On Time Horizons in Health Economic Evaluations

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Highlights

- Available guidance on time horizons is not clear or consistent with regard to population-level effects owing to infectious disease transmission or other linkages, and the practice on setting time horizons is inconsistent.
- At least for infectious diseases, the state of the epidemic at the end of the policy period cannot be evaluated precisely. Evaluations over longer policy periods mitigate this challenge, but are subject to greater uncertainty and return averages of possibly time-varying effects.
- Incremental analysis of the effects of interventions implemented at a point in time within the policy period improves accuracy and helps identify opportunities in realigning the timing and mix of interventions under consideration.

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Abstract

The issue of time horizons has received scant attention in discussions pertaining to health economic evaluations unlike discounting or translation of health outcomes into life-cycle measures (e.g. Quality Adjusted Life Years (QALYs) or Disability Adjusted Life Years (DALYs)). The available guidelines do not offer clear and consistent guidance for many problems addressed in health economic evaluations. In practice, variation of time horizons between studies for the same diseases is a matter of concern, as results on cost-effectiveness depend on the time horizon.

Our paper contributes to establishing a consistent approach to setting time horizons across common types of health economic evaluations and mitigating potential bias where the choice of a time horizon may affect results of the evaluation.

We find that available guidance is clear only for patient-focused interventions, but not in the presence of population-level effects owing to transmission of infections or other linkages. We distinguish between a policy period – over which an intervention is delivered or initiated – and an evaluation period over which the effects are measured. One important challenge in establishing a time horizon for evaluation is that, at least for infectious diseases, the state of the epidemic at the end of the policy period cannot be evaluated precisely and incorporated in the results of an economic evaluation. While longer policy periods partly mitigate this challenge, they are subject to greater uncertainty, and outcomes may not adequately reflect the cost-effectiveness of current policies because outcomes reflect an average over the policy period. Incremental analysis on interventions implemented in sub-periods of the policy period (especially at the beginning) potentially improves accuracy and helps to identify potential for improving cost-effectiveness by varying the path of implementation or the mix of interventions offered over time.

I. Introduction

The measurement of health outcomes and costs over time in health economic evaluations poses several challenges – capturing health effects which often extend well beyond the study period (notably owing to longer survival), the scope of future costs, weighing health outcomes and costs over time through discounting, and setting time horizons for policy implementation and evaluation.

Some of these issues have been well explored. The immediate effects of health interventions are typically transformed into quality-adjusted life years (QALYs, endorsed by the Panel on Cost-Effectiveness in Health and Medicine, see Feeny et al., 2016) or in global health to disability-adjusted life years (DALYs) (Kyu et al., 2018; Jamison Gelb, Horton et al. 2017). Claxton and others (2019) and Haacker, Hallett and Atun (2019) provide recent access points to a longstanding discussions on discounting in global health going back some 40 years (Weinstein and Stason, 1977). The issues around future costs, and in particular their scope, included in health economic evaluations are well understood (van Baal Wong, Slobbe, et al., 2011), but not considered consistently in practice (Sanders et al. (2016); van Baal, Morton, Meltzer, and Brouwer (2019)).

In contrast, the issue of time horizons in health economic evaluations has not been addressed comprehensively, even though the choice of a “time period over which to evaluate an intervention is a vexing question” (Tan-Torres et al., 2003). Influential guidance on cost-effectiveness analysis (Table 1) provides general recommendations, e.g., advising that the time horizon “should extend far enough into the future to capture important differences in consequences” (Owens et al., 2016).

Applying such general recommendations across common types of health economic evaluations is a challenge. The most clear-cut case is a patient-focused evaluation of an intervention for which costs and effects can be measured or projected through the life course of the patient(s), or a shorter period if there are no lasting health and cost effects. This approach works because we can be certain that all the effects of the intervention have been realised by that time.

Setting an appropriate time horizon is less straightforward, if the disease targeted by an intervention is communicable or when behavioural externalities are present, as the effects of an intervention spread across the population and are not tied to the lifetime of the immediate beneficiaries of an intervention.

