



Estimating the costs of non-medical consumption in life-years gained for economic evaluations

Klas Kellerborg^{a,*}, Bram Wouterse^a, Werner Brouwer^{a,b}, Pieter van Baal^a

^a Erasmus School of Health Policy & Management, Erasmus University Rotterdam, the Netherlands

^b Erasmus School of Economics, Erasmus University Rotterdam, the Netherlands

ARTICLE INFO

Keywords:

Economic evaluation
Future costs
Welfare economics
Consumption

ABSTRACT

Including the costs of non-medical consumption in life years gained in economic evaluations of medical interventions has been controversial. This paper focuses on the estimation of these costs using Dutch data coming from cross-sectional household surveys consisting of 56,569 observations covering the years 1978–2004. We decomposed the costs of consumption into age, period and cohort effects and modelled the non-linear age and cohort patterns of consumption using P-splines. As consumption patterns depend on household composition, we also estimated household size using the same regression modeling strategy. Estimates of non-medical consumption and household size were combined with life tables to estimate the impact of including non-medical survivor costs on an incremental cost-effectiveness ratio (ICER). Results revealed that including non-medical survivor costs substantially increases the ICER, but the effect varies strongly with age. The impact of cohort effects is limited but ignoring household economies of scale results in a significant overestimation of non-medical costs. We conclude that a) ignoring the costs of non-medical consumption results in an underestimation of the costs of life prolonging interventions b) economies of scale within households with respect to consumption should be accounted for when estimating future costs.

1. Introduction

Medical interventions can increase life expectancy of patients and, as a consequence, may cause consumption of both medical and non-medical goods and services during the additional life time. This consumption in gained life time can be related to treatment of additional diseases (medical costs) or simply related to food, housing or clothing (non-medical costs). By definition, these costs would not have occurred if life had not been prolonged. While this may be a seemingly straightforward observation about the economic consequences of prolonging life, including these additional costs in economic evaluations conducted from a health care (medical costs) or a societal perspective (medical and non-medical costs) has been the topic of considerable debate (de Vries et al., 2018). As a result, the inclusion of both future medical and future non-medical costs, is still uncommon (de Vries et al., 2018). Disagreement is strongest concerning the inclusion of non-medical costs, sometimes also referred to as survivor consumption (Feenstra et al., 2008; Gandjour, 2006; Garber and Phelps, 1997, 2008; Lee, 2008; Lundin and Ramsberg, 2008; D Meltzer, 1997; Meltzer, 2008; Nyman, 2004, 2011; Richardson and Olsen, 2006). While the debate on whether to include

these costs in life years gained is ongoing, only a few studies have concentrated on the empirical estimation of future non-medical costs and their influence on outcomes of economic evaluations (Kruse et al., 2012; Manns et al., 2003; D Meltzer, 1997; Meltzer et al., 2000). These studies consistently found that including non-medical costs in economic evaluations increased the incremental cost-effectiveness ratios (ICERs) substantially, but that the impact varied with age of patients.

Estimates of non-medical consumption used in economic evaluation so far have used estimates of costs of consumption by age coming from a single cross section (Kruse et al., 2012; Manns et al., 2003; D Meltzer, 1997; Meltzer et al., 2000) and have ignored two issues. First, economies of scale within households were ignored as consumption in these studies was calculated by dividing household consumption by household size. Economies of scale allow members of larger households to achieve the same level of utility with less consumption (Nelson, 1988). Second, as data from a single cross section were used, correcting the age profile of consumption for period and cohort effects was not possible. Empirical studies on consumption conducted outside the context of economic evaluation have shown that life-time household consumption patterns are hump-shaped, peaking at middle ages and decreasing afterwards

* Corresponding author. P.O. Box 1738, 3000 DR, Rotterdam, the Netherlands.
E-mail address: kellerborg@eshpm.eur.nl (K. Kellerborg).

