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# MODELING AGE DIFFERENCES IN COST-EFFECTIVENESS ANALYSIS

## *A Review of the Literature*

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Abstract

**Objectives:** Cost-effectiveness analysts often present cost-effectiveness results by age to help inform decisions about the use of an intervention. Yet it is not known how well studies model the risks and costs associated with age. We reviewed published studies to examine their modeling of age differences.
**Methods:** MEDLINE searches identified all cost-effectiveness analyses published between 1985 and 1997 that included adults 50 years of age and older, were based on data for developed countries, and compared cost-effectiveness ratios for adults of different ages or for initiation of an intervention at different ages; 36 articles met these criteria. They were reviewed to determine the extent to which they incorporated age-specific data. Studies that justified using the same data for all ages were counted as having varied the data element by age.
**Results:** All studies varied life expectancy by age. Most also varied the incidence/prevalence of the target condition and the case fatality rate. Only 36% varied the effectiveness rate of the intervention by age. Costs were usually assumed constant: 42% of studies varied the cost of treating adverse effects and 17% varied the cost of treating the target condition. Whether a data element was varied did not appear to be related to the pattern of cost-effectiveness ratios by age.
**Conclusions:** Many studies have not modeled age differences in sufficient detail to ensure that differences in cost-effectiveness ratios by age are accurate and a sound basis for decisions. As cost-effectiveness analysis becomes more widespread, analysts should strive to incorporate more complete age-specific data.

**Keywords:** Age factors, Age, Cost-effectiveness analysis, Cost-utility analysis, Health policy

Risks of disease differ by age, with risk for adults usually increasing with age. Risk can rise steeply starting at age 60 or 65. In part because older people have more background comorbidities and functional loss, which can complicate the course of any single disease, the effectiveness of prevention or treatment, its adverse effects, and its costs may also differ by age. When one or more of these elements vary with age, the cost-effectiveness of an intervention will be different for different age groups.

Recognizing these realities, cost-effectiveness analysts often present cost-effectiveness ratios by age group. Such results are intended to help inform policy decisions about the use of

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an intervention, decisions that may take the form of different recommendations for different age groups. There are numerous examples of age-specific recommendations (7;42;43). If cost-effectiveness results are to be a valid basis for informing these decisions, accuracy is essential. Yet it is not known how well studies model the risks and costs associated with age.

In this article we review cost-effectiveness studies that analyzed interventions for adults and presented results by age. We found a wide range of practice, from studies that varied only life expectancy by age to studies that incorporated extensive age-specific information. Cost data were particularly likely to be assumed constant across age groups, but even a factor as important as the effectiveness rate of the intervention was varied by age in less than half the studies.

In the Methods section we discuss the data that would ideally be used in analyses that report results by age and describe the procedures used to identify relevant studies. The Results section presents our review of the literature for the years 1985–97 to show in detail the extent to which analyses attempted to model differences by age and the general patterns of cost-effectiveness reported in them. The Discussion section turns to the implications of the results for the use of cost-effectiveness analysis to inform decisions.

## METHODS

A cost-effectiveness ratio is based on the comparison of an intervention with an alternative or “comparator.” For example, screening may be compared with waiting until the disease becomes clinically apparent, or surgery may be compared with medication. The health effects and costs of both the intervention and the comparator are first estimated. The cost-effectiveness ratio is then calculated as net cost (difference in costs between intervention and comparator) divided by net health effect (difference in health effects between intervention and comparator). Thus, if intervention A costs $15,000 per person and has a life expectancy of 78.5 years, while comparator B costs $5,000 per person and has a life expectancy of 78.0 years, the cost-effectiveness of A, when compared with B, is $20,000 per life-year $[(15{,}000 - 5{,}000)/(78.5 - 78.0)]$.

### Requirements for an Accurate Analysis by Age

A cost-effectiveness analysis requires data on the health-related outcomes that can result from an intervention or its comparator, both desired outcomes and adverse effects, and on the costs associated with those outcomes. An analysis that examines cost-effectiveness by age requires age-specific information. If health is measured by life expectancy, the analyst needs data on the probability of death under the intervention and the comparator that are specific to each age group considered. The effectiveness of the intervention against that risk and any adverse effects may also be age-related. If the costs of the intervention or the comparator involve hospitalization, physician visits, medications, home health services, etc., the analyst will need age-specific information on the numbers and costs of these services. For some interventions costs may be the same at all ages, but this should not be assumed to be the case without justification; the comorbidities and functional losses of elderly persons suggest that their costs may be higher.

