Education and debate

Prognosis without treatment as a modifier in health economic assessments

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How long someone has to live intuitively seems important in rationing decisions. Incorporating it into economic assessments, as described here, could make decisions fairer

Editorial by Klein

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Explicit rationing—decisions not to fund certain treatments—has become a fact of life in many health-care systems.^{1–4} Health economic assessments often underpin rationing decisions, although it remains unclear whether society's values are well reflected by the utilitarian approach of maximising the units of health attainable from available resources.^{5,6} Health economic assessments are used to determine the additional cost per unit of health gain for different treatment options. Cost effectiveness analysis is the most common method of assessment^{7,8} and, for life shortening conditions, primarily focuses on the additional cost per life year gained. We propose that prognosis without treatment is an important contextual modifier of life years gained in evaluating treatments for life shortening conditions. We present initial data supporting this hypothesis and describe resource allocation strategies that use this information.

Limitations of life years gained

Life years gained represent the extra life expectancy resulting from a treatment. By definition, the comparison is with the life expectancy associated with an established standard of care for the condition. Depending on the condition, the established standard of care may be interventional or supportive.

Using life years gained in health economic assessments has several problems. The first is that they are inapplicable to treatments that do not prolong life. Most of the other problems relate to the fact that a year of life in a particular clinical setting may not have the same value as a year of life in a different clinical setting.

QALYs and contextual modifiers

Initial attempts at improving the fairness of life years gained resulted in the development of quality adjusted life years (QALYs). In a QALY, each unit of time in a health state is weighted by both the objective quality of that time and its subjective worth. Consequently, QALYs can also be used in economic assessments of treatments of non-life shortening conditions and of

Stylised Kaplan-Meier survival curves from a hypothetical clinical study comparing an interventional treatment with supportive care

treatments in life shortening conditions that do not prolong life. However, controversy exists over the methods used to construct the weighting schemes for QALYs and whose subjective opinion should be canvassed.⁹ In addition, the traditional additive independence model for QALYs (that is, that periods in different health states can be summed after conversion to QALYs regardless of the order in which they occur) has recently been challenged.¹⁰ The subjective worth of a period in a given health state may be different when it is part of an improving profile rather than a declining one.¹⁰ This can be considered part of the broader idea that the context of a period of life years gained may contain relevant modifying factors in addition to those contained within the time gained from treatment.

Age is another contextual modifying factor that has been mooted.^{9,11} Such an adjustment is in line with one of the tenets of general economics—the rule of diminishing marginal utility. This rule summarises the commonsense observation that the more you have of

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something, the less you value each additional unit of it. For example, when considering the cumulative acquisition of food, money, or electrical goods, the first biscuit, £10, or television is usually more valued than the second, the second more than the third, and so on). Although there is little evidence that elderly people make different treatment decisions from younger adults,¹² the question of how much a year of elderly life is valued compared with a year of younger life, and by whom, remains unanswered.^{11 13} In addition, on a practical point, beyond the gross distinction between paediatric and geriatric conditions, data on the average ages of patients likely to have specific treatments are not readily available to inform any health economic modification.

We propose a novel contextual modifier for life shortening conditions that has the potential to be both a more acceptable and a more practical use of the rule of diminishing marginal utility. We suggest adjusting life years gained on the basis of the prognosis without treatment. This terminology presupposes that the comparative standard of care is supportive, and this assumption will be used for simplicity throughout this article. When the comparator is another intervention, the same concept would be more accurately expressed as prognosis with standard treatment.

Evidence for use of prognosis without treatment

Advocates of expensive treatments that produce only modest improvements in survival in life threatening conditions often argue that the time gained from treatment should be viewed differently when patients will live only a few months without it. To explore this claim in more detail, we did a pilot study in Edinburgh. We gave 10 doctors, 10 nurses, and 10 medical secretaries a hypothetical scenario in which resources were available to treat only one of three patients (see bmj.com for full details). Each patient had an unspecified disease that would be fatal, but they would be well until they died. No other patient details were given to reduce the effect of confounders on respondents' decisions. The available treatment, which had no side effects, would add three months to the life of whoever received it. Without treatment one patient would die in 6 months, one in 12 months, and the other in 24 months.

Participants were asked if they could decide which patient they would treat. Twenty eight of the 30 respondents were able to decide, suggesting that prognosis without treatment is relevant to decisions on resource allocation. Similar observations have been made about the factors influencing the distribution of a limited supply of zidovudine to patients with HIV infection and of donor livers to potential transplant recipients.¹⁴ We asked respondents in the Edinburgh study why they had made their particular choice. Their explanations could be grouped into three main categories:

- Immediate risk of death (treatment of patient who would die the soonest without treatment)
- Percentage increase in life years (treatment of patient who would get the greatest percentage increase in life expectancy from the treatment)

Hypothetical comparison of life years gained and percentage increase in life years

Two clinical scenarios are competing for extra resources of £3.2m:

Scenario 1—New antimicrobial drug for treating a complication of AIDS

Treatment with standard care costs £2000 for each patient and median survival is 6 months

Treatment with the new drug costs £10 000 and median survival is 9 months

Cost per life year gained is £32 000 (incremental cost of the new treatment (£8000) divided by 0.25 (the 3 month gain from treatment expressed as a fraction of a year))

