Practical Guidance for Including Future Costs in Economic Evaluations in the Netherlands: Introducing and Applying PAID 3.0

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ABSTRACT

Objectives: A consensus has been reached in The Netherlands that all future medical costs should be included in economic evaluations. Furthermore, internationally, there is the recognition that in countries that adopt a societal perspective estimates of future nonmedical consumption are relevant for decision makers as much as production gains are. The aims of this paper are twofold: (1) to update the tool Practical Application to Include Future Disease Costs (PAID 1.1), based on 2013 data, for the estimation of future unrelated medical costs and introduce future nonmedical consumption costs, further standardizing and facilitating the inclusion of future costs; and (2) to demonstrate how to use the tool in practice, showing the impact of including future unrelated medical costs and future nonmedical consumption in a case-study where a life is hypothetically saved at different ages and 2 additional cases where published studies are updated by including future costs.

Methods: Using the latest published cost of illness data from the year 2017, we model future unrelated medical costs as a function of age, sex, and time to death, which varies per disease. The Household Survey from Centraal Bureau Statistiek is used to estimate future nonmedical consumption by age.

Results: The updated incremental cost-effectiveness ratios (ICERs) from the case studies show that including future costs can have a substantial effect on the ICER, possibly affecting choices made by decision makers.

Conclusion: This article improves upon previous work and provides the first tool for the inclusion of future nonmedical consumption in The Netherlands.

Keywords: economic evaluation, future costs, nonmedical consumption, unrelated medical costs.

VALUE HEALTH. 2020; ■(■):■–■

Introduction

Although cost-utility analysis (CUA) is increasingly used to assess whether new interventions in healthcare yield sufficient value for money,[1] there are still several methodological issues that require attention. One such issue is the extent to which future costs should be included in CUAs,[2,3] where future costs are costs that arise from extending individuals' lives and include all costs in the life-years gained (LYG) from an intervention. They are typically divided into medical (relevant for both societal and healthcare perspectives) and nonmedical costs (only relevant for the societal perspective). Nonmedical costs here refer to consumption (eg, costs for housing and food) minus production (benefits from additional work in LYG). For medical costs, a distinction is made between *related* (eg, costs for check-ups by a cardiologist after a heart attack) and *unrelated* costs (eg, costs for treating pneumonia after said heart attack). Future related medical costs are typically included in CUAs. Including future unrelated medical costs, however, has been frequently debated. Early in the debate, the extent

to which future costs should be included was discussed using theoretical models aiming to optimize societal welfare. This led to multiple views on the topic,[4,5] the most compelling being that all future costs and benefits should be considered.[5] Later, the discussion was extended with the more practical view that because future unrelated medical consumption benefits are generally included, the costs thereof should be included to be consistent.[6] This argument was also used to state that future nonmedical costs should *not* be included, arguing that the benefits thereof are not systematically included in the Quality Adjusted Life-Year (QALY).[7] There are different views, however, on the extent to which the benefits from nonmedical consumption and production are actually included,[8–10] and there is so far no compelling (empirical) evidence regarding this.[3] The inclusion of future unrelated medical costs in CUA is now required in The Netherlands[11] and recommended in the United States.[12] Although production in LYG is often considered part of productivity costs in CUA using a societal perspective, the inclusion of future nonmedical consumption costs is only recommended in the United States.[12]

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To facilitate the inclusion of future unrelated medical costs in The Netherlands, the Practical Application to Include Future Disease Costs (PAID 1.0) was introduced in 2011[13] and updated in 2016 (PAID 1.1). This tool provides age and sex-specific average medical spending estimates, which can be specified to exclude the costs of specific providers and diseases. Estimates are based on a conceptual model that combines various streams of the literature. Costs by age are corrected for "time-to-death" by estimating costs separately for survivors and decedents. Time to death refers to the finding that healthcare costs are often higher in the last period of life.[14] Since older people are more likely to die, not correcting for this leads to an overestimation of the impact of age on medical expenditures[14] and ignores the fact that saving a life at a given age leads to the postponement of this high-cost last period of life.[15] Future related medical costs of specific diseases already included in the analysis can be excluded to prevent double-counting.

This article provides an extensive update of PAID to PAID 3.0. First, it uses most recent available cost of illness (COI) data (2017). Second, and the largest difference from PAID 1.1, future costs of nonmedical consumption are included. We provide guidance, supported by 3 case studies, on how to use PAID 3. PAID 3.0 can be used free of charge via https://imta.shinyapps.io/PAID3/ and consists of a webapp made in Shiny in R.