Estimates of the health effects and costs for an intervention and its comparator should be as complete and accurate as possible, since the cost-effectiveness ratio depends on the differences between them. Small errors will be magnified when differences are taken. For example, if the intervention involves more medications than the comparator, and data on medications are incomplete, the difference in costs between the two will understate the net cost of the intervention. And if the elderly use higher levels of medication than younger

**Table 1.** Illustrative QALY Calculations for Two Age Groups

| Health state | QALY weight | Elderly: Probability of health state: Intervention | Elderly: Probability of health state: Comparator | Elderly: Net QALY | Young: Probability of health state: Intervention | Young: Probability of health state: Comparator | Young: Net QALY |
|---|---|---|---|---|---|---|---|
| Excellent | 1.0 | 0.2 | 0.2 | 0 | 0.6 | 0.5 | +0.10 |
| Good | 0.8 | 0.6 | 0.3 | +0.24 | 0.4 | 0.3 | +0.08 |
| Poor | 0.4 | 0.2 | 0.5 | −0.12 | 0.0 | 0.2 | −0.08 |
| *Total QALYs* | — | 0.76 | 0.64 | +0.12 | 0.92 | 0.82 | +0.10 |

Calculations are per person; see Methods section for description of calculations. The "net QALY" column shows the difference in QALYs between the intervention and the comparator for each health state and in total (last row).

people, the understatement will be greater for them and differences among age groups will be misrepresented.

Quality-adjusted life-years (QALYs) are a more complete measure of health outcomes than life expectancy (20). QALYs capture improvements (or declines) in function, symptoms, and pain as well as changes in years of life. QALYs are calculated by multiplying the time a person spends in a health state by a number between 0 and 1, called a QALY weight, which reflects the desirability of that health state. In general, the elderly will be in poorer health than younger people, and thus their time, for either the intervention or the comparator, will be multiplied by lower weights.

Yet an intervention may be more cost-effective for older than younger people exactly because the elderly face higher risks, experience poorer health states, or require more costly services. Table 1 shows how this can happen with a simplified illustration of QALY calculation. In the example, there are three health states: excellent health (QALY weight = 1), good health (QALY weight = 0.8), and poor health (QALY weight = 0.4). The total QALYs shown for the intervention and comparator in the last row were calculated by multiplying the probability of each health state times its QALY weight and summing over all health states. Net QALYs, the difference between intervention and comparator, are also shown in the last row. Under both the intervention and the comparator, an elderly person has a higher probability of experiencing poor, or, at best, good health. But since the health effect due to the intervention comes from its ability to improve health and an elderly person is more likely to experience a substantial improvement in health (from poor to good), the net health effect is larger for an elderly than a younger person (0.12 vs. 0.10). Note that this simple example does not take into account differences in life expectancy at different ages.

A cost-effectiveness ratio is the net result of all these factors operating together. The longer life expectancy of a younger person may be offset by greater benefit for an elderly person. Costs may be higher for the elderly, but the difference in costs between the intervention and the comparator may be smaller; that would be the case, for example, if the cost of an intervention (e.g., medication) is nearly the same regardless of age while the cost of the alternative (e.g., hospitalization) is substantially higher for the elderly. In order for the cost-effectiveness ratio for an age group to be accurate and valid, the elements that go into it must be based on age-specific data whenever age differences might be important. It may sometimes be valid to assume that an element, such as the probability of benefit or the cost of treatment, is the same across age groups, but this assumption should be well founded. Nor should analysts assume that small differences in a single factor can be ignored. In combination with other age-specific data, those differences may produce substantial differences in cost-effectiveness.

### The Literature Review

We used three terms to search MEDLINE for articles published from 1985–97: cost-effectiveness analysis, cost-utility analysis, and cost-benefit analysis. MEDLINE used the term cost-benefit analysis for all three kinds of studies in the early years of the period. To identify studies that presented results by age, we conducted searches that combined each of the three terms with the text word "age" or "aged." These searches resulted in 569 articles. Other terms (e.g., "elderly") were tested but did not turn up appropriate articles. The abstracts of all articles identified were reviewed to exclude cost-benefit analyses, articles in languages other than English, or subjects inappropriate for the purposes of this paper (e.g., an analysis of an intervention for children).

The 131 abstracts that remained were printed and reviewed to identify studies that included (but were not necessarily limited to) adults age 50 or older, that were based on data for developed countries, and that compared results for adults of different ages or for initiation of an intervention at different ages. If an abstract left any of these points in doubt, the article was selected. A few additional articles were discovered serendipitously or through review articles turned up by the searches, resulting in a total of 51 articles.

