Standardizing the inclusion of indirect medical costs in economic evaluations

Running title: Standardizing indirect medical costs

Pieter HM van Baal[1,2*], Albert Wong[1,4], 'Laurentius CJ Slobbe[3], Johan J Polder[3,4], Werner BF Brouwer[2], G Ardine de Wit[5,6]

[1]National Institute for Public Health and the Environment (RIVM)

Expertise Centre for Methodology and Information Services

[2]Erasmus University Rotterdam

Institute of Health Policy & Management and Institute for Medical Technology Assessment

[3]National Institute for Public Health and the Environment, Centre for Public Health Forecasting, Bilthoven, the Netherlands

[4]Tilburg University, Department Tranzo

[5]National Institute for Public Health and the Environment, Centre for Prevention and Health Services Research, Bilthoven, the Netherlands

[6] Julius Center for Health Sciences and Primary Care, University Medical Center, Utrecht, the Netherlands

*Corresponding author: Pieter van Baal

e-mail: vanbaal@bmg.eur.nl

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Abstract

A shortcoming of many economic evaluations is that they do not include all medical costs in life years gained (also termed indirect medical costs). One of the reasons for this is the existence of practical difficulties in the estimation of these costs. While some methods have been proposed to estimate indirect medical costs in a standardised manner, these methods fail to take into account that not all costs in life years gained can be estimated in a standardised manner. Costs in life years gained caused by diseases related to the intervention are difficult to estimate in a standardised manner and should always be explicitly modelled. However, costs of all other (unrelated) diseases in life years gained can be estimated in a standardised manner.

In this paper we propose a conceptual model how to estimate costs of unrelated diseases in life years gained in a standardised manner. Furthermore, we describe how we estimated the parameters of this conceptual model using various data sources and studies conducted in the Netherlands. Results of the estimates are embedded in a software package called *PAID 1.0: Practical Application to Include future Disease Costs*. *PAID 1.0* is available as a Microsoft Excel tool and enables researchers to "switch off" those disease categories that were already included in their own analysis and to estimate future health care costs of all other diseases for incorporation in their economic evaluations.

We assumed that total health care expenditures can be explained by age, sex and time to death while the relation between costs and these three variables differs per disease. To estimate values for age and gender per capita health expenditures per disease and health care provider stratified by time to death we used Dutch Costs of Illness (COI) data for the year 2005 as a backbone. The COI data consisted of age and sex specific per capita health expenditure uniquely attributed to 107 disease categories and 8 categories of healthcare providers. Since the Dutch COI figures do not distinguish between costs of those who die at a certain age (decedents) and those who survive that age (survivors), we decomposed average per capita expenditures into a part that is attributable to decedents and survivors using other data sources.

Key words: economic evaluation, medical costs in life years gained, modeling, cost effectiveness analysis

Introduction

Life saving (or death postponing) interventions induce medical consumption in so-called life years gained. This medical consumption in life years gained has also been labeled as 'indirect' medical costs and in the theoretical economic literature a further distinction has been made between related and unrelated medical costs in life years gained (1). Subsequently, there has been discussion as to whether all of this medical consumption in life years gained (related and unrelated) should be included in economic evaluations (1-8). In practice, as prescribed in (pharmacoeconomic) guidelines (e.g. (9,10)), many economic evaluations do take into account those costs in life years gained that are related to the intervention under evaluation, while ignoring other medical costs altogether. However, the costs that are termed 'related' and therefore included in practice do not necessarily adhere to the definitions of 'related' and 'unrelated' employed in the theoretical literature (11). In the practice of economic evaluations, related costs are usually defined on the level of diseases and only the costs occurring in life-years gained of diseases at which the intervention is targeted are taken into account. For instance, in an economic evaluation of statins for the prevention of cardiovascular disease, usually all costs of future cardiovascular disease are included and costs of all other diseases in life-years gained are excluded. In an evaluation of a colorectal cancer screening program, only the future (averted) costs of colorectal cancer are included. However, if these interventions result in gains in life expectancy, it is likely that costs for other diseases, besides the diseases at which the intervention is targeted, will occur, so that the cost-effectiveness might change (4,12-15). Theoretically, the distinction between related and unrelated has nothing to do with diseases and costs are only unrelated if they, conditional on reaching a certain age, are independent of the intervention (1). In the above-mentioned examples on cardiovascular disease and colorectal cancer, some of these disease-specific costs may be theoretically called related while others are not. Furthermore, costs of other diseases, which are not included in the economic evaluation, may also be partly related.