(Alessie and Ree, 2009; Fernández-Villaverde and Krueger, 2007). The hump can partly be explained by differences in household composition by age after taking into account economies of scale of consumption within households. This implies that prolonging the life of a patient living in a multi-person household may have a different impact on consumption than doing the same for a patient living in a single-person household. Therefore, household size and economies of scale within households are relevant when estimating the costs of non-medical consumption resulting of life extension; not doing so leads to an over-estimation of the impact of future costs on ICERs for multi-person households. However, even after controlling for household size, consumption exhibits a (hump-shaped) age pattern. This means that we also have to take the age-pattern into account when including non-medical consumption in cost-effectiveness analysis. An estimate based on the age distribution of consumption in one particular year might not suffice, as consumption can depend on (economic) events in that particular year. Similarly, different birth cohorts have different consumption patterns, ceteris paribus (Dahlberg and Nahum, 2003). This is relevant, as many health care interventions are targeted at specific birth cohorts, which thus might have different age profiles of consumption. Consequently, correctly identifying the age pattern means controlling for period and cohort effects. This requires datasets with all relevant variables, observed over several years. If such data sources are available, identifying an age-period-cohort model is not trivial, because age, periods, and cohorts, are linearly dependent. Several solutions to this problem have been applied, which always involve relaxing the linear dependency between the three variables, by restricting one or more of the effects, requiring strong assumptions (Deaton, 1997). Fernández-Villaverde and Krueger (Fernández-Villaverde and Krueger, 2007), for instance estimated consumption age profiles using a kernel function, while Alessie and Ree (2009), used linear splines for the age and cohort effects and, both studies modelled period effects using dummies for different calendar years or quarters.

This paper will present estimates of future non-medical costs and relates the estimates to the theoretical discussion. We add to the existing literature on future non-medical consumption by (i) using state-of-the-art methods to estimate non-medical spending patterns while accounting for age, period and cohort effects, (ii) including economies of scale within households in these estimates, and (iii) highlighting the consequences of including these costs in economic evaluations. As a starting point for our analyses, and as a comparator in estimating the impact of including future non-medical costs on the ICER, we take an economic evaluation conducted from a societal perspective in which future medical costs and productivity gains are already included while excluding future non-medical costs. This seems the most relevant and common comparator given current practice in cost effectiveness analysis.

2. Theoretical model

To better understand the role of future non-medical costs in economic evaluation and the controversies surrounding its inclusion, we will first describe a formal model of the decision rules of cost effectiveness adopting a societal perspective. As a starting point we will take an intervention (x) that influences quality of life (Q), production (P), medical consumption (M) and non-medical consumption (C) in two periods (denoted with subscripts 1 and 2). Note that both the direct healthcare investments in x as well as the impact of x on other medical spending are included in M . We are interested in the amount i we should spend on x . The impact of the intervention on health, production and consumption in period 2 is partly determined by its impact on the probability to survive from period 1 to period 2 denoted by S :

$$H = Q_1(i) + \beta S(i) Q_2(i) \tag{1}$$

$$N = M_1(i) + C_1(i) - P_1(i) + \beta S(i) \{M_2(i) + C_2(i) - P_2(i)\} \tag{2}$$

Equation (1) shows lifetime discounted health (where β acts as the

time preference discount factor) denoted H as a function of the level of spending i on intervention x and Equation (2) shows lifetime discounted net resource use denoted N (medical and non-medical consumption minus production) as a function of the level of spending i on intervention x . From a societal perspective, an ICER can be interpreted as the change in net resource use, which is defined as medical and non-medical consumption minus production, divided by QALYs gained. Assuming decreasing marginal health gains from spending on x , the decision rules of cost effectiveness imply that we should invest in the intervention up until the point that the ICER equals the consumption value of health (denoted V): $\frac{dN/di}{dH/di} = V$. Using Equations (1) and (2) we can write this as:

$$\frac{\frac{\partial M_1}{\partial i} + \frac{\partial C_1}{\partial i} - \frac{\partial P_1}{\partial i} + \beta S(i) \left\{ \frac{\partial M_2}{\partial i} + \frac{\partial C_2}{\partial i} - \frac{\partial P_2}{\partial i} \right\} + \beta \frac{\partial S}{\partial i} \{M_2(i) + C_2(i) - P_2(i)\}}{\frac{\partial Q_1}{\partial i} + \frac{\partial Q_2}{\partial i} \beta S(i) + \frac{\partial S}{\partial i} \beta Q_2(i)} = V. \tag{3}$$