Methods

As stated by Meltzer,[5] if the aim of economic evaluations is to maximize social welfare given available resources, all costs following from an intervention should be considered. This implies that both medical costs, related and unrelated, and nonmedical costs should be included. The incremental cost-effectiveness ratio (ICER), including all costs can be written as follows:

$$ICER = \frac{\Delta\,[LY \times (RMC + PC)]}{\Delta\,QALY} + \frac{\Delta LY \times UMC}{\Delta\,QALY} + \frac{\Delta LY \times NMC}{\Delta\,QALY}, \quad (1)$$

where

- LY = life years;
- RMC = related medical costs;
- PC = productivity costs;
- UMC = unrelated medical costs;
- NMC = costs of nonmedical consumption.

Splitting the ICER equation into 3 ratios distinguishes the elements that are currently included in economic evaluation, related medical costs, and productivity costs, from the additional costs that are not usually considered: future unrelated medical costs and future costs of nonmedical consumption. Equation (1) also illustrates that differences in unrelated medical costs and future costs of nonmedical consumption are purely the result of differences in survival. In our estimation of the ICER, in which future costs are included, we use per capita medical and nonmedical consumption cost patterns by age as a starting point.

Lifetime costs of unrelated medical and nonmedical consumption $LY \times [UMC + NMC]$ for an individual aged a dying at age n, can be written as shown in Eq. (2):

$$LY \times [UMC + NMC] = \sum_{a}^{n-1}\sum_{i} sc_i(a) + \sum_{i} dc_i(n) + \sum_{a}^{n} nmc(a), \quad (2)$$

where

- a = age in years;

- n = age at death;
- dc = decedent costs (healthcare costs in last year of life);
- sc = survivor costs (healthcare costs in other years);
- nmc = average costs of nonmedical consumption;
- i = index of unrelated diseases.

Unrelated Medical Costs

Rather than taking a bottom-up approach and predicting the risk of all unrelated diseases and connecting these to costs, we take a top-down approach and use total per capita healthcare costs by age and sex as a starting point for estimating unrelated medical costs. Using methods identical to those of van Baal and colleagues,[13] we first break down total healthcare costs by disease, enabling the exclusion of costs for diseases already included in the analysis. Although we explain these methods in the ensuing text, for a more detailed description we refer to the original paper by van Baal and colleagues.[13] Disease-specific per capita healthcare costs were estimated using data from the Dutch COI from 2017.[16] Rather than using the system of health accounts [17] perspective (used in PAID 1.1), we use the classification from the National Institute for Public Health and the Environment (RIVM). Although the system of health accounts is internationally recognized, the RIVM definition includes more healthcare costs, such as international care. Whereas average per capita spending hardly changed between 2013 and 2017, age and disease patterns have changed. For example, between 2013 and 2017, costs of psychological disorders increased 14% when using 2017 prices—far more than costs in other disease categories, such as diseases of the central nervous system (2% when using 2017 prices).

COI data are specified by sex and 21 age-classes, which we interpolated using cubic splines to obtain age-year-specific per capita expenditures, and which are calculated from population spending totals. The data are further attributed to 100 disease categories and 11 healthcare provider categories (overview in Appendix A in Supplemental Materials found online at https://doi.org/10.1016/j.jval.2020.07.004.) These disease categories include "Not disease-related" and "Not allocated," meaning that these are also included in our definition of unrelated medical costs. Because healthcare costs are strongly determined by both age and time to death,[18] individual lifetime healthcare costs can be estimated as shown in the first 2 parts of Eq. (2). To obtain estimates for survivors and decedents, average per capita expenditures are divided into 1 part attributable to those dying and 1 part to those surviving at that particular age, assuming average costs are a weighted average of costs for survivors and decedents (age and sex indices are left out here for notational purposes):

$$ac_i = (1 - m) \times sc_i + m \times dc_i, \quad (3)$$

where

- ac_i = average per capita healthcare expenditure for disease i;
- m = mortality rate.