Besides the lack of consensus regarding the theoretical appropriateness of including future medical costs, we think that an important reason why many guidelines still do not advocate the inclusion of all future medical costs is the lack of practical tools to facilitate their inclusion. Since economic evaluations of life saving (preventive and curative) interventions are conducted in a variety of settings, including those of new (and often expensive) drugs, a standardised way to account for medical costs in life years gained is of great importance. However, the question then becomes: how can we standardize the inclusion of indirect medical costs? The simplest way to include indirect medical costs in a standardized way is to multiply age-specific per

capita medical consumption with the life years gained in an economic evaluation. For example, if an intervention causes a person to die at his 80th birthday instead of his 79th the indirect medical costs are then estimated by simply taking the average per capita health expenditures of an 80 year old person. However, adding age-specific average per capita health consumption has been shown to result in biased estimates of the apparent costs of ageing. Zweifel and colleagues (16) were the first to conclude, using longitudinal Swiss sick fund data, that health care expenditures depend on time to death, rather than on time since birth (age). Higher average health care cost at a higher age are caused mainly by the fact that many elderly people die, with associated high health care utilization in the period just before dying. The role of proximity to death (also known as the 'red-herring' hypothesis) has been confirmed in other studies (17-20). Further research revealed that the strength of the proximity to death effect differed starkly between health care providers (20,21) and between different diseases (22). Wong et al. (22) found that the time to death effect was strongest for the most lethal diseases such as lung cancer, septicaemia, heart and renal failure. The diseases where the time to death effect could not be found had a non-life threatening nature, and were either chronic or only had planned non-urgent inpatient treatment. Gandjour & Lauterbach were the first to link the 'red herring' literature to the practice of economic evaluations (23). By modelling total per capita health expenditures conditional on age and proximity to death they demonstrated that cost-effectiveness analyses overstate the incremental cost-effectiveness ratio (ICER) of preventive interventions if they do not explicitly model the high costs of the last year of life, as these costs are only postponed by prevention (23). Although the paper of Gandjour & Lauterbach showed that adding age-specific per capita costs without accounting for the high expenditures near death results in overestimates of medical costs in life years gained, their approach also has its limitations since it cannot be combined with most economic evaluations in practice. This holds because of the fact that the costs of related diseases are already included in most economic evaluations, and therefore it is incorrect to add *all* medical costs in life years gained to the ICER, even when corrected for the costs in the last year of life (11). Clearly, only the costs of all other (unrelated) diseases should be included. One solution to this problem may be *not* to model the costs of related diseases in case of life saving interventions. Then, the approach proposed by Gandjour &Lauterbach could be considered appropriate. However, simply adding per capita costs stratified by age and proximity to death ignores cost differences between diseases as well as the fact that some of these per capita costs will indeed importantly change as a result of the intervention. A successful weight loss intervention will change the per capita expenditures on diabetes and cardiovascular disease. However, it will probably not alter the expenditures on for instance dementia. A colorectal cancer screening prevention will probably influence future spending on colorectal cancer (and possibly also other types of cancer) but will not influence future spending on all other diseases. Therefore, while it is impossible to

standardize the inclusion of indirect medical costs for all diseases and for all interventions it might be possible to standardize inclusion of the indirect medical costs of *all other* diseases besides the diseases at which the intervention is targeted. This would make ICER estimates more precise as well as improve the comparability of results of different economic evaluations.

In this paper, we describe a methodology which can be used to include costs of unrelated diseases in gained life years in a standardized way in economic evaluations. This methodology has been implemented in a toolkit designed to facilitate inclusion of indirect medical costs in economic evaluations in practice in the Netherlands: the *Practical Application to Include future Disease costs (PAID 1.0* ***hyperlink to PAID 1.0.xls***). This tool enables researchers to incorporate indirect medical costs in their economic evaluation in a tailor-made fashion. Depending on the diseases for which costs are already included in the basic economic evaluation, future costs of all other diseases can be added using PAID 1.0, in combination with the survivor curves from the basic economic evaluation. This paper highlights the methodology underlying PAID 1.0. In the following section, we will explain the conceptual model and the data sources and methodology used to estimate the parameters of the conceptual model behind PAID 1.0. In the results section, we will present the estimated model parameters embedded in PAID 1.0.

Methodology

Suppose, someone conducts an economic evaluation of a stroke care intervention resulting in a substantial increase in life expectancy. He or she has already estimated the costs of stroke in this study as they are expected to change due to the intervention. An important question in that context obviously is *how* the costs of all other diseases should then be estimated?

Conceptual framework

If the goal is to develop a general framework to estimate the costs of all diseases not directly related to an intervention it is convenient to start by breaking total health care expenditures down by diseases. Conceptually, lifetime health care costs are then the sum of disease-specific expenditures one incurs throughout his or her life. Since disease-specific expenditures are strongly determined by age and time to death (22) individual lifetime health care costs can be estimated using the following formula:

$$lhc(g) = \sum_{a}^{n-1} \sum_{i} sc_i(a,g) + \sum_{i} dc_i(n,g) \qquad (1)$$

with

lhc(g) *lifetime health care costs for an individual gender g*

a *age in years*

n *age at death*

dc *decedents costs: per capita health care costs in the last year of life*

sc *survivor costs: per capita health care costs in all other years*

i *index for diseases*

Equation (1) simply states that individual health care expenditures are the sum of per capita disease-specific expenditures in the last year of life and 'other' years, and can be thought of as lifetime health expenditures if current health expenditure pattern would remain constant. Now suppose an intervention that increases life expectancy influences the health expenditures for *Z*, a set of related diseases. The costs of all other diseases can then be simply estimated by summing over the remaining disease categories:

$$\sum_{a}^{n-1}\sum_{i\notin Z} sc_i\,(a,g) + \sum_{i\notin Z} dc_i\,(n,g) \qquad (2)$$

with

Z *the set of related diseases*

By first breaking down lifetime health care expenditures into disease components it is simple to exclude costs of certain diseases to avoid double counting of costs and to model the costs of those diseases of which treatment patterns are expected to change separately.