The design of an evaluation with respect to time horizons becomes more complex when an evaluation considers the impact of a policy, by which we refer to an intervention delivered or initiated (e.g., by placing patients with HIV on antiretroviral therapy, who then receive treatment for life) successively across a targeted population over a period of time. A common motive for such an evaluation is the desire to assess progress towards policy targets, for example reducing incidence or the number of deaths from a disease below a threshold. In such an evaluation, it is necessary to make decisions on the time horizon for the assumed implementation of the policy of which the effects are studied (although the policy might continue after this period, outside the scope of the evaluation), and the time horizon over which the effects are evaluated. While some considerations call for adopting

longer time horizons (e.g. sufficient ones to assess progress towards disease elimination), others go against it (e.g., increasing uncertainty for more distant periods).

Our objectives are informing choices on setting time horizons across common types of health economic evaluations, and improving accuracy where results may be sensitive to the choice of a time horizon. We first provide an overview of available guidelines and of the practice on setting time horizons. We then discuss options on setting time horizons for the evaluation of policies. Finally, we describe approaches that can help refine the practice on setting time horizons for health economic evaluations.

II. Background

The important role of the time horizon in health economic evaluations is reflected in influential guidelines. These guidelines broadly recommend the time horizon should “be of sufficient length to capture all costs and effects relevant to the decision problem,” “extend far enough into the future to capture important differences in consequences,” or “be long enough to capture all the differential effects of the options” (Table 1).

These guidelines do not make explicit reference to the role of transmission effects for interventions related to communicable diseases, however. The focus on lifetime effects of “treated individuals” or the beneficiaries of an intervention, and the absence of references to disease transmission suggests a focus only on direct patient-level effects of an intervention. Only one guideline differentiates between a policy period – “all interventions should be evaluated under the assumption that they are implemented over a period of 10 years” (Tan-Torres et al., 2003) – and the period over which the effects are evaluated.

Some more specific guidance has emerged for interventions like vaccines where disease transmission is an important consideration. Ultsch et al. (2016), for instance, suggest the “time horizon of a dynamic model should last until the steady state is achieved in order to deliver valuable results” in an economic evaluation of immunization.

The practical importance of time horizons is underscored by a number of studies. McCreesh et al. (2018) demonstrate that results on cost-effectiveness of expanding treatment eligibility for people living with HIV strongly depend on the time horizon chosen. Kim et al. (2017), in a review focusing on the United States, report similar findings for treatment of Hepatitis C or various cardiovascular diseases. These studies suggest that the choice of the time horizon is not rendered moot by discounting, for time horizons commonly used. Focusing on the United States, Kim et al. (2017) also report that a majority of a sample of 800 cost-effectiveness studies adopted a time horizon of at least 50 years, but many of the studies adopting a shorter time horizon did so even though a long-term outlook seemed appropriate, considering the type of disease and intervention studied. Only a small minority of studies provided a sensitivity analysis with respect to the time horizon.

Table 1. Perspectives on Time Horizons in Influential Guidelines

Torrance, Siegel, and Luce, 1996 (1st Panel on Cost-Effectiveness)	"The time horizon of the analysis for a cost-effectiveness study should extend far enough into the future to capture the major health and economic outcomes-both intended effects and unintended side effects. As a result, some analyses follow patients for the duration of their lives. For certain interventions, such as the removal of environmental toxins, the effects of a program may run even longer, requiring a time horizon that extends for generations. Frequently, the appropriate time horizon extends beyond the availability of primary data, and modeled data must be used in the analysis." "When a positive discount rate is used, as is recommended for the Reference Case Analysis, the time horizon of the study will in many cases be effectively limited by the discount rate."
Drummond and Jefferson, 1996 (Guidelines for Authors and Peer Reviewers of Economic Submissions to the BMJ)	"The time horizon should be long enough to capture all the differential effects of the options. It should often extend to the whole life of the treated individuals and even to future generations. If the time horizon is shortened for practical reasons this decision should be justified and an estimate made of any possible bias introduced."
Tan-Torres and others, 2003 (WHO Guide to Cost-Effectiveness Analysis)	"All interventions should be evaluated under the assumption that they are implemented over a period of 10 years. However, costs and health effects related to the intervention should be followed for the duration of the lifetime of the beneficiaries."
Wilkinson and others, 2014 ("iDSI" Reference Case)	"The time horizon used in an economic evaluation should be of sufficient length to capture all costs and effects relevant to the decision problem." "Lifetime time horizon should be used in first instance. Shorter time horizon can be used where shown that all costs and effects that are relevant to the decision problem have been captured."
Owens, Siegel, Sculpher, and Salomon, 2016 (2nd Panel on Cost-Effectiveness)	"The time horizon of the CEA should extend far enough into the future to capture important differences in consequences. [...] Using a time horizon that does not encompass all consequences can provide a misleading estimate of the cost-effectiveness of an intervention. [...] At a minimum, modeling should be used to estimate gains in life expectancy due to differential survival. As noted, the time horizon should also be sufficient to capture relevant costs. [...] When a positive discount rate is used, as is recommended for Reference Case analyses, the time horizon of the study will in many cases be effectively limited by the discount rate."