Cost per percentage increase in life years (quoted for 100%) is £16 000 (£8000/0.5, (where gain from treatment/prognosis without treatment = 3 months/6 months = 0.5))

Allocating all the additional resource to this treatment would gain 100 life years or a 200 000 per cent increase in life years

Scenario 2—New chemotherapy for metastatic cancer

Treatment with standard care costs £2000 and median survival is 3 months

New treatment costs £10 000 and median survival is 5 months

Cost per life year gained is £47 904 (£8000/0.167)

Cost per percentage increase in life years (quoted for 100%) is £12 121 (£8000/0.66)

Allocating all the additional resource to this treatment would gain 67 life years or a 264 000 per cent increase in life years

If we assume allocation on utilitarian grounds alone, if life years gained were used in the economic analysis all the £3.2m would be used for the new antimicrobial drug in AIDS. If percentage increase in life years was used, the resources would be allocated to the chemotherapy. Alternatively, a local or national resource allocation body could decide to fund either new treatment based on a preset acceptable cost per life year gained or cost per percentage increase in life years.

- Life expectancy with treatment (treatment of patient whose total life expectancy—that is, prognosis without treatment plus additional lifespan derived from treatment—would be the greatest).

Could any of these novel strategies be used to inform explicit rationing decisions at the societal level? Assuming median survival to be representative of survival per se, data to inform each of the strategies could easily be extracted from the Kaplan-Meier curves of the relevant randomised controlled clinical trial (figure, see bmj.com for further analysis). However, as a stand alone strategy only percentage increase in life years (PILYs) would be suitable for use in economic assessments. This is because the other two novel strategies would ignore, or potentially underemphasise, whether the treatment was having any effect. The box shows how percentage increase in life years could be costed and a hypothetical comparison with life years gained.

What further work is required?

Although we have shown that using percentage increase in life years in economic assessments is feasible, we do not know whether it is ever more appropriate than using life years gained. This could be determined through a simple questionnaire ranking strategies for allocating resource between hypothetical patients when the prognosis without treatment and gain from treatment differ. Our pilot study used timescales of prognosis and gain comparable to those found with and without chemotherapy in metastatic cancers of the breast, colon, and lung. Although it

Summary points

Quality adjusted life years (QALYs) are commonly used in economic evaluations of new and existing treatments

Contextual elements may provide important additional modifiers

Prognosis without treatment seems to be important in people's resource allocation decisions for life shortening diseases

Resource allocation strategies based on percentage increase in life years (PLYs) or percentage increase in QALYs could be used to incorporate prognosis without treatment directly

Further exploration of such modifiers is needed to optimise the fairness of health economic assessments

makes sense to explore similar timescales initially, we will eventually need to determine the time limits of both prognosis without treatment and gain from treatment under which the preference for a particular resource allocation strategy holds true. Prognosis without treatment may, for example, be relevant only if life years gained are insufficiently different between therapies to use on their own or only when median survival is less than two years with standard care. Lower limits of applicability may also exist. It would be unsurprising, for example, if percentage increase in life years were not considered relevant when patients had only a few days left to live without treatment and gained only a small number of extra days from a new treatment.

The different methods of modifying life years gained described above are not necessarily mutually exclusive. Several could therefore be used together within a single economic assessment. For example, the principles of both quality of life and percentage change could be combined by considering any QALYs gained from a particular treatment within the context of the QALYs associated with not giving that treatment. If percentage increase in life years or percentage increase in QALYs are clearly identified as preferable to life years gained or QALYs, we will need a debate about whose opinions count the most and what sort of consensus society needs to institute changes in the way that health economic assessments are conducted. The existing tools should not be discarded lightly.

Using percentage based strategies, alone or as an adjunct to existing methods, may eventually be deemed fairer in conditions with poor prognosis, whereas QALYs and life years gained without additional modification may be thought more appropriate for use in conditions with a good prognosis. In this situation, one solution would be for blocks of resources to be centrally ring fenced for poor prognosis conditions and then allocated to different treatment

scenarios taking into account percentage change, while resources for other conditions could be allocated using the standard life years gained or QALY methods. Analogous proposals have been made for allocating resources nationally (macroallocation) to highly specialised healthcare services before subsequently rationing them between users of the service according to predefined guidelines (microallocation).¹⁵ Ultimately, it may be possible to determine an acceptable threshold cost for percentage increases to help decide whether a treatment is worth using at all. Publicly raising the issue of whether information on prognosis without treatment is as a valid modifying factor in health economic assessments is the first step in all of these processes.

Contributors and sources: RC, FN, and DJ have a background in medical oncology and oncology drug development. SM, JJO, and DJW have a background in cardiovascular clinical pharmacology. RC, DJ, DW, and SM have all contributed to or chaired local, regional, or national medicines review committees, advising on drug related resource allocation issues. DW is currently the chairman, and AW is the head of health economics, for the Scottish Medicines Consortium, the national medicines review body for Scotland. This paper is based on surveys, ideas, and concepts developed through discussions between all authors over the past three years. RC is the guarantor.

Competing interests: None declared.

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(Accepted 1 April 2005)

Endpiece

Everyone's right

It must become a right of every person to die of old age. And if we secure this right for ourselves we can, coincidentally, assure it for the planet.

Alice Walker, African-American author

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