need additional calcium to supplement their diet, the major question may not be so much when but whether supplemental calcium is used to meet recommended guidelines.

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If Almost Nothing Goes Wrong, Is Almost Everything All Right? Interpreting Small Numerators

To the Editor.—Twelve years ago in an article entitled "If Nothing Goes Wrong, Is Everything All Right?" Drs Hanley and Lippman-Hand[1] provided a helpful rule of thumb for interpreting numerators of 0. They showed that if 0 events are observed in N trials, the upper limit of the 95% confidence interval (CI) for the frequency of events is approximately 3/N. Thus, if there are no deaths among 50 patients treated with a new medication, the upper limit of the 95% CI for the risk of death is about 3/50, or 6%. On the other hand, if no deaths occur in a study of 1000 patients, the upper limit of the 95% CI for the mortality rate is 3/1000, or 0.3%.

I have found that similar approximations work for other small numerators and that they can be a helpful shortcut when scanning journal articles. In each case, as the denominator increases, the numerator for the upper limit of the exact 95% CI approaches a limit (Table). (This Table can be derived using any statistical package that calculates exact binomial 95% CIs, such as STATA.[2]) As a rough but easily remembered approximation, the numerators of the 95% CI upper limits for observed numerators of 0, 1, 2, 3, and 4 are about 3, 5, 7, 9, and 10.

For example, in a study of Nissen fundoplication in neurologically impaired children with gastroesophageal reflux,[3] the reported perioperative mortality was 6% of 52 patients (ie, three deaths); no CI was supplied. Using the shortcut, the rough 95% CI upper limit for the observed numerator of three deaths would be 9/52 or 17.3%, reasonably close to the true value of 16.0%. This rapid 95% CI estimation enables the reader to put in perspective the safety of the operation demonstrated in the study.

This also works when the numerator, rather than being very small is very close to the denominator that the observed proportion is close to 1. In this instance, to estimate the lower limit of the 95% CI, one subtracts the numerator from the denominator (yielding a difference of 4 or less), and then calculate an upper limit of the 95% CI for the complement of the observed proportion. As an example, consider a recent study on the use of artificial neural networks for the diagnosis of myocardial infarction.[4] The neural network program correctly identified 35/36 patients with myocardial infarction, or 97.2%; the 95% CI published in the article was 97.2% to 97.5%. This seems narrow for a CI based on only 36 patients. To use the shortcut, we first subtract numerator from denominator. That is, 35/36 patients with myocardial infarction were identified by the network, so 1/36 must have been missed. The upper limit of the 95% CI for 1/36 is about 5/36, or about 14%. Since the upper confidence limit for the proportion of false negatives is about 14%, the lower limit for the proportion of true positives (sensitivity) must be about 86% (100%−14%), quite different from the lower limit of 97.2% published in the article, but close to the true value of 85.4%.

Upper Limit of Exact 95% Confidence Intervals From the Binomial Distribution

	Observed Numerator*				
Denominator	0	1	2	3	4
10	2.6	4.5	5.6	6.5	7.4
20	2.8	5.0	6.3	7.6	8.7
50	2.9	5.3	6.9	8.3	9.6
100	3.0	5.4	7.0	8.5	9.9
200	3.0	5.5	7.1	8.7	10.1
500	3.0	5.5	7.2	8.7	10.2
1000	3.0	5.6	7.2	8.8	10.2

*The confidence intervals in the 0 numerator column are one-sided; all others are two-sided.

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2. Computing Resource Center. *STATA Reference Manual: Release 3.* 5th ed. Santa Monica, Calif: Computing Resource Center; 1992:175-180.
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Cost-effectiveness of Noninvasive Testing for Osteomyelitis

To the Editor.— The article by Dr Eckman and colleagues[1] regarding cost-effectiveness analysis in the diagnosis of foot infections is an extensive analysis that is fundamentally flawed because of an error in the assumptions about the costs of the procedures. The cost of the technetium Tc 99m bone scan is listed as $719 and the cost of the indium In 111–labeled leukocyte scan is put at $447. It may be that these numbers reflect the charges of the studies in the Boston, Mass, area, but these numbers do not reflect the cost of the studies.

First, the listed costs of the studies are not representative. The 1993 Medicare resource-based relative value scale–based reimbursement for a three-phase bone scan is $204.06 (global payment comprising professional and technical fees), which is only a fraction of the $719 listed in Table 4 in the article.

Second, the factor of concern is not the charge for the study, but the marginal cost of performing the study. This is particularly true with capitated patients where there is no revenue derived from performing the test. I can assure you that the cost to a department of performing an indium In 111–labeled leukocyte scan (based on the cost of the isotope, effort to label the cells, time to image the patient, and the like) is much larger than the cost of doing a technetium Tc 99m MDP (medronate methylene diphosphonate) bone scan.

The type of analysis that was attempted in this study is of great value, but the economic factors must be specified with more precision to justify the conclusions.

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1. Eckman MH, Greenfield S, Mackey WC, et al. Foot infections in diabetic patients: decision and cost-effectiveness analyses. *JAMA.* 1995;273:712-720.

In Reply.—Economic analyses of health care strategies must carefully differentiate costs from charges.[1] Costs represent the actual amount paid for resources consumed in providing a service, while charges represent the price requested for reimbursement of that service. Because market forces affect charges, large and seemingly arbitrary differences between costs and charges for different services may exist.[2] We agree with Dr Makler that it is important to use costs, which correspond more closely to actual resource consumption, and not charges, when performing cost-effectiveness analyses.

Makler believes that the costs listed in our analysis are not representative, quoting the 1993 Medicare resource-based