The toolkit PAID 1.0 contains estimates of age- and gender specific costs for a range of diseases stratified by last year of life and other years as in equation (1). *PAID 1.0* is available as a Microsoft Excel tool **(hyperlink to PAID 1.0.xls)** and enables researchers to select the diseases whose costs are already modelled and therefore should be excluded to calculate per capita costs for all other diseases as in equation (2). The costs of all other disease figures can then be combined with the survivor curves of the intervention and comparator under study to estimate differences in costs of unrelated diseases. The number of survivors in the scenarios can be multiplied with survivor costs of unrelated diseases estimated by PAID 1.0 and the number of deaths in both scenarios can be multiplied by the decedent costs of unrelated diseases estimated by PAID 1.0 (see PAID 1.0 user manual for more details on how to use PAID 1.0 **insert hyperlink to PAID 1.0 user manual.pdf**).

Estimating the input of PAID 1.0: disease-specific per capita health expenditures stratified by last year of life and 'other years'

To produce consistent estimates of disease-specific per capita costs for decedents (costs per capita in the last year of life) and survivors (costs per capita in all other years) as in equation (1) we combined information from several data sources. As backbone we used Cost of Illness (COI) data for the Netherlands in 2005 (24). In that study the 2005 total direct health care costs in different health care settings in the Netherlands were uniquely attributed to 107 disease categories (including rest categories as 'not disease related') and 8 categories of health care providers, specified by gender and 21 age classes. Appendix A displays tables of the health providers (Table A1) and diseases (Table A2) distinguished in the 2005 COI study. The 2005 COI study was a sequel to earlier 1999 and 2003 Dutch COI studies (25-27) and COI estimates were made using the health care costs definitions of the System of Health Accounts (SHA) (28) for reasons of international comparability. To translate the age categories from the COI data into age-year specific per capita health expenditures we interpolated the 21 age classes using cubic splines.

Since the Dutch COI figures do not distinguish between costs of survivors and decedents, the most important step in the estimation of equation (1) was the decomposition of average per capita expenditure into a part that is attributable to those who die at a certain age and those who survive that age. This decomposition was accomplished by assuming that average costs in a single year at a particular age is the weighted average of those surviving that year and those dying that particular year (Note that all input parameters and model calculations are age and gender specific, but that for notational purposes age and gender indices were omitted):

$$ac_i = (1-m) * sc_i + m * dc_i \qquad (3)$$

with

ac_i *average per capita health care expenditure for disease i*

m *mortality rate*

Per capita health care expenditures for survivors and decedents for a particular disease can then be calculated if we know the mortality rate and the ratio (r_i) between health care costs for those dying at a particular age and those surviving that age:

$$
\begin{aligned}
dc_i &= r_i * sc_i \\
ac_i &= sc_i + (r_i - 1) * m * sc_i \\
sc_i &= \frac{ac_{i,j}}{1 + (r_i - 1) * m}
\end{aligned}
\tag{4}
$$

To divide the average per capita costs per disease according to the above specified relations we used additional data sources. Mortality rates for 2005 from Statistics Netherlands were employed (29). Given mortality rates, the only additional input needed is disease-specific cost ratios of decedents and survivors. However, these were only available for hospital expenditures (22). Since, the effect of proximity to death on health care expenditures differs strongly per health care provider, we could not use these ratios directly to decompose all disease-specific per capita health expenditure. Therefore, we used these ratios only to decompose hospital expenditures:

$$
sc_{i,j=1} = \frac{ac_{i,j=1}}{1 + (r_{i,j=1} - 1) * m} \tag{5}
$$

with index j denoting the health care provider. j=1 refers to the hospital sector.

In Wong et al (22) disease-specific ratios were estimated for 75 diseases categorized using the International Shortlist for Hospital Morbidity Tabulation (ISHMT) format which is highly compatible with the COI categories, resulting in 71 matches of 107 disease categories which amounts to 60% of total hospital expenditure in 2005 (Table A2 in Appendix A displays the matches of COI categories to the ISHMT categories). For the non-disease related expenditure (11.7 % of total expenditure), we assumed the ratios to equal one and thus, conditional on age and gender, equal costs for survivors and decedents. For the remaining disease categories we used the age- and sex-specific mode of the 71 matched disease ratios. The mode was estimated by kernel density estimates using average costs per disease as weights.

