%–75% of women during natural or induced

menopause.³ Many women discontinued their hormone therapy because of the WHI results but continued to experience significant symptoms and sought medicinal help from their physicians. The only medications with scientific proof of efficacy, other than estrogen and progestins, are SSRIs, clonidine and, more recently, gabapentin.^{3–7}

As demonstrated by Loprinzi and colleagues,⁷ breast cancer patients with depression reported a reduction in hot flashes when taking SSRIs. Subsequently, other SSRIs were shown to have similar beneficial effects. However, SSRIs are much less effective in this regard than HRT (which is more than 85% effective).³

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Competing interests: Dr. Wolfman has received an honorarium from Wyeth for speaking to physicians about issues to do with menopause.

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I was dismayed when I read the commentary by Roger McIntyre and associates¹ regarding antidepressants and menopause. The final paragraph, advising practitioners to “familiarize themselves with the beneficial effects of serotonergic antidepressants on climacteric symptoms” is essentially a push to prescribe these medications for symptomatic menopausal women.

This suggestion is backed up by one reference, a position statement of the North American Menopause Society.² This article is a literature review (I am unaware of any properly conducted clinical studies on this subject) which in fact recommends other interventions (e.g., lifestyle and dietary supplements) as first-line therapy, with SSRIs coming in later, together with progesterone and gabapentin.

Overall, I believe this commentary is misleading. It encourages physicians to prescribe a potent class of medications for climacteric symptoms without the benefit of any careful clinical studies.

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