Disease-specific costs for survivors and decedents can be estimated using Eq (4), using mortality rates and the sex- and age-dependent ratios between costs for decedents and survivors (r_i):

$$dc_i = r_i \times sc_i, \quad (4)$$

$$ac_i = sc_i + (r_i - 1) \times m \times sc_i,$$

$$sc_i = \frac{ac_i}{1 + (r_i - 1) \times m},$$

Mortality rates from 2017 were obtained from Statistics Netherlands.[19] We used the same disease-specific ratios for costs between decedents and survivors for the hospital sector as used in previous versions of PAID. For ambulatory healthcare, drugs and appliances, and nursing and residential care, ratios from 1999 based on total expenditures were used.[20] To obtain disease-specific ratios for these providers, we exponentiated disease-specific hospital ratios by a scaling constant describing the relation between costs for decedents and survivors between hospital care and other providers (see Appendix C in Supplemental Material found online at https://doi.org/10.1016/j.jval.2020.07.004). For providers for which no ratios were available, we assumed that costs for decedents were equal to costs for survivors, as it is predominantly in hospitals that differences in survivor and decedent costs are observed.[18–21]

Nonmedical Consumption

To estimate costs of nonmedical consumption by age, we used data from the cross-sectional Dutch Household Consumption survey from 2004 adjusted to 2017 price levels using consumer price indices from Statistics Netherlands. In previous literature, economies of scale within households have been found to be important when estimating nonmedical consumption,[22,23] implying lower per person consumption costs when household size is larger. For instance, spending on housing can be divided among more people when household size is larger; however, the utility obtained from housing is likely to be the same whether someone lives on their own or not. This has important implications for estimating future costs of nonmedical consumption because preventing a death in a single-person household will result in more future nonmedical consumption than preventing a death in a multiperson household.[24] To estimate costs of nonmedical consumption for an average household by age, we fit 2 generalized additive models using penalized B-splines on age. The first model estimates annual consumption per household equivalent. Consumption per household equivalent is calculated from household consumption using the Organisation for Economic Co-operation and Development modified equivalence scale.[25] The Organisation for Economic Co-operation and Development modified equivalence scale assigns a weighting factor of 0.5 to each additional adult household member and 0.3 to each child in a multiperson household. The second model estimates the probability of a household having more than 1 adult; we are interested in making predictions for an average household. Using this equivalence scale implies that preventing a death in a single-person household results in twice as much nonmedical consumption as compared with a multiperson household with two adults. Details on these models and testing of assumptions can be found elsewhere.[23] The models are used to estimate average annual nonmedical consumption by age of preventing a death in an average household as in Eq. (5):

$$nmc(a) = [hh\ equiv(a) \times h(a) \times w] + [hh\ equiv(a) \times (1 - h(a))], \quad (5)$$

where

- h = probability of household having >1 adult;
- $hh\ equiv$ = annual nonmedical consumption per household-equivalent;
- w = weight of deceased household member: .5 for an adult and .3 for a child.

Case Studies

We demonstrate the impact of including future costs on the ICER via 3 case studies. Benefits are discounted at 1.5% per year and costs at 4% per year, in adherence with Dutch guidelines.[11] For the first case study, a life is hypothetically saved at ages 0 to 100, whereas in the second and third case studies, we replicate survival curves from previous studies. In the first case study, life tables for estimating life expectancy at all ages are used and combined with quality-of-life data from Gheorghe and colleagues.[26]

For the second case study, we replicated survival curves from a previously published cost-effectiveness study on oxaliplatin plus fluoropyrimidines versus fluoropyrimidines only as adjuvant treatment of stage 3 colon cancer,[27] wherein oxaliplatin showed an incremental QALY gain of 1.02 and 0.68 LYG, incremental costs of €9961, and a corresponding ICER of €9766. The sample consisted of patients previously diagnosed with stage 3 colon cancer who were randomized to either treatment or control groups. The median age of patients was 60 years. This study is then updated by including estimates of future medical costs, after excluding costs related to colon cancer, and including future nonmedical consumption.

For the third case study, we used the results from a clinical trial assessing survival of pembrolizumab monotherapy compared to platinum-based chemotherapy in a group of previously untreated patients with locally advanced or metastatic non–small-cell lung cancer.[28] The paper from which the survival curves are extracted does not perform a CEA, and therefore there are no "baseline" ICER or QALY gains. In this clinical trial, the median age at baseline was 64 years of age, and 71% of patients were male. This case study demonstrates how to use PAID when survival is short. We recommend using estimates of living 1 year longer when studies have a relatively short time-horizon (<5 years as rule of thumb), especially when survival between the new treatment and comparator are highly different in the first study-year. In that case, using decedent costs would create large differences in costs at baseline between the new treatment and the comparator for unrelated diseases. This is implausible because it implies a different past trajectory of costs for the same person before getting the treatment and conflicts with the definition of unrelated medical costs. Costs for living 1 year longer at a particular age, $c(a)$, can be calculated as follows:

$$c(a, g) = sc(a, g) + dc(a + 1, g) - dc(a, g), \quad (6)$$

where

- c = costs of living one year longer;
- a = age in years;
- g = gender.