For other health care providers besides hospitals no empirically estimated disease-specific ratios were available. However, for some major health providers (providers of ambulatory health care, drugs and appliances, nursing and residential care) we had access to decedent/survivor ratios for total expenditure in 1999 estimated in previous research using data from insurance claims (17). To estimate disease-specific ratios for these three health care providers (ambulatory health care, drugs and appliances, nursing and residential care), we exponentiated all disease-specific hospital ratios by a constant:

$$r_{i,j>1} = r_{i,j=1}^{x_{j>1}} \quad (6)$$

with

j *index denoting the health care provider; j=1 implies hospital care.*

$r_{i,j>1}$ *ratio (costs decedents) / (costs survivors) for disease-specific health expenditure of disease i for health care provider j other than hospital care*

$x_{j>1}$ *scaling constant for health care provider j other than hospital care*

Thus, if for example the disease-specific hospital ratios for diseases *a*, *b* and *c* equal 4, 9 and 16, and the scaling factor *x* for long-term care equals 0.5, the disease-specific ratios for this health care provider would equal 2, 3 and 4. Equation (6) implies that for each health care provider the age- and gender-specific distributions of ratios [(disease costs decedents)/(disease costs survivors)] are proportional on the log scale. Suppose we use equation (6) for a given baseline disease (denoted by *i*=1), then this can be rewritten as:

$$r_{i=1,j>1} = r_{i=1,j=1}^{x_{j>1}} \Rightarrow \log(r_{i=1,j>1}) = x_{j>1}\log(r_{i=1,j=1}) \Rightarrow x_{j>1} = \frac{\log(r_{i=1,j>1})}{\log(r_{i=1,j=1})}$$

Since we assume $x_{j>1}$ to be equal for all diseases, we can similarly state that:

$$x_{j>1} = \frac{\log(r_{i>1,j>1})}{\log(r_{i>1,j=1})}$$

Thus,

$$x_{j>1} = \frac{\log(r_{i=1,j>1})}{\log(r_{i=1,j=1})} = \frac{\log(r_{i>1,j>1})}{\log(r_{i>1,j=1})} \quad \textit{for all values of } i \quad (7)$$

Equation (7) describes how the effect of proximity to death on health care expenditures differs between health care sectors. A value of *x* higher than one implies that for that health provider the relation between time to death and health care expenditures is stronger for all diseases than in the hospital sector. A value for *x* lower than one implies that the relation is less strong. An alternative way of scaling the ratios would be to multiply all hospital ratios by a constant. However, since some ratios were smaller than one, we chose to scale the hospital ratios on a log scale. This way, we ensured that the relation between time to death and health care expenditure did not change from negative (ratio smaller than one) to positive (ratio greater than one) or vice versa. Equation (7) can be rearranged to describe how the proximity to death relationship differs between diseases:

$$\frac{\log(r_{i>1,j>1})}{\log(r_{i=1,j>1})} = \frac{\log(r_{i>1,j=1})}{\log(r_{i=1,j=1})} \quad \textit{for all values of } i \quad (8)$$

In the example mentioned above, it is easy to check that log(16)/log(4) = log(4)/log(2)=2.

To ensure that the sum of disease costs of decedents and survivors match those in such a way that the ratio for total expenditures in that health care sector equals the empirically estimated ratios (17), we exponentiated all disease-specific hospital ratios by the constant *x* such that the following assumption is not violated:

$$r_{tot,j>1} = \frac{\sum_i dc_{i,j>1}}{\sum_i sc_{i,j>1}} = \frac{\sum_i r_{i,j=1}^{x} * sc_{i,j>1}}{\sum_i sc_{i,j>1}} \quad (9)$$

Combining equation (9) with equation (5) we can write total survivor expenditures for health care providers other than hospital care calculated using the estimated ratio for total expenditures as function of mortality rates, average costs per disease for that health care provider, disease-specific hospital ratios and the scaling constant :

$$sc_{tot,j>1} = \frac{\sum_i ac_{i,j>1}}{1+(r_{tot,j>1}-1)*m}$$

$$sc_{i,j>1} = \frac{ac_{i,j>1}}{1+(r_{i,j=1}^{x_{j>1}}-1)*m} \quad (10)$$

$$sc_{tot,j>1} = \sum_i sc_{i,j>1} = \sum_i \frac{ac_{i,j>1}}{1+(r_{i,j=1}^{x_{j>1}}-1)*m}$$

Equation (10) now contains only one unknown variable: the scaling factor *x*. Age-, gender- and health care provider-specific values for *x* were found by numerically minimizing the error, as defined by the distance between total survivor costs calculated using the empirically estimated ratios for total expenditures for these three health care providers (ambulatory health care, drugs and appliances, nursing and residential care) and the total survivor costs calculated as the sum of the disease-specific survivors costs:

$$\left(sc_{tot,j>1} - \sum_i \frac{ac_{i,j>1}}{1+(r_{i,j=1}^{x}-1)*m} \right)^2 \quad (11)$$

For the remaining provider categories (mainly being overhead type health care costs, see Table A1 in the Appendix) it is assumed that costs are equal for decedents and survivors and that costs depend solely on age and gender.