These articles were alternately assigned, following the order of their appearance in the printed abstracts, to one of the authors for full review. An abstracting form was used to promote comparability of reviews. It asked for the first author and year of publication, study design (e.g., decision analysis), time horizon, methods (e.g., study perspective, measure of health effects), intervention/comparator, population, data sources, year of costs, use of discounting, cost-effectiveness ratios by age, and sources of age differences. Each author reviewed the other's completed forms.

Fifteen articles reviewed at this stage turned out not to be appropriate because they did not present results by age. The remaining 36 articles are included in this paper. We reviewed these 36 articles a second time, using a second abstracting form that listed the individual data elements required for cost-effectiveness analysis, to determine the extent to which analysts searched for and incorporated age-specific data. We noted when assumptions were varied by age or when justification was offered for not varying assumptions by age. If there was no explicit statement in the article, we assumed that the authors had not used age-specific data and had not tested for differences by age.

## RESULTS

Table 2 lists the 36 studies by type of intervention (primary prevention, screening for existing disease, or therapy) and pattern of cost-effectiveness ratios by age. Three of the studies contained two comparisons of interventions in which cost-effectiveness ratios had different patterns by age, and one article contained three comparisons with different patterns by age. For example, an analysis of HMG-CoA reductase inhibitors for coronary heart disease reported one pattern for primary prevention, another pattern for secondary prevention in women, and a third for secondary prevention in men. We tabulated and reported all 41 comparisons. No consistent pattern of cost-effectiveness ratios by age was evident across the studies reviewed, overall or by type of intervention. Of 41 comparisons, the cost of an intervention per unit of health effect gained fell with age in 16 comparisons, rose with age in 15, fell and then rose with age in eight, rose and then fell with age in one, and had no pattern in one.

Table 3 reports the number and percentage of studies that used age-specific data, by type of data. We counted studies that included a statement justifying the use of the same data for different age groups as having varied the item by age. Although all studies incorporated a higher risk of death and hence lower life expectancy for older age groups, most did not

**Table 2.** Studies by Type of Intervention and Pattern of Cost-effectiveness Ratios by Age[a]

| Intervention/Pattern | Primary prevention | Screening | Therapy | Total |
|---|---|---|---|---|
| Cost falls at older ages | Balestra (2) | Danese (11) | Bass (4) | 16 |
| | Geelhoed (19) | Eddy (15)[b] | Bloom (6) | |
| | | Lee (30)[c] | Edelson (16) | |
| | | Salzmann (35) | Goldman (21)[d] | |
| | | Tsuji (41) | Gronvald (22) | |
| | | | Johannesson (23) | |
| | | | Kalish (25) | |
| | | | Mark (31) | |
| | | | Weinstein (44) | |
| Cost rises at older ages | Oster (32) | Eddy (15)[f] | Bennett (5) | 15 |
| | Sisk (40)[e] | Krahn (27) | Chang (8) | |
| | | Lee (30)[g] | Cronenwett (9) | |
| | | | Desch (13) | |
| | | | England (17) | |
| | | | Fitzgerald (18) | |
| | | | Johannesson (24)[h] | |
| | | | Katz (26) | |
| | | | Richards (34) | |
| | | | Salpeter (36)[i] | |
| Cost falls, then rises with age | Cummings (10) | de Koning (12) | Goldman (21)[k] | 8 |
| | Goldman (21)[j] | Eddy (14) | Johannesson (24)[l] | |
| | Oster (33) | Shimbo (39) | | |
| Cost rises, then falls with age | | | Krumholz (28) | 1 |
| No pattern by age | | Schechter (37) | | 1 |
| Total | 7 | 12 | 22 | 41 |

[a] Based on 41 comparisons in 36 articles (see text).
[b] In the comparison of Pap smears to screen for cervical cancer until age 74 and no screening, cost per life-year saved is lower if screening begins at older ages than at younger ages.
[c] Routine exercise testing for stable angina with angiography if ST-segment depression ≥1 mm compared with testing and angiography for ≥2 mm.
[d] HMG-CoA reductase inhibitors for secondary prevention of coronary heart disease in women.
[e] Vaccination against pneumococcal bacteremia is cost saving at all ages ≥65, with savings and health benefits lower at older ages.
[f] In the comparison of Pap smears for cervical cancer with no screening starting at ≥ age 65, cost per life-year saved is higher for older ages than for younger ages.
[g] Routine exercise testing for stable angina with angiography if ST-segment depression ≥2 mm compared with ≥3 mm, and testing and angiography for ≥3 mm compared with no routine testing.
[h] Antihypertensive medication compared with no special medication, both without future costs of survivors.
[i] Isoniazid prophylaxis for low-risk tuberculin reactors compared with no isoniazid; cost saving at all ages, with lower savings at older ages.
[j] HMG-CoA reductase inhibitors for primary prevention of coronary heart disease in women and men.
[k] HMG-CoA reductase inhibitors for secondary prevention of coronary heart disease in men.
[l] Antihypertensive medication compared with no special medication, both with future costs of survivors.

fully take age differences into account. For example, only 13 (36%) of the studies varied the effectiveness rate of the intervention by age. Almost two-thirds (23 of 36) assumed the same rate of effectiveness regardless of a person's age and did not justify that assumption. Since risk factors and health problems are typically more prevalent among elderly people, such an assumption would imply higher absolute levels of health benefit for older compared with younger age groups.