Furthermore, although the approach discussed earlier assumes independence between the healthcare intervention and cost of nonmedical and unrelated medical consumption, we provide a framework allowing for a correlation between the intervention and unrelated medical costs—applied in the third case study. We show the impact of adjusting PAID estimates of unrelated medical costs for this correlation, which is relevant when the studied population is expected to have a different healthcare use for unrelated diseases than the average population. Estimates can be adjusted using the framework as displayed in Eq. (7), where per capita costs are shown as the product of disease prevalence and

Figure 1. (A and B) Average per capita medical costs and nonmedical consumption by age. (C and D) Medical costs, split into survivor and decedent costs by age.
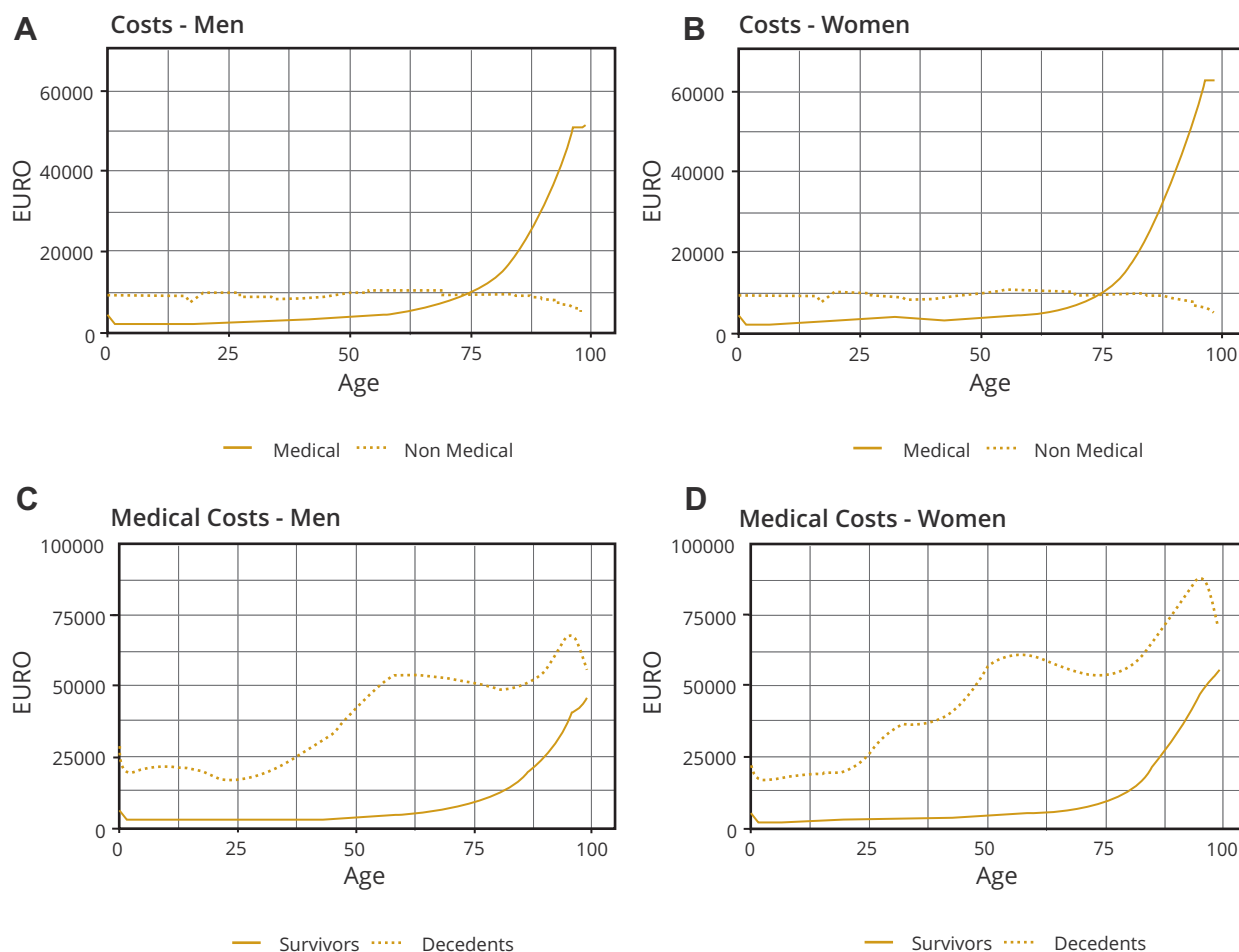
per patient costs:

