8. Are underlying trends in disease distribution and severity taken into account? Are other pertinent population trends assessed?
9. Are technological changes and evolution of practices taken into account?
10. Are the distributions of benefits and costs important and are they considered?

Conclusions
1. Are the conclusions consistent with the analysis and appropriately qualified?
2. Are conclusions robust? Have assumptions and key uncertainties been subjected to a sensitivity analysis?

SUGGESTIONS FOR FURTHER RESEARCH

Our suggestions for further research are cognizant of broadened clinical experience with cimetidine in recent years and newly emerging empirical evidence of health system effects of the drug. Any analysis must take account of the shifting epidemiologic pattern of ulcer disease. We believe that sound CEAs comparing effects of different strategies over an ulcer patient's lifetime would provide valuable guidance to medical decisions for patients with ulcer disease.

As discussed earlier in this case study, a number of well-controlled clinical trials have assessed the clinical effects of cimetidine in the past few years. These trials have not dealt with every important clinical comparison (e.g., maintenance antacids v. cimetidine), but they have provided a much sounder empirical base for projecting some of the clinical consequences of the drug. Since clinical use of cimetidine is so widespread, a broad group of clinicians could be consulted for subjective estimates of likely consequences in areas where clinical trials are lacking. It would be possible to begin by sending participating physicians a summary of empirical clinical findings with cimetidine. A systematic method, such as a Delphi process, could then be used to reach group consensus on key probabilities.

There is still little empirical information on health system effects of cimetidine to serve as a basis for estimating resource costs and savings. Any analysis of the health system effects of an intervention in ulcer disease must take as a baseline the epidemiologic trends in the disease discussed in this case study. As mentioned previously, the rate of surgery for ulcer disease shows a steeper decline in 1978 than would be predicted from the previous trend. Confirmation of this drop and additional evidence linking it to cimetidine would provide a sounder basis for projecting direct cost savings in one area, and for attributing such savings to the use of cimetidine. Additional evidence of health system effects of cimetidine may emerge from the ongoing research that we have described.

In further analyses of cimetidine, one fundamental concern must be the time frame of the analysis. Calculations based on a single year, for example, will overlook the important distinction between avoidance of surgery and delay in surgery. From the evidence we have cited in this case study, there is a good reason to believe that a year of maintenance cimetidine imparts a delay in inevitable surgery rather than a long-lasting cure of ulcer disease.

More generally, with diseases such as peptic ulcer, which are chronic, and with interventions such as cimetidine, whose long-term effects may be very important, a benefit-and-cost analysis might best focus on a cohort of patients, projecting effects over their lifetimes. Rather than attempt to enumerate all resource implications for a cross-section of the population in a single year, it might be more helpful to estimate the present-value lifetime resource costs and health effects for a given population of ulcer patients. Then, on the basis of available research evidence and subjective clinical judgments, one could estimate the consequences for a given type of patient of pursuing different management strategies. This approach would allow compari-