Analyses of therapeutic interventions were most likely, and analyses of screening least likely, to vary the effectiveness rate by age (Table 4). This difference in methods did not stem solely from data availability; one evaluation of mammography versus breast physical exam to screen for breast cancer varied the incidence and specificity of the examinations

**Table 3.** Number and Percentage of Articles That Used Age-specific Data, by Type of Data (Based on 36 Articles)

| Type of data | Number | Percentage |
|---|---|---|
| Life expectancy | 36 | 100% |
| Incidence/prevalence of target condition | 32 | 89 |
| Case fatality rate | 31 | 86 |
| Risk of intervention's adverse effects | 21 | 58 |
| Cost of treating adverse effects | 15 | 42 |
| Effectiveness rate of intervention | 13 | 36 |
| Cost of treating target condition[a] | 6 | 17 |
| Quality of life[b] | 4 | 24 |

[a] An article was counted as having varied costs by age or justified the lack of variation if it varied any component of these costs or considered whether any component varied with age.
[b] Based on the 17 articles (18 comparisons in Table 5) that used QALYs; of these 17, 13 did not vary the QALY weights by age.

with age, while a later study assumed that the effectiveness of mammography did not vary with age (12;14). In general, however, there seemed to be no association between varying or not varying the effectiveness rate by age and the pattern of cost-effectiveness results.

Although studies differed in their measures of health effects, these differences were not clearly associated with a particular pattern of results (Table 5). Seventeen articles (21 comparisons) expressed health effects as years of life saved. Another 17 articles (18 comparisons) used QALYs, which combine likely changes in length and quality of life; four of these used QALY weights that varied by age (13;24;34;40). The remaining two studies measured cases of disease prevented or detected (18;22).

The four studies that used different QALY weights for different age groups found that the more intensive intervention was more costly per QALY gained at older ages. For three of the four, it is difficult to attribute these results to age adjustments in QALY weights, however. Declining duration of the intervention's effectiveness by age heavily influenced the results for vaccination to prevent pneumococcal disease, but variations in the QALY weights had little effect (40). For adjuvant chemotherapy for primary breast cancer, cost per QALY gained was higher at older ages even before quality-of-life adjustment by age, presumably because mortality and recurrence rates rose with age (13). Similarly, in an analysis of antihypertension medication, costs per life-year and per QALY had the same

**Table 4.** Variation in Effectiveness Rate by Type of Intervention and Pattern of Cost-effectiveness Ratios[a]

| | Effectiveness rate not varied by age | | | Effectiveness rate varied by age | | | |
|---|---|---|---|---|---|---|---|
| Intervention/ pattern | Primary prevention | Screening | Therapy | Primary prevention | Screening | Therapy | Total |
| Cost falls at older ages | 2 | 4 | 5 | — | 1 | 4 | 16 |
| Cost rises at older ages | — | 2 | 7 | 2 | 1 | 3 | 15 |
| Cost falls, then rises with age | 3 | 2 | 1 | — | 1 | 1 | 8 |
| Cost rises, then falls with age | — | — | — | — | — | 1 | 1 |
| No pattern by age | — | 1 | — | — | — | — | 1 |
| Total | 5 | 9 | 13 | 2 | 3 | 9 | 41 |

[a] Based on 41 comparisons from 36 articles. See footnotes for Table 2.

**Table 5.** Quality-of-life (QOL) Adjustment by Type of Intervention and Pattern of Cost-effectiveness Ratios[a]

| | No QOL adjustment | | | QOL adjustment | | | |
|---|---|---|---|---|---|---|---|
| Intervention/ pattern | Primary prevention | Screening | Therapy | Primary prevention | Screening | Therapy | Total |
| Cost falls at older ages | 1 | 3 | 7 | 1 | 2 | 2 | 16 |
| Cost rises at older ages | 1 | 2 | 2 | 1 | 1 | 8 | 15 |
| Cost falls, then rises with age | 3 | 2 | 1 | — | 1 | 1 | 8 |
| Cost rises, then falls with age | — | — | 1 | — | — | — | 1 |
| No pattern by age | — | — | — | — | 1 | — | 1 |
| Total | 5 | 7 | 11 | 2 | 5 | 11 | 41 |

[a] Based on 41 comparisons from 36 articles. See footnotes for Table 2.

pattern (24). The results of the fourth study seemed more dependent on the QALY weights; the analysis did not extend through patients' life expectancies, reported results after 4 years of home parenteral nutrition for intestinal failure, and did not appear to vary effectiveness or risk of the intervention by age (34).