$$sc(a)_i = p(i|a) \times sc(a|i)_i, \tag{7}$$

$$dc(a)_i = m(a|i) \times dc(a|i)_i,$$

where

- $p(i|a)$ = probability of disease i conditional on age a;
- $m(a|i)$ = mortality rate at age a conditional on having disease i;
- $sc(a|i)$ = survivor costs at age a conditional on having disease i;
- $dc(a|i)$ = decedent costs at age a conditional on having disease i.

Given the relationships displayed in Eq. (7), we adjusted unrelated costs to reflect higher prevalence and mortality for stroke among patients with lung cancer.[29] We adjusted the unrelated costs for stroke by extracting the costs for stroke separately, multiplying stroke costs with the relative risk of stroke—1.47—as estimated by Chen and colleagues[29] and adding these back to the sum of unrelated medical costs, as shown in the equations below.

$$sc(a) = \sum_{i \neq j} sc_i(a) + sc_j(a) \times \lambda, \tag{8}$$

$$dc(a) = \sum_{i \neq j} dc_i(a) + dc_j(a) \times \lambda,$$

where

- j = unrelated disease with higher costs (e.g. stroke);
- λ = multiplier.

To demonstrate how to use PAID with survival data on an individual level, we fitted 2 parametric survival models, assuming a Weibull distribution to overall survival results presented in the Kaplan–Meier plot[28] from which we randomly drew individual survival times.

Results

Unrelated Medical Costs and Nonmedical Costs

Panels A and B in Figure 1 show how average healthcare expenditures rise sharply after age 75, whereas per capita nonmedical consumption shows a less strong age pattern but decreases at old age and peaks at middle age (identical numbers

Table 1. The impact of including future costs on the ICER for case studies 2 and 3.

	Case study 2 (€ per QALY*)	Case study 3 (€ per life-year)	
		Unadjusted	Adjusted for stroke
Original ICER	9580	N/A	N/A
Impact including unrelated medical costs on ICER	3761 (13 341)	5546	5619
Impact including nonmedical costs on ICER	5440 (15 020)	9126	9126
Total impact on ICER	9201 (18 781)	14 672	14 745

*Total ICER shown in brackets.

for males and females because estimates are not sex specific). These graphs show that up until around age 75, people have higher nonmedical costs than healthcare consumption, whereas afterward, healthcare exceeds nonmedical consumption.

Age-specific per capita medical costs for survivors and decedents are presented in graphs C and D, showing comparable patterns in spending by sex, although women's expenditures are higher, especially at older ages. These graphs show that differences between survivor and decedent costs are highest in the first year of life and between 50 and 75 years and become smaller at the highest ages. This can largely be attributed to causes of death and related periods of illness before dying at different ages. In the first year of life, death often follows a period with high use of medical care. The same holds for middle age. At the highest ages, survivors and decedents typically incur higher healthcare expenditures, narrowing the difference in costs.

Case Studies

For the first case study, we estimated the impact of including future costs on the ICER when death is prevented at a certain age (see Fig. 2). It shows that the older people get, the more expensive it is to save them.

The results of the second and third case study are summarized in Table 1. Figures 3 and 4 show differences in costs and survival over time for the two case studies. Including future unrelated medical costs in case study 2 leads to an increase of €3761 in the ICER; including nonmedical consumption adds another €5440 to the ICER.