Results

To show the effect of the decomposition of average per capita health expenditures by costs related to those dying and those surviving, Figure 1 displays average per capita costs in the last year of life and other years specified by gender and age, stacked for the different health care providers (in this graph we have omitted costs for all other health care providers as these depend on age solely and not on time to death). The first two panels display the average per capita health expenditure (panel A for men and panel B for women) resulting from interpolating the COI study (summed over all 107 disease categories). The four panels thereafter, display the estimates summed over all 107 disease categories that are the result of the decomposition of the COI data into costs of decedents and costs of survivors. Please note that the Y-axis of different panels have different scales. From Figure 1 it can be concluded that costs in the last year of life are very high at a very young age and decrease sharply thereafter. The major cause for this decrease is the fact that mortality in the first year of life is often preceded by a period of intensive hospital care, whereas mortality among children, youngsters and especially young adults is mostly caused by (traffic) accidents. At middle age, costs in the last year of life increase again. Total costs of survivors increase exponentially at old age mainly due to frailty, disability, co-morbidity and subsequent needs for nursing and residential care. Survivor costs in hospital, for GP's and for medicines do not depend strongly on age, so the age related increase in total health care expenditure is produced mainly in the long term care sector. At older ages, the share in long term care costs increases sharply in the costs of survivors. Interestingly, absolute cost levels are somewhat higher in women than in men, especially at a higher age. This may be explained to a certain extent by the fact that the nursing and residential care population mainly consists of women.

Table 1 displays some estimates of some disease-specific ratios for different health care providers for men aged 75. From this table it can be seen that the relation between time to death and health care expenditures is strongest for the hospital care providers. As a result, the scaling factors estimated needed to calculate disease-specific decedent survivor ratios are all below one. Furthermore, the disease-specific ratio is highest for lung cancer and lowest for depression.

Table 2 displays estimates of lifetime health expenditure broken down by health care provider. Lifetime health care expenditure was estimated by calculating the expected value of equation (1) using mortality rates for 2005 summed over all diseases. To show the importance of including time to death, we compared the percentage of health care expenditure consumed in the last year of life with a naïve estimate in which we did not make a distinction between costs in the last year of life and other years as derived from the original COI data. Table 2 makes clear that the share of hospital costs is much higher in the last year of life than in other years. However, also for long term care a large share of lifetime health care expenditure is realized in the last year of life (28% for men and 25% for women). It should be noted that although this seems very large, the share that is expected to be spent on long term care in the last year of life would also be substantial if costs in the last year of life (conditional on age) are the same as in other years (10% for men and 11% for women). Seen this way, it can be concluded that the effect of including proximity to death effect is most outspoken for hospital expenditures.

To zoom in on the differences in health care expenditure patterns between diseases, Figure 2 displays a similar graph as Figure 1, but now for two different disease categories instead of total expenditures: neoplasms and diseases of the circulatory system. Please note that Y-axes have different scales.

Figure 2 clearly illustrates the differences between disease categories. Per capita expenditure for neoplasms is on average lower than for circulatory diseases. However, in the last year of life, per capita health expenditure is much higher for neoplasms. More specifically, the average health care expenditure for neoplasms is largely determined by hospital expenditure in the last year of life.

Table 3 presents estimates of lifetime health care costs broken down into costs in the last year of life and other years for different disease categories. Table 3 demonstrates for example that cancer is a major cost component in the last year of life, but hardly in other years. The same goes for diseases of the blood and blood-forming organs.

Discussion and conclusions

Since economic evaluations of life saving (preventive) interventions are conducted in a variety of settings, including those of new (and often expensive) drugs, a standardised way to account for indirect medical costs is of great importance. While some methods have been proposed to estimate medical costs in life years gained (23), these methods do not take into account that in most economic evaluations a part of these indirect medical costs have already been covered,

namely those costs related to the disease or intervention that was evaluated. These future costs that are expected to change as a result of an intervention should always be explicitly modelled and, hence, this is common practice in the majority of economic evaluations. Subsequently, simply adding per capita health expenditures stratified by age and proximity to death will result in double counting of the costs of related diseases (11). In this paper, we have proposed a methodology to estimate the costs of all other diseases in life years gained in a standardised manner that avoids this double counting. Starting from the framework developed by Gandjour & Lauterbach (23) we presented a methodology to adjust per capita health expenditure stratified by age and proximity to death for the costs of the diseases already included in the main economic evaluation. In this conceptual model it is assumed that total health care expenditures can be explained by age, sex and time to death while the relation between costs and these three variables differs per disease. We presented estimates of our conceptual model which are embedded in a toolkit called PAID 1.0, tailored for economic evaluations in the Netherlands. Disease-specific average per capita expenditures from the Dutch Costs of Illness 2005 study were decomposed into a part that is attributable to those who die at a certain age and those who survive that age. To accomplish this we used estimates of ratios of disease-specific (hospital expenditures in the last year of life)/(hospital expenditures in other years) and ratios of decedent and survivors costs of total expenditures for other health care providers than hospitals. Our results on the effect of the last year of life with respect to total health expenditures calculated as the sum of disease-specific health expenditures for all health care providers are in line with previous research conducted in the Netherlands (11).