Equation (3) shows the role of non-medical consumption costs in economic evaluations. These costs are influenced by changes in survival times levels of non-medical consumption ($\beta \frac{\partial S}{\partial i} C_2(i)$) and, conditional on survival, changes in the level of consumption. The discussion on the inclusion of non-medical costs so far has only focused on the first part ($\beta \frac{\partial S}{\partial i} C_2(i)$) and it is usually assumed that non-medical consumption, conditional on being alive, is not affected by healthcare interventions ($\frac{\partial C_1}{\partial i} = 0, \frac{\partial C_2}{\partial i} = 0$).

Using a similar welfare economic framework as in equation (3), Meltzer concluded that decisions based on cost-effectiveness information are only consistent with welfare maximization when all future costs, including non-medical consumption, are included (D Meltzer, 1997). However, this also requires that the denominator of Equation (3) captures the full benefits of the intervention including the utility derived from leisure and non-medical consumption. Whether this is the case is unclear (D Meltzer, 1997). For this reason, Nyman has argued that future non-medical costs could be excluded from economic evaluations since the related utility gains are not captured either, as quality of life instruments used in economic evaluation are designed to only capture health-related utility (Nyman, 2004, 2011). In response to Nyman, it has been suggested that even if quality of life instruments have not been developed to explicitly capture the utility related to non-medical consumption it might still be the case that some benefits of non-medical consumption are implicitly included (Gandjour, 2006; Lundin and Ramsberg, 2008). Equation (3) can provide us more insight in these arguments. First of all, at least some level of consumption is required to stay alive after a life prolonging intervention. In other words: marginal changes in survival through the intervention ($\frac{\partial S}{\partial i} > 0$) would require that at least some parts of $\beta \frac{\partial S}{\partial i} C_2(i)$ is included in the numerator of the ICER. Similarly, interventions that increase quality of life should include consumption costs, if the marginal increases in quality of life ($\frac{\partial Q_1}{\partial i} + \frac{\partial Q_2}{\partial i} \beta S(i)$) also (implicitly) require additional non-medical consumption. Furthermore, the benefits of non-medical consumption are not only captured through changes in quality and life and survival but also through baseline levels of quality of life and survival. Non-medical consumption (e.g. healthy food, safe cars, sports) is a known determinant of life expectancy (Cutler et al., 2006). Any change in quality of life ($\frac{\partial Q_2}{\partial i}$) due an intervention therefore captures some benefits of non-medical consumption as these changes are multiplied by life expectancy using the term $S(i)$. For an intervention that affects survival, we have to weigh the additional life years gained with some level of quality of life (as reflected in the term $\frac{\partial S}{\partial i} \beta Q_2(i)$ in Equation (3)). If that level of quality of life indeed requires a certain level of non-medical

consumption, this should be included as costs. Finally, even if the QALY does not fully capture utility derived from non-medical consumption, the cost-effectiveness threshold, based on the consumption value of health V , might. This value is often derived from willingness to pay (WTP) exercises, and it's likely that individual based their valuation on the full welfare gains with possibly higher V 's for higher consumption levels, in line with the commonly observed positive association between income and WTP for QALY gains (see e.g. [Bobinac et al., 2010](#)).