For the third case study, we estimated a mean survival of 25.1 months for the intervention group (pembrolizumab) and 15.3 months for the comparator group (chemotherapy). Figure 4 (bottom) shows difference in survival. As stated above, in this

Figure 2. Case study 1. The hypothetical impact of including future unrelated medical costs and future nonmedical consumption (NMC) on the ICER when death is prevented (for free) at a certain age.
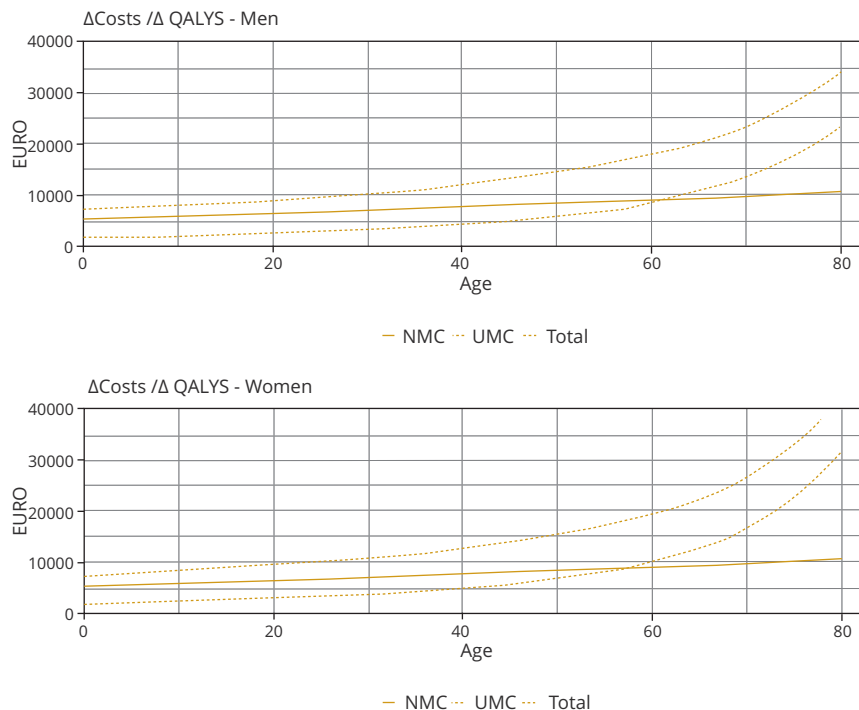
Figure 3. Case study 2. The added costs for including unrelated consumption and nonmedical consumption (top), and the difference in survival between intervention and comparator group (bottom).
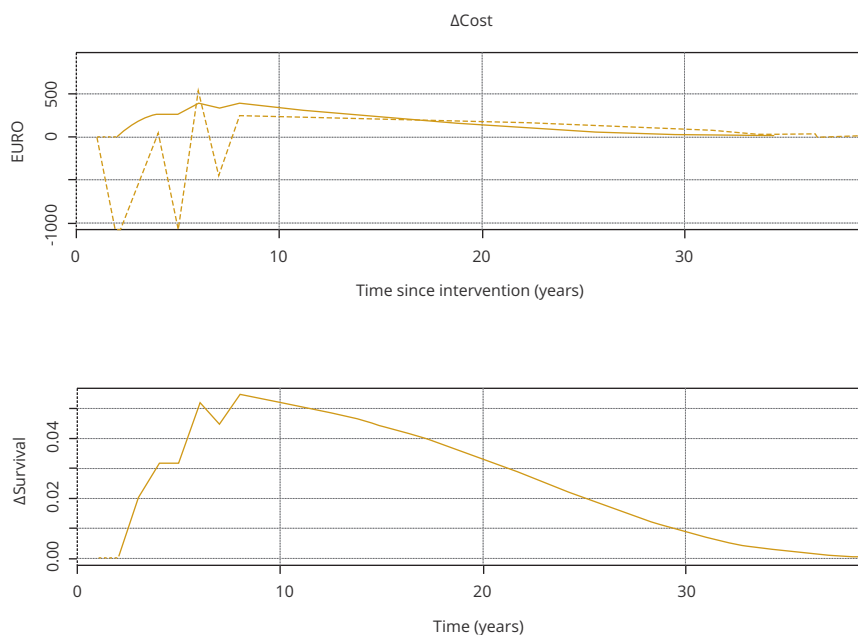
study no baseline ICERs and QALYs were available. Therefore, only the impact of inclusion on the ICER can be estimated, and impact is shown as cost per LYG. We estimated a discounted LYG of 0.77 for the intervention group compared to the comparator. Inclusion of future unrelated medical costs increased the ICER by €5546, or €5619 after adjustments for stroke incidence. Including future nonmedical consumption further increased the ICER to €9126. Note here that the impact on the ICER will be different when QALYs instead of life-years are used. If the LYG will be in less than perfect health, this will increase the impact on the ICER.