In our methodology we accounted for the fact that the relation between age, gender, and proximity to death per capita costs differs between diseases (22). This allows the relation between time to death and health care costs to be altered if the costs of related diseases are excluded (11). Consequently, for our methodology it is pivotal to know for each disease what the role of age and proximity to death on disease-specific per capita health expenditure is. Our conceptual model is similar to the concept of ‘other cause’/’background’ mortality which is often used in simulation models to decompose total mortality rates into a part related to the intervention and a part unrelated to the intervention. To decompose average per capita health expenditures into costs in the last year of life and all other years we had to make several assumptions. Most importantly, we assumed that the disease-specific ratios estimated in Wong et al. (22), based on 60% of hospital expenditures, could be generalized to total hospital expenditures and that the disease-specific ratios could be used to decompose disease-specific costs in some other health care providers under some constraints. Furthermore, the validity of PAID 1.0 crucially depends on the validity of the COI study and the allocation of the health expenditures to disease categories in that study. Another limitation is that we dichotomized

proximity to death into two categories. A next version of PAID could be improved by stratifying into more periods. This latter becomes more important if we consider the timing of health expenditures and the role of discounting therein. We used total health care expenditure in the Netherlands from 2005 as a starting point. This implies, that age-specific cross-sectional data is interpreted in a longitudinal fashion, as is done when constructing life tables and also in many Markov models. The implicit assumption is that current observed patterns of health expenditures remain constant. Of course, the longer the period that is modeled, the more problematic this assumption becomes. We do not claim that the parameters included in our conceptual model are the only ones that are needed to estimate indirect medical costs. Technological progress, innovation, changes in morbidity patterns, but also developments in the labor market and institutional changes may have an impact on future health care costs, but have not been included. Although we recognize these limitations, we are convinced that it is better to provide an estimate using all current, albeit imperfect, knowledge than no estimate at all. While the former estimate may be imprecise, the latter is surely wrong.

In economic evaluations, modelling techniques are applied frequently to estimate the effects of life prolonging interventions on health and health care costs. Usually, in these models, an intermediate effect such as blood pressure, newly detected cases through screening, or short-term survival (as estimated in using observational data, an RCT or meta analyses) is connected to causally related events (most importantly: death) that could not be observed within the trial period of the intervention because the follow up period is too short. Thus, models are used to reach beyond the time horizon of trials. As a result, costs and effects beyond the observed period have to be estimated from other data sources. In cost-effectiveness studies that capture both health effects and costs of related diseases during added life years, PAID 1.0 allows to estimate future health care costs, correcting for costs of diseases already included in the basic evaluation taking into account that the relation between health care expenditure and proximity to death differs per disease and health care provider. In the case that costs are included for only a limited follow-up period while at the same time health effects are modeled for the whole course of life after the follow-up period, PAID 1.0 can be used for the inclusion of age-specific costs of survivors and decedents. PAID 1.0 is populated with country-specific (Dutch) data and not immediately transferable for use in other countries. The most important ingredient to construct a similar tool for other countries is a top-down Costs of Illness study, covering all health care expenditure which are already conducted in a variety of countries (30). The relation between health care costs and proximity to death is less well researched for different countries, but we expect this variable to be less susceptible to variation between countries than health care expenditure itself (31). Therefore, if country specific information on the influence of time to

death on health expenditure is lacking, an option might be to ‘borrow’ data from other countries, e.g. those presented in this paper.

Concluding, we think that the use of PAID 1.0 improves comparability between economic evaluations in the Netherlands and we hope that our proposed methodology may inspire researchers from other countries to further refine and improve standardized estimation of indirect medical costs.

