Letter

How should clinicians interpret results reflecting the effect of an intervention on composite end points?

Evidence-Based Medicine recently published a thoughtful commentary by Montori et al., addressing the above question, prompted by the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS), which was abstracted in the same issue. The ACHOIS investigators compared a screen-and-treat programme for gestational diabetes with routine pregnancy care and used as their main end point a composite of 4 outcomes: shoulder dystocia, Duchenne-Erb palsy, fracture, and death—a natural choice given that a main purpose of gestational glycaemic control is to prevent the baby from being born too big. The topic is important and several points are worth noting.

Montori et al. listed 3 questions to help decide the appropriateness of a composite outcome:

(a) Are the component outcomes of similar importance to the patients?
(b) Are the more and less important outcomes occur with similar frequency?
(c) Do the more and less important outcomes occur with similar relative reductions of the risk (RRRs)?

It seems to me that a clinically meaningful composite endpoint analysis would require either condition (a) or (c) to be satisfied, whereas condition (b) is a secondary matter. In the ACHOIS study, shoulder problems were much more common, and obviously much less serious, than death. With respect to RRRs, Montori et al. were uncertain how to answer question (c). If (b) had been satisfied, the decision problem would be a little easier to explain to expectant mothers, but it is (a) and (c) that decide whether a logically defensible lumped analysis can be devised.

If the infant dies, a broken clavicle does not come? The composite endpoint analysis requires either condition (a) or (c) to be satisfied, whereas condition (b) is a secondary matter. In the ACHOIS study, shoulder problems were much more common, and obviously much less serious, than death. With respect to RRRs, Montori et al. were uncertain how to answer the question (c). If (b) had been satisfied, the decision problem would be a little easier to explain to expectant mothers, but it is (a) and (c) that decide whether a logically defensible lumped analysis can be devised.

What happens if a patient experiences 2 of the outcomes? The composite endpoint approach in ACHOIS implies that, if the infant dies, a broken clavicle does not matter. This statement would also be true in the case of co-occurrence of, say, palsy and fracture. The endpoint definition capitalises the form “one or more of the following…” and in other words, co-occurrence of component undesirable outcomes does not really matter. Otherwise, the questions above have to be modified to deal intelligently with co-occurrence.

Correction

In the October 2006 issue of Evidence-Based Medicine, calculation errors were detected in the table of the abstract for the article by Prince et al. The numbers needed to treat (NNTs) for compliant patients were incorrect.

The correct NNTs for calcium v placebo in compliant patients are these:

Any fracture NNT 21 (95% CI 13 to 235)

Appendicular fracture NNT 22 (CI 13 to 225)
Upper limb fracture NNT 34 (CI 24 to 238)