Figure 4. Case study 3. The additional costs by time for the lung cancer intervention (top left), and the additional costs by time when adjusted for increased stroke risk (top right). Difference in survival between intervention and comparator group (bottom).
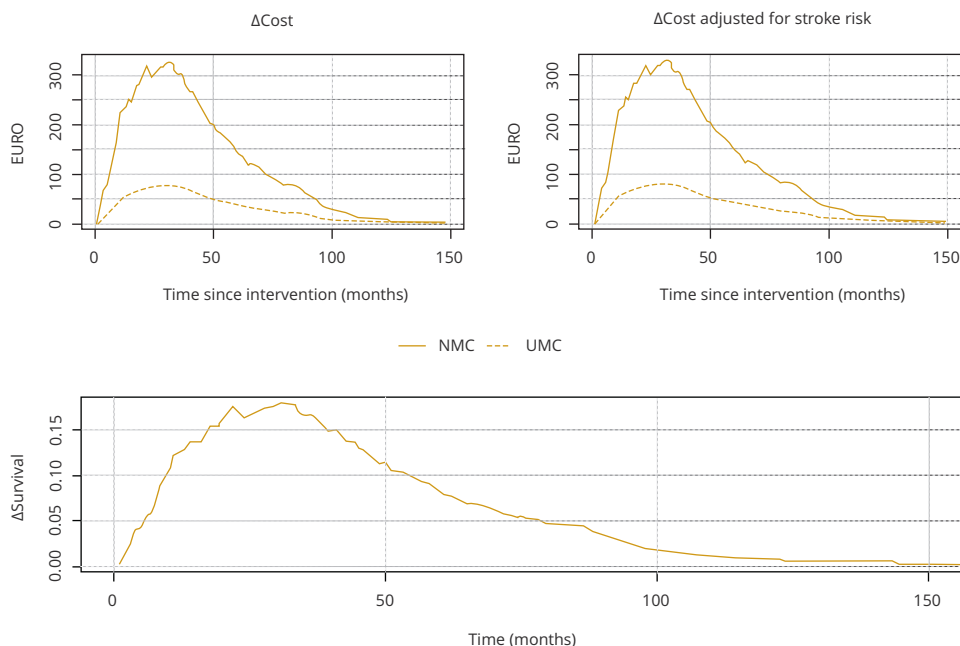
Discussion and Conclusion

In 2011, a practical tool to include future unrelated medical costs in a standardized manner was introduced.[13] In this paper, we updated the tool with the most recent data on medical costs and included estimates for future nonmedical consumption. Recent COI data were combined with mortality data and decedent-survivor cost ratios to provide disease-specific estimates of medical expenditures per capita in survivors and decedents. Related costs of an intervention are then excluded from total medical expenditure. Nonmedical consumption was estimated taking into account household economies of scale. Using case studies, this paper further demonstrated how to use the tool in practice.

The first case study refers to the situation of saving a life at a given age, with no intervention costs. It shows that the impact of including future costs becomes larger at higher ages, mainly owing to rising healthcare expenditures with age, whereas in comparison to future medical costs, the impact of including nonmedical consumption remains relatively stable over time. The consumption curve (Fig. 1) follows a U-shape as seen in previous literature[22,36]; however, when dividing these costs by QALY changes, the curve flattens considerably. Another factor affecting the relative impact of including future costs at younger ages versus older ages is that the more expensive (older) years are discounted more highly when lives are saved at younger ages. Furthermore, the impact of including future nonmedical consumption is larger than including future unrelated medical costs until approximately the age of 60. This may seem surprising when looking at Figure 1, which shows that per capita nonmedical consumption is larger than medical consumption until approximately the age of 75. When estimating the impact of including future unrelated medical costs on saving a life at different ages, however, we consider time to death. As a result, high medical spending in the last year is postponed, and additional medical spending is less than suggested by Figure 1.

In the second case study, a published evaluation comparing interventions for colon cancer is replicated. Including future unrelated medical costs increases the ICER by almost 40%, and when all future costs are included, the ICER more than doubles. In The Netherlands, a cost-effectiveness threshold ranging from €20 000 up to €80 000 per QALY gained is applied, where the height depends on the principle of proportional shortfall.[30,31] Using the iMTA Disease Burden Calculator,[32] we calculated a proportional shortfall for this case study of 0.37, which implies that the relevant threshold in this case study is €20 000.[31] Including future costs in this study could thus make this intervention not cost-effective because it pushes the ICER near the threshold. It is important to note that an intervention being not cost-effective is not an undesirable outcome, but simply the result of correctly estimating the change in costs for an intervention.