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Tables & Figures

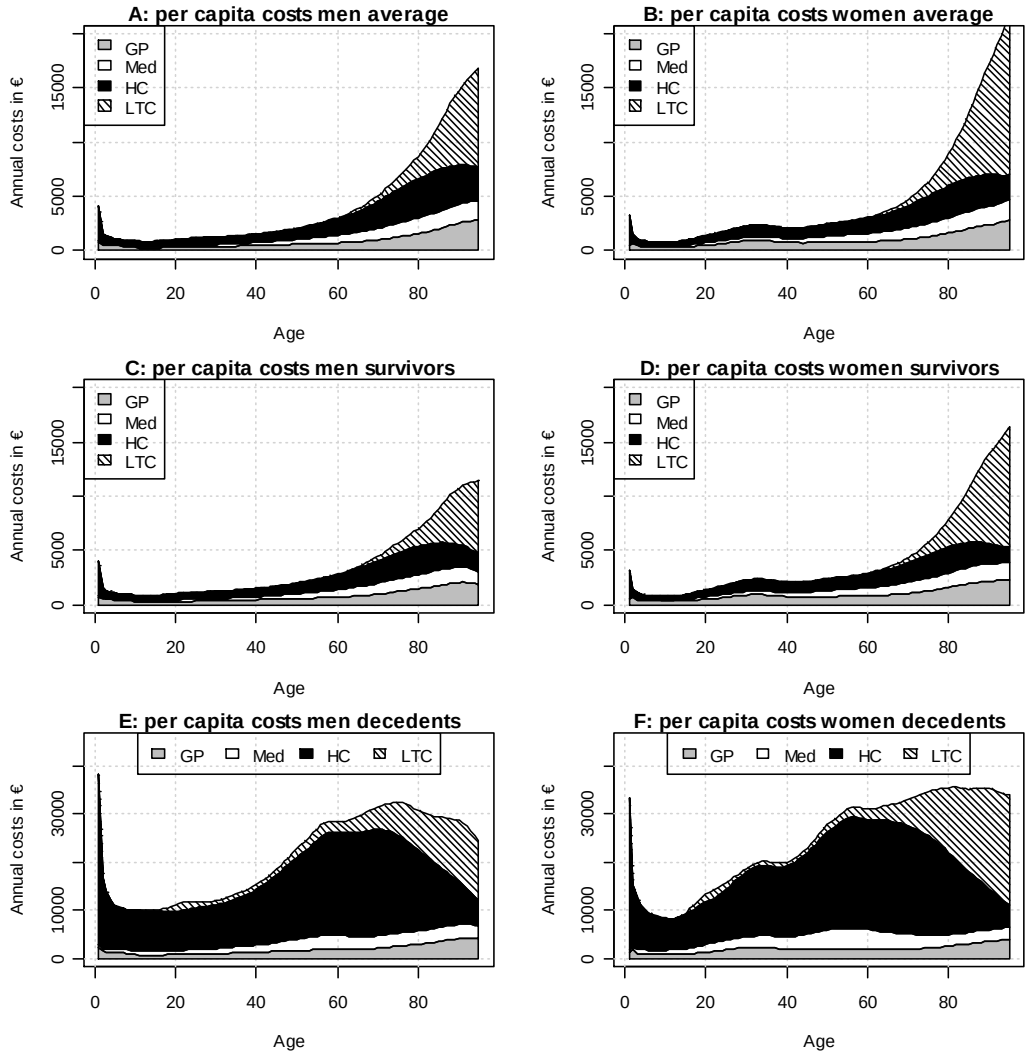

Figure 1: Average annual health care expenditure per capita (euros, price level 2005) in the Netherlands 2005 by age and gender, for four health care providers and stratified by last year of life and other years (GP=Providers of ambulatory health care, Med= retail sale and other providers of medical goods, HC = Hospitals, LTC= Nursing and residential care facilities)