A similar picture emerges in relation to cost-effectiveness analyses in global health (Figure 1), as measured by the studies captured in the Global Health Cost Effectiveness Analysis Registry (CEVR, 2019). The time horizon adopted in these studies reflects properties of the disease (e.g., shorter for rotaviral enteritis, which is an acute and time-limited viral infection), but there is high dispersion of time horizons used in studies within disease categories. Less than one-half of studies adopt a lifetime horizon, and only about 5 percent provide an analysis for multiple time horizons. The studies covered translate direct health outcomes into DALYs (a condition for inclusion in this database), which is a common method of accounting for life-time health consequences of an intervention, but it is not clear how the corresponding future costs have been accommodated (problematic in particular for HIV/AIDS, where survival depends on continuing treatment). As a matter of concern, three of the four diseases covered most frequently in the studies analysed (namely, HIV/AIDS, malaria, and tuberculosis) are both chronic and communicable: i.e., diseases for which the consequences of an intervention spread across populations and therefore beyond the lifetime of patients or populations targeted directly.

Figure 1. Time Horizons Across Cost-Effectiveness Studies for Selected Diseases in the Global Cost-Effectiveness Analysis Registry

III. Discussion

Our discussion is guided by three considerations. First, as pointed out by O'Mahoney et al. (2015), it is helpful to distinguish different dimensions of time horizons. Specifically, we consider a policy period over which intervention is assumed to be implemented (although it could be expected to continue, but outside the scope of the evaluation), and an evaluation period over which the effects of an intervention or of a policy are realized and measured, which can be equal to or extend beyond the policy period. We set aside a third dimension discussed by O'Mahoney et al. (2015) – intervention duration, i.e., “length of time over which the intervention is applied per person or cohort” – which, for our purposes, can be captured under the evaluation period.

Second, we distinguish three stylized settings which raise different methodological or practical issues – (i) analysis of an intervention which is delivered or initiated at one point in time; (ii) analysis of an intervention which is delivered over some policy period and evaluated over the same period, and (iii) an analysis in which the evaluation period extends beyond the policy period. We note that there are shades between these stylized cases regarding the scope of outcomes and costs covered.

Third, we recognize that an evaluation may adopt a shorter time horizon than theoretically warranted, for practical or political reasons – e.g., measuring progress towards global targets like the Sustainable Development Goals through 2030 (United Nations General Assembly, 2015).

The most straightforward case is the **analysis of an intervention delivered or initiated at a point in time**. For non-communicable diseases, the effects can be tracked by following the beneficiaries of the intervention over time, or applying some modelling, to establish the relevant changes in health outcomes and costs, up to a lifetime horizon if required. For communicable diseases (or in the presence of linkages or externalities), establishing an appropriate evaluation period is less straightforward, as the health effects extend beyond the targeted population, and the relevant time horizon becomes dependent on the disease transmission and progression dynamics. In this setting, it is desirable to project the consequences of an intervention across the population until the effects peter out (Ultsch et al., 2016). Adopting a shorter horizon results in truncation of health gains or costs, and leads to biased estimates on cost-effectiveness.