In the third case study, we demonstrate how to adjust for short time horizons and show that PAID estimates can easily be applied to several forms of models. Furthermore, we show how to adjust estimates when costs for unrelated diseases in the studied population are suspected to differ from the costs for the general population. This is adjusted for here by using the increased risk of stroke among patients with lung cancer. In this case, the difference between future unrelated medical costs, whether adjusted or unadjusted, is relatively small. If the costs of a disease for which the risk is increased were large and the additional risk substantial, the impact of such adjustment would be larger, as shown by Manns et al in their paper on end-stage renal disease care.[33]

An important limitation to the study is that there are no more recently estimated decedent-survivor cost ratios than those used here. Although more recent estimates of mean overall spending in the last year of life compared to other years show comparable numbers,[34] more detailed estimates may show different patterns. An update of these ratios would be useful for future research. A further limitation with regard to decedent–survivor cost ratios is that we did not have estimates for all providers, and disease-specific estimates for 3 providers were derived by combining hospital estimates with provider-specific sector estimates. In a similar vein, the classification of costs among providers was different for 2017 COI data, and therefore fewer costs could be adjusted using these ratios. It is also worth noting that data from the household survey are relatively old; although data are adjusted to 2017 prices, changes in spending patterns by age may not be captured. Furthermore, we estimated nonmedical consumption by age and assumed no correlation between nonmedical consumption and disease. Although there is relatively little literature covering this topic, there are some findings that suggest such a correlation. For example, it may be that medical consumption crowds out nonmedical consumption for the severely ill, although this is unlikely in the Dutch context, given that almost all healthcare spending is publicly financed.[35] The findings that nonmedical consumption decreases from a certain age,[22,36,37] however, may imply that as health decreases (as it does at older ages) so does nonmedical consumption. Further research in this area is needed.

Finally, we do not address uncertainty in this paper. Uncertainty could stem from the 2 key elements of our estimates: survival and costs. The original costs in this case are averages provided by Statistics Netherlands and are therefore with little surrounding uncertainty. However, there are still sources of uncertainty, such as decedent-survivor cost ratios; the larger the time to death effect (larger ratios), the smaller the impact of future costs on the ICER.[5]

In general, including future costs may have a systematic effect on reimbursement decisions because the "upward" effect on the ICER changes differently by population and intervention. As the cost of extending life increases with age, this implies that the age at which an intervention is given will be of increased importance for the cost-effectiveness of an intervention. Another parameter that affects the magnitude of the impact of including future costs, and thus decisions, is the ratio of life-years gained to QALYs gained for a particular intervention. It has been shown that the larger this ratio, the larger the impact of including future costs.[5]

In this paper, no specific attention is paid to future related medical costs and future productivity because these are typically already included in economic evaluations, and extensive guidance on how to estimate and include these costs is already available in The Netherlands.[38] When looking at the total impact of including future costs, production gained at working ages would presumably lead to those years being the least costly. This would, however, also depend on how productivity is measured. In The Netherlands, these costs are typically quantified using the friction costs method and thus are limited to the friction period. Using the human capital approach or including informal and household production would affect the impact of inclusion at different ages. The latter methods would imply higher negative costs (more productivity gains from living longer) and thereby lower ICERs. Another issue worth mentioning is that, although there is agreement that including future unrelated medical costs would improve the internal consistency of the ICER, implying that costs are included when related benefits are included, how much QALYs capture the benefits from nonmedical consumption (and also production) is currently unclear.[6] Furthermore, it is also unclear to what extent thresholds to which ICERs are compared include

these benefits.[3] The impact of including future nonmedical consumption and the comparison with existing thresholds should thus be interpreted with caution.

To conclude, this article provides an update and extension of PAID and demonstrates through case studies the application and impact of including future costs in economic evaluations. Updated ICERs show that including future costs, even just unrelated medical costs, can have a substantial effect on the ICER, which could affect decision makers' choices. For future research, it would be interesting to see the estimates used in a variety of economic evaluations.

Supplementary Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2020.07.004.

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