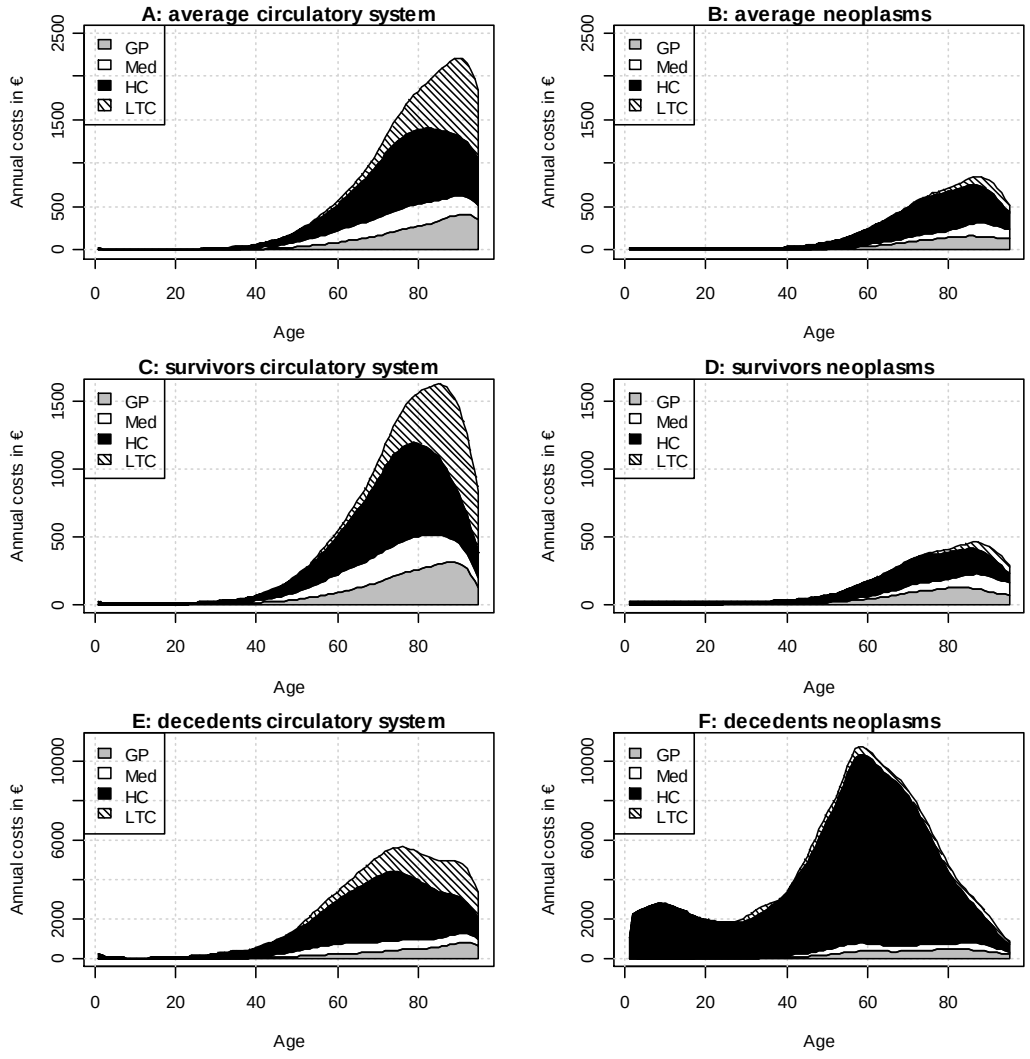

Figure 2: Average annual health care expenditure per capita in the Netherlands 2005 by age and gender, stratified by last year of life and other years, for two different disease categories, (GP=Providers of ambulatory health care, Med= retail sale and other providers of medical goods, HC = Hospitals, LTC= Nursing and residential care facilities)

Table 1: Ratios of (decedent costs) / (survivor costs) for men at age 75

	Ratio for total costs	Scaling factor *x*	Lung Cancer	Stroke	Depression
Hospitals (HC)	8.5	-	121.1	6.3	2.8
Nursing and residential care facilities (LTC)	7.6	0.90	73.7	5.2	2.5
Providers of ambulatory health care (GP)	2.2	0.42	7.6	2.2	1.6
Retail sale and other providers of medical goods (Med)	2.3	0.46	8.9	2.3	1.6

Table 2: Estimated lifetime health care costs (euros, price level 2005) stratified by last year of life and all other years and health care provider

	Men			Women		
	Last year of life	Other years	% costs in last year of life*	Last year of life	Other years	% costs in last year of life*
Total	30017	207979	13 (4)	34766	279059	11 (4)
Hospitals (HC)	15571	80389	16 (3)	13017	91452	12 (2)
Nursing and residential care facilities (LTC)	8046	20897	28 (10)	15373	45633	25 (11)
Providers of ambulatory health care (GP)	3011	44596	6 (3)	3020	65980	4 (3)
Retail sale and other providers of medical goods* (Med)	2767	34872	7 (4)	2664	45323	6 (3)
Other health care providers	622	27225	2 (2)	691	30671	2 (2)

**between brackets the percentage of costs in the last year of life if the relation between proximity to death and health care expenditures is ignored and only the costs of illness data is used*

Table 3: Estimated lifetime health care costs stratified by last year of life and other years specified by disease category

	Men			Women		
	Last year of life	Other years	% costs in last year of life	Last year of life	Other years	% costs in last year of life
Total	30017	207979	13 (4)	34766	279059	11 (4)
Infectious and parasitic disease	535	7019	7 (3)	454	7454	6 (2)
Neoplasms	5091	8976	36 (5)	3744	11562	24 (3)
Endocrine, nutritional and metabolic diseases	805	5190	13 (4)	1117	7261	13 (5)
Diseases of the blood and the blood-forming organs	331	859	28 (6)	340	1081	24 (6)
Mental and behavioral disorders	6136	29522	17 (6)	10080	47875	17 (7)
Diseases of the nervous system	1727	16094	10 (4)	1532	20152	7 (3)
Diseases of the circulatory system	4822	27450	15 (5)	5882	25456	19 (6)
Diseases of the respiratory system	2372	10634	18 (5)	1499	10835	12 (4)
Diseases of the digestive system	1294	19537	6 (2)	1183	22806	5 (2)
Diseases of the genitourinary system	1209	6096	17 (6)	1050	10540	9 (4)
Pregnancy, childbirth and the puerperium	15	669	2 (0)	47	12480	0 (0)
Diseases of the skin and subcutaneous tissue	315	3855	8 (3)	348	4422	7 (3)
Diseases of the musculoskeletal system and connective tissue	1189	13506	8 (3)	2112	23292	8 (3)
Congenital malformations	34	1839	2 (0)	28	1728	2 (0)
Certain conditions originating in the perinatal period	65	2781	2 (0)	54	2484	2 (0)
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	2166	20914	9 (3)	1840	27201	6 (3)
Injury, poison and certain other consequences of external causes	1061	6900	13 (5)	2063	10304	17 (7)
Not allocated/ Not disease related	850	26136	3 (3)	1396	32123	4 (4)

**between brackets the percentage of costs in the last year of life if the relation between proximity to death and health care expenditures is ignored*