The relevance of these point is illustrated by Haacker, Gorgens, and Fraser-Hurt (2016) for male circumcision for HIV prevention. For a male individual circumcised at age 20, projected HIV infections averted among the population circumcised are spread over about 10 years. HIV infections averted among sexual partners and through mother-to-child transmission exceed the direct effects by a factor of 1.5, and are spread over a longer period of about 20 years. HIV-related treatment costs peak only after 30 years and are spread over about 70 years. These findings – indirect effects of a similar order of magnitude as the direct effects of a prevention intervention and the realisation of indirect benefits over a longer time horizon – apply to other communicable diseases, such as tuberculosis and malaria, although the time horizons are unusually long for HIV.

The second case is an economic evaluation involving a **policy period (perhaps of some considerable length) and an evaluation period equal to the policy period**. This approach is typical for policy-oriented studies designed to analyse both the effectiveness and cost-effectiveness of an intervention/policy and its contributions to controlling a disease. For example, this approach has been adopted in global policy targets and related studies, including on “ending AIDS” (UNAIDS, 2014), “eliminating Hepatitis C” (WHO, 2016), the investment case for the 6th Global Fund Replenishment (Global Fund, 2019), Lancet Commissions on “Global Health 2035” (Jamison et al., 2013), diabetes in sub-Saharan Africa (Atun et al., 2017), tuberculosis (Reid et al., 2019), and cancer (Atun et al., 2015), and in numerous academic papers covering similar ground (e.g., Eaton et al., 2014 and Stover et al., 2016 on HIV; Bertram et al., 2018 on NCDs; Ozawa et al., 2016 on immunization).

The long policy period averaging 17 years in these 11 reports and studies is motivated by the objective of assessing the effectiveness of a policy, or of its components, in terms of reducing incidence and mortality and meeting “elimination” targets. Adopting a long time horizon, though, comes at a cost in terms of the accuracy and practical relevance of results on cost-effectiveness. One reason is uncertainty – the larger the weight of developments further out, the more uncertain the results on cost-effectiveness become. Moreover, if cost-effectiveness is calculated as the ratio of health effects and costs, each summed over the policy period (possibly weighed by some discount rate), the result reflects an average cost-effectiveness over the policy period. This average figure can mask changes in the cost-

effectiveness of a policy and its components over the policy period. Hence, adopting a long time horizon can result in weak guidance on **current** policies. This shortcoming is particularly relevant for the design of policies to control infectious diseases, where the effectiveness of interventions depends on the prevalence of the disease and other endogenous factors. E.g., in case of HIV, average cost-effectiveness ratios over the policy period have been shown to mask changes in cost-effectiveness across sub-periods (such that that front-loading of investments improves cost-effectiveness overall; Anderson, Ghys, Ombam, Hallett, 2018) and changes in the relative effectiveness of prevention interventions (so that the optimal policy mix changes over the policy period; Shattock et al., 2016).

Hence, setting a long policy period for evaluation may be appropriate to study the potential effectiveness of a policy in controlling a disease, and mitigates bias owing to truncation of health gains or costs in the presence of long time lags. However, the issue of averaging can be addressed by estimating the **incremental contributions** of interventions implemented at some point in time within the policy period – in particular at the beginning, which is most relevant for contemporaneous policy analysis. E.g., the coverage rate of some intervention(s) could be varied for the first period, keeping policies for the remainder of the policy period unchanged. If this incremental analysis produces results (and – for several interventions – rankings) different from the average cost-effectiveness, this could result in a reassessment of sequencing or pace of scale-up of the policy.

The second challenge regarding the design of health economic evaluations with respect to time horizons is the valuation of the consequences beyond the end of the policy period. In addition to outcomes over the policy period, there are costs and health outcomes beyond this period which can be attributed to actions within the policy period. In practice, this problem is frequently addressed by **extending the time horizon of the evaluation beyond the policy period** – the third type noted above.

