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LETTER TO THE EDITORS

Last year in the summer issue of this journal, Khandker et al. (3) published the results of an interesting modeling study following the cost-effectiveness of various strategies for detecting cases of colon cancer. In addition to the baseline alternative, the authors investigated eight different screening strategies and calculated the incremental cost-effectiveness of these eight strategies. Table 1 contains the results of their study in terms of cost and effectiveness as well as incremental cost-effectiveness (see Table 3, Khandler et al.).

The authors concluded in their article that:

> . . .in the base case model most of the screening options had a cost-effectiveness ratio of less than $20.000 per life-year saved in 1994 dollars. Although the definition of what is an acceptable cost-effectiveness ratio remains arbitrary, the median cost per life-year saved reported for 310 health care interventions was $19,000 using 1993 dollars. Thus, other than that for 5-year colonoscopy, cost-effectiveness ratios for all screening options considered in this study can be considered to be at or below the median (3).

In my opinion this conclusion is misleading, and will easily lead to wrong decisions if policy makers base their decisions on the above conclusion alone. Without doubt, policy decisions must be based on incremental analysis, but are the incremental cost-effectiveness ratios, as presented in the above table, the relevant figures? To answer this question, we should ask ourselves whether the considered alternatives are compatible options or incompatible options. Alternative interventions are said to be compatible if more than one and possibly all alternatives may be selected. Alternatives are said to be incompatible if only one alternative can be selected. (Incompatible alternatives have also been called mutually exclusive, competing, or interdependent alternatives.) The screening options presented cannot be executed at the same time: choosing one screening option implies that the other screening options will not be executed. Therefore, the eight options are incompatible alternatives. How can we select the best option from a set of incompatible alternatives? Some methods have recently been proposed to solve the problem of detecting the best option from a set of incompatible options (1;4). A graphic representation is a useful aid in determining the best candidate in a set of incompatible options (2). In Figure 1, the base case and the eight screening options are presented, based on the numbers in Table 1.

Figure 1 enables us to detect dominated alternatives. A less effective, more costly alternative is said to be strongly dominated by a more effective, less costly alternative. These dominated alternatives should never be chosen and can be excluded. In a graphic representation, these dominated options can be identified very easily. Each option with a position northwest (above left) of another option can be excluded. If we compare 3-year flexible sigmoidoscopy with annual fecal occult blood testing (FOBT), we see that the first option is both more costly and less effective. Hence, 3-year flexible sigmoidoscopy can be excluded. This conclusion can also be reached by looking at the graph, where the 3-year flexible sigmoidoscopy is located northwest of annual FOBT. Often, more than one dominated option can be excluded, but in this specific case all other options remain

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Table 1. Cost-effectiveness Estimates in 1994 Dollars

	Cost ($ per person)	Effectiveness (life-years)	Incremental cost:effectiveness ratio
Baseline (no screening)	$643	18.14	–
Annual FOBT	$2,058	18.24	$14,394
3-year flexible sigmoidoscopy	$2,079	18.23	$16,261
5-year flexible sigmoidoscopy	$1,713	18.23	$12,636
Annual FOBT/ 3-year flexible sigmoidoscopy	$2,854	18.25	$20,334
Annual FOBT/ 5-year flexible sigmoidoscopy	$2,639	18.25	$18,204
5-year double-contrast barium enema	$2,577	18.25	$17,553
5-year colonoscopy	$3,906	18.25	$28,724
10-year colonoscopy	$2,602	18.25	$17,696

Source: Khandker et al. (3).

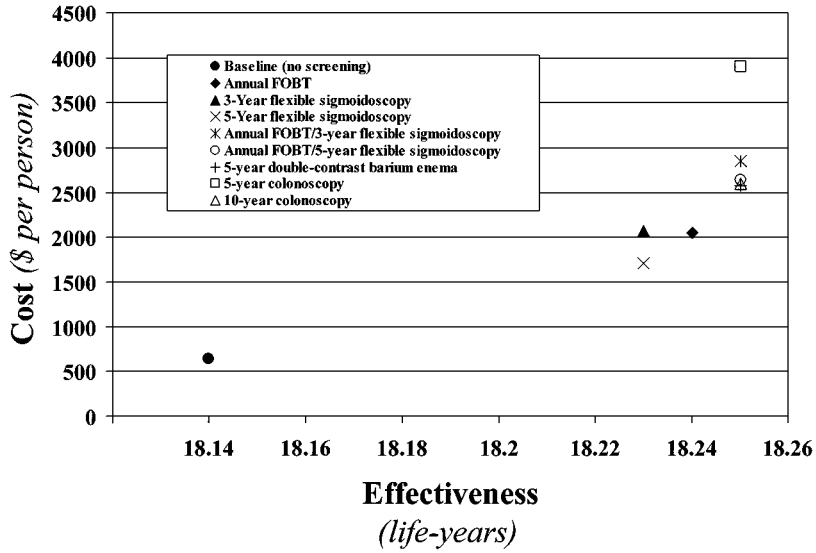

Figure 1. Comparison of a base case and eight screening options, based on the numbers in Table 1.

possible candidates. Together they form the southeast boundary of the set of incompatible alternatives.