Costs were the data items most frequently assumed to be constant across age groups (Table 3). Fewer than half the studies used age-specific information on the cost of treating adverse effects. Only six used age-specific data on the cost of treating the target condition or justified not varying it (4;17;22;31;35;44) Even these did not always fully account for differences in this cost; we counted an article as having varied treatment costs by age if it varied any component by age (or considered whether that component might vary by age).

The duration of most studies was the life expectancy of the target groups, but three studies truncated the analysis short of life expectancy (6;34;39). These three incorporated health effects and cost for shorter periods. This approach may have favored results for the elderly since it reduced the effect of their shorter life expectancies.

A few studies contained notable flaws not clearly associated with age comparisons. Some omitted important costs: physician costs (2), nursing home costs (2), and costs of adverse effects (1). Five did not state the perspective of the analysis. Three did not state that they discounted future costs and health effects.

## POLICY IMPLICATIONS

We reviewed cost-effectiveness studies published between 1985 and 1997 that presented cost-effectiveness ratios for different age groups. Most studies did an incomplete job of incorporating age differences. Many did not use age-specific data for the effectiveness, risks, and costs of the interventions evaluated, and did not appear to question whether use of the same rates and costs for all age groups was reasonable.

It is not clear how often the lack of adjustment for age stems from insufficient data, and how often it reflects that key variables do not in fact vary by age. For example, the cost-effectiveness analysis of pneumococcal vaccination for elderly people (40) found only one source that reported the effectiveness of pneumococcal vaccination by age (38). Moreover, that source reported that immunocompetent status was more important for effectiveness than age. The increasing inclusion of elderly people in clinical trials, along with the growing appreciation of differences among age groups over age 65, should improve data availability



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over time. In the United States, data from the Medicare program provide age-specific costs for people 65 years and older, but comprehensive costs for comparisons with younger age groups are generally lacking.

Several observers have expressed concern that cost-effectiveness analysis tends to favor younger people over the elderly (1;3;29;45). Use of life-years or QALYs rather than lives saved appears to be the major reason for the concern. Our review suggests that age differences have not been modeled with enough rigor to show definitively whether cost-effectiveness methods tend to favor one age group over another. It is not, however, a foregone conclusion that more rigorous analyses would favor younger age groups. As the illustration in Table 1 suggests, even if older people are less responsive to an intervention or have higher costs or risks of complications, they may still derive greater net health benefit for the funds spent. Elderly people often have higher incidence and prevalence of health problems, a higher risk of developing complications from disease and thus greater benefit from avoiding it, and higher costs of subsequent treatment. Individually and collectively, they may therefore have more to gain in better health and reduced costs from an intervention.

The discounting procedure used in cost-effectiveness analysis may also favor elderly people. To account for people's preferences for present over future outcomes, a discount rate is applied to future costs and health effects. The farther into the future costs and health effects occur, the lower their present value after discounting. Discounting thus attenuates the effect of elderly people's shorter life expectancy by reducing the present value of the additional but more distant life-years of younger people. Screening and treatment of hypertension, for example, produce more immediate costs but also more immediate health benefits for older people, who have higher incidence rates.

Cost-effectiveness analyses, like the data on which they are based, have used age as a proxy for factors with health and cost implications, such as comorbidities, severity of illness, and mortality rates. Age may fail to capture the likely benefits, risks, and costs for a particular individual or subgroup of individuals within an age group. Until research brings greater insight into the exact factors associated with health benefits and risks, however, policy analysts have little choice but to use age, despite its limitations. Continuing to probe for those underlying factors is clearly important for both clinical practice and cost-effectiveness analysis.

We conclude that many studies have not modeled age differences in sufficient detail to ensure that differences in cost-effectiveness ratios by age are accurate and a sound basis for decisions. As cost-effectiveness analysis becomes more widespread, analysts should strive to incorporate more realistic estimates regarding age. Even with improvements in methods, decision makers should continue to probe the underlying assumptions and values of any analysis and to supplement cost-effectiveness results with considerations of equity and distribution.

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