There are several established methods of extending aspects of the evaluation beyond the policy period, such as translating health outcomes into QALYs (Feeny et al., 2016) or DALYs (Kyu et al., 2018), or assigning monetary values to improved health outcomes (Jamison and others, 2013; Robinson, Hammitt, and O’Keeffe, 2019). While QALYs and DALYs are widely used in academic studies in public and global health, policy-oriented reports and studies often specify “economic returns” in form of monetary valuations of health outcomes (including 8 of the 11 reports and studies quoted earlier). The issues around the accounting for future costs (“related” or “unrelated”) are well understood, and academic guidelines generally recommend a symmetric approach to health outcomes and costs with respect to the time horizon (Tan-Torres and others, 2003; Wilkinson and others, 2014; Owens, Siegel, Sculpher, and Salomon, 2016; see Table 1). However, the academic practice on including future costs is inconsistent (Sanders and others, 2016; de Vries, van Baal, and Brouwer, 2019).

Extending this approach to interventions implemented over some policy period is also possible, e.g., by including savings in treatment costs owing to reduced incidence that occur after the end of the policy period. Examples include assessments of comprehensive HIV control policies (Schwartländer et al., 2011) or of an HIV prevention programme (Njeuhmeli et al., 2011).

Where the implementation of an intervention is studied over a period of time, though, the accounting for the future costs poses some additional challenges. Costs within the policy period include some of the lifetime costs of disease (or reflects corresponding savings) caused by the health events

within the period, and it is important to account for lifetime costs and current spending in a way that avoids double-counting. This point is illustrated in Figure 2, which shows lifetime costs of treatment associated with two policies. Scenario 2 envisages improved prevention effort (not costed here), but the same treatment eligibility as in Scenario 1. Because there are fewer new infections in Scenario 2, the costs caused by new cases, and the costs overall, are lower in Scenario 2 than in Scenario 1. Irrespective of any new cases, the costs of care and treatment are at least A+B, for the population already affected by the diseases at the beginning of the policy period, of which cost B occurs after the end of the policy period. The improved prevention effort, which results in lower number of new cases, reduces the lifetime costs of care and treatment for new cases by E+F, or from C+D+E+F to C+D. E+F thus represents financial savings against the additional costs of implementing the prevention policy described by Scenario 2. However, if spending during the policy period are already included in the policy analysis, only the *remaining* savings in lifetime costs of people affected by the disease at the end of the policy period should be counted (represented by F in comparing Scenario 2 to Scenario 1).

Figure 2. Accounting for Lifetime Costs of Disease Beyond Policy Period

Generally, implementing these approaches is conceptually straightforward. In many policy analyses, however, the lifetime costs of disease are also policy-dependent. E.g., if the eligibility for accessing some treatment for some diseases expands, the projected lifetime costs for people affected by the disease, and for all new cases, changes. This is an example of an “unfunded liability” (Premchaud, 1995) which is created by a legislative or regulatory change and commits resources in future budget periods. Such unfunded liabilities can be captured with the framework described in Figure 2, but this might blur the link between expenditures over time and the underlying and preceding policy decisions. Accrual accounting methods to assess such future costs are commonly used in public finance (IFAC and CIPFA, 2018; OECD and IFAC, 2017) – e.g., to estimate the liabilities posed by insurance programs (Congressional Budget Office, 2018) – but rarely applied in public and global health.

The approaches on accounting for consequences beyond a policy period described above may not fully account for the implications of the policy beyond the endpoint of the policy period even with a very

long evaluation period. For example, the state of an infectious diseases epidemic at the end of the policy period may have implications for the future trajectory of the epidemic. Assessing the implications (and even the direction) of such dynamic effects is not straightforward. Does a disease control strategy result in a permanently lower trajectory of incidence (and hence improved health outcomes, and lower costs of care and treatment) following the end of the policy period? Or will the epidemic rebound in the absence of continued investments in prevention, and incidence could be higher than otherwise following the policy period? Or will incidence remain low, but only subject to some continuity policy which comes at a cost?

In health economic evaluations, there is no straightforward and fully satisfactory way to get around this endpoint problem. One approach would be to prolong the time horizon of the policy period to a point from which disease dynamics and costs no longer matter practically, e.g., because of discounting. However, longer time horizons result in less reliable estimates on cost-effectiveness of current policies (as discussed).