In the next step, we have to define which of the remaining options is really the best. This selection can be done by comparing the options with each other, starting with the base case option. The first option on the southeast boundary, starting from the base case option, is 5-year flexible sigmoidoscopy. The incremental cost-effectiveness ratio between these two options can be found in Table 1: $16,261. If this is below the acceptable level (which might be the case), 5-year flexible sigmoidoscopy is a better candidate than the base case. The next option on the southeast boundary is annual FOBT. Whether annual FOBT is a better candidate than 5-year flexible sigmoidoscopy depends on the

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incremental cost-effectiveness ratio between these two candidates. The incremental cost-effectiveness ratio is not presented in the table but can easily be calculated, based on the cost and effectiveness data in the table. The incremental cost-effectiveness ratio is \$34,500 [= (2,058 − \$1,713)/(18.24 − 18.23)]. (With an extra decimal in the numbers of effectiveness, this incremental cost could have been calculated more precisely, but this would probably have no effect on the conclusions. If we consider \$34,500 to be below the acceptable level, annual FOBT should be chosen as the better candidate over 5-year flexible sigmoidoscopy. The search for better candidates continues by comparing the next option on the southeast boundary, which is 5-year double-contrast barium enema, with the best candidate up till now, annual FOBT. This comparison can be performed again by incremental analysis. The incremental cost-effectiveness ratio between these two options is \$51,900 [= (\$2,577 − \$2,058)/(18.25 − 18.24)]. If we consider (about) \$50,000 to be an acceptable level for producing a year of life, then the 5-year double-contrast barium enema is a better option than annual FOBT. If not, we should stick with annual FOBT, because all other options have even higher incremental cost-effectiveness ratios, which can easily be seen in Figure 1.

In their study, Khandker et al. calculated average cost-effectiveness ratios instead of incremental cost-effectiveness, because they compared all options with the option of doing nothing. For policy decisions it is necessary to calculate incremental cost-effectiveness ratios, in which the incompatible options are compared directly with each other.

To summarize our conclusions, the maximum value that society is willing to pay for life-years (or for quality-adjusted life-years) determines the optimal candidate within a set of incompatible alternatives. If society is willing to pay \$20,000 for a year of life, 5-year flexible sigmoidoscopy is the best candidate. If society is willing to pay \$40,000 for a year of life, annual FOBT is our candidate. If society is willing to pay \$60,000 for a year of life, 5-year double-contrast barium enema is the best candidate. All other options on the southeast boundary, lying north of 5-year double-contrast barium enema, should never be chosen because they have very high incremental cost per life-year gained (almost infinite), in comparison with 5-year double-contrast barium enema. In the above analysis I did not pay attention to the level of uncertainty, which might shed a somewhat different light on the above absolute conclusions.

It is almost 25 years since Neuhauser and Lewicki (5) published their article, titled *What do we gain from the sixth stool guaiac?* To paraphrase this title: What can we learn from the sixth stool guaiac? Neuhauser and Lewicki calculated that the addition of a sixth guaiac stool test to a series of five guaiac stool tests would imply that society is willing to pay about \$47,000,000 for finding one case of colon cancer! In essence, the problem, as analyzed by Neuhauser and Lewicki, is the same as the one described above: choosing the best strategy of a set of incompatible alternatives. We could have learned that the only way of selecting the best candidate is applying an incremental way of thinking in a correct way.

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Dr. Khandker's reply:

The comments on the Khandker et al. (2000) paper are useful to the extent that they provide a basis for making pairwise comparison of the screening options. The general conclusion, however, remains largely unaffected. As the commentators note, "If the society is willing to pay $20,000 for a year of life, 5-year flexible sigmoidoscopy is the best candidate. If society is willing to pay $40,000 for a year of life, annual FOBT is our candidate." Qualitatively, these conclusions are not different from the ones derived by Khandker et al. — "Sigmoidoscopy every 5 years and annual fecal blood testing were the two most cost-effective strategies. . . ." It is interesting that a more rigorous approach retains the fundamental results. Assuming that society leans toward a lower threshold for willingness to pay for a year of life, the conclusions are also consistent with cost minimization from a societal perspective.

In general, the remarks are useful because they provide a foundation for considering alternative scenarios without any predetermined baseline. In addition, the approach also provides alternative guidance for societies or settings where the cost-effectiveness threshold varies considerably. However, a lack of baseline may sometimes lead to unwanted consequences since baseline provides a direction from where we start to where we end up, an essential for policy evaluation. Furthermore, as a practical matter, when alternative uses of money are compared across a broad spectrum of interventions, one can easily end up with a close-to-infinite number of possible scenarios to compare.

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