In some cases, it is possible to evaluate the state of a disease at the end of the policy period (subject to assumptions on continuation policies) without explicitly running projections until the end of time. Such methods are used in engineering or macroeconomics (e.g., Bellman, 1957; Ljungquist and Sargent, 2018), but they require that the state of a dynamic system can be summarized by one or very few state variables. This requirement is generally not met in health economics, as the population affected would typically be differentiated by sex, age, disease progression, treatment status, transmission risk (for infectious diseases), etc., resulting in a large number of state variables.

In one special case, it is more feasible to evaluate the state of a disease at the end of the policy period. This is when the effects of a policy dissipate over time, or the epidemic attains a “steady state” (Ultsch et al., 2016; Mauskopf et al., 2018), in which the relevant outcomes and costs under alternative scenarios are constant or grow at a constant rate. From this point, the present discounted value of the changes in long-term outcomes (following the point at which steady-state is reached) can be calculated as a multiple of the current value of the relevant variables.

IV. Conclusions

Available guidelines on health economic evaluations (summarized in Table 1) broadly agree that the evaluation should extend over the lifetime of the beneficiaries, or a shorter period if that is sufficient (i.e., if the intervention regards a disease which does not affect survival and does not have other lasting consequences in terms of either effects or costs). We find this guidance incomplete and inadequate in informing choices in settings commonly encountered in health economic evaluations – especially concerning infectious diseases – for two reasons. First, the “lifetime of the beneficiaries” is well-defined only for patient-focused interventions, but not when population-level effects occur because of disease transmission or behavioural and other externalities. Second, health economic evaluations frequently regard interventions offered over some policy period, and different considerations apply regarding the choice of the policy period and of the evaluation period over which the effects are measured, and for the scope of effects captured over the evaluation period.

We find that there is no fully satisfactory general method to account for the consequences of interventions beyond the end of the policy period, except for special cases: when the effects of a policy dissipate eventually – over the lifetime horizon for patient-focused evaluations, if the population-level effects of an intervention taper off (as in the example on male circumcision), or if an epidemic attains a steady state.

However, our discussion points to several methods which can help improve the accuracy of health economic evaluations. For example, it has been observed that cost-effectiveness ratios tend to improve with longer time horizons (Kim et al., 2017; McCreesh et al., 2018). **Sensitivity analysis** with regard to the time horizon is rarely conducted (Kim et al., 2017), yet understanding how costs and effects evolve over time is a valuable insight in its own right. Moreover, if results depend on the time horizon adopted, this finding could point to misspecification of the evaluation, e.g., when important results are truncated and results on cost-effectiveness are therefore biased. One common cause of such misspecification is inconsistent accounting for costs and effects. While health economic evaluation commonly accounts for the health consequences beyond the policy period (by translating immediate health impacts to deaths or cases averted in QALYs or DALYs), it is less common to account for the future costs.

Where a long policy period is adopted it is nevertheless important to bear in mind drawbacks of such an approach. Especially in the context of a disease control strategy, the cost-effectiveness of interventions, and their ranking, may change over the policy period. Results on cost-effectiveness ratios pertaining to the policy period overall may therefore be misleading in terms of identifying the most effective (possibly time-variant) policies. Incremental analysis of variations on the policy (especially on interventions delivered at the beginning of the policy period) can serve as a validity check on policy analyses and help to refine optimal policy design over time. Relatedly, accrual accounting offers a useful framework for linking costs and health outcomes to underlying decisions and events.

In summary – unlike other aspects of health economic evaluations over time like discounting or translating immediate health outcomes into life-cycle measures like QALYs or DALYs, the issue of time horizons has received relatively little attention, and available guidelines do not offer clear guidance for commonly used policies in different settings. This is the case even though results of health economic evaluations have been shown to be sensitive to the choice of the time horizon. Perhaps one reason for this neglect is that the issue of time horizons does not lend itself to simple general solutions. Our contribution is to describe common settings in health economic evaluations with regard to time horizons, to propose a more differentiated approach to time horizons differentiating between policy periods and evaluation periods, while describing methods to improve accuracy and relevance of evaluations covering long policy periods.

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