It should be noted that in practice, economic evaluations conducted from a societal perspective tend to include changes in productivity (P) associated with the intervention. For these costs (or benefits) it is also unknown to what extent the associated utility changes are fully captured in QALY gains ([Nyman, 2011](#)). When the additional production generated by the intervention is taken into account, it seems consistent to also include the part of this production that is consumed by the individual itself on the cost side. In this paper, we take the position that leaving out real costs and benefits (even in a 'balanced' way) from an economic evaluation risks welfare lowering decisions. Even if the benefits of non-medical consumption are not perfectly reflected in the QALY measure, the appropriate response should not be to exclude the real societal costs of non-medical consumption to balance the incomplete QALY, as this leaves policy makers uninformed about real societal impacts (in terms of costs and benefits) of their decisions. Rather the response should be to capture these benefits in another way, as the overall challenge is to provide decision makers with a full account of societal impacts, including all costs and all benefits.

In Equation (3), the intervention can also affect the level of consumption through the terms $\frac{\partial C_1}{\partial i}$ and $\frac{\partial C_2}{\partial i}$. An example we mentioned above is an intervention that improves quality of life, for which additional consumption is required. Other channels can be out-of-pocket payments for medical consumption, and changes in the marginal utility of consumption because of changes in health. In the remainder of this paper we will focus on a solely lifesaving intervention (e.g. a decrease in fatal accidents). The assumption we make is that this intervention is targeted at the general population, and those affected the intervention will have a quality of life pattern that is equal to that of the general population. This allows us to follow the approach taken in the existing literature on non-medical consumption and assume that this consumption is not directly impacted by the intervention ($\frac{\partial C_1}{\partial i} = \frac{\partial C_2}{\partial i} = 0$). We can concentrate on the estimation of changes in lifetime non-medical consumption that are purely the result of increases in life expectancy ($\frac{\partial S}{\partial i} C_2(i)$), and we can use the age profile of consumption of the general population for $C_2(i)$. We return to the issue of how health care interventions might change levels of non-medical consumption in the discussion. We will focus on the estimation of the non-medical consumption costs versus QALYs ratio ($\frac{\beta \frac{\partial S}{\partial i} C_2(i)}{\frac{\partial Q_1}{\partial i} + \frac{\partial Q_2}{\partial i} \beta S(i) + \frac{\partial S}{\partial i} \beta Q_2(i)}$) in our theoretical model. This ratio directly shows the impact including non-medical consumption cost would have on an existing ICER. Moving from our theoretical model to the more general case where interventions have an impact beyond two periods and where spending, survival and quality of life vary by age, we will refer to $\frac{\Delta nmc}{\Delta Qalys}$ in the remainder of this paper. $\Delta Qalys$ stands for the total discounted QALYs gained over the lifetime and Δnmc for the total discounted incremental costs of non-medical consumption due to increases in survival.

3. Methods

3.1. Data

Data from the Dutch budget survey (Budgetonderzoek) from 1978 to 2004 were used to estimate non-medical consumption by age. The budget survey was a yearly cross-sectional survey collected among the

non-institutionalized population of the Netherlands which ran from 1978 until 2004 (while the survey was not conducted in 2001 and 2002) and was coordinated by Statistics Netherlands.¹ The budget survey data are publicly available from <http://www.dans.knaw.nl>. The survey included expenditures on a detailed and comprehensive set of consumption categories (e.g. consumption related to eating, transport, housing, vacation but also consumption related to hobbies) as well as information on income, family composition and background information on all members of the household. Households took part in the survey for an entire year and expenditures were monitored using diaries which were collected by interviewers on a regular basis during the year. Consumption on both durable as well as non-durable goods was tracked with the use of these diaries. The consumption data includes value added taxes on consumer goods. Such taxes are transferred back through the state to society, and could therefore be seen as redistributions of wealth rather than costs (although redistribution is not costless). Therefore, the true costs of non-medical consumption may be somewhat overestimated in our study. The sample consists of households who answered all the necessary questions, with a household breadwinner age of 18 or higher, which resulted in a sample size of 56,566 households with an average household size of 2.78 persons and annual household costs of non-medical consumption of 11,288 euro (2017 prices). For our purposes, we excluded all consumption related to medical care. In the Netherlands, health care insurance is compulsory and out-of-pocket spending on medical care is low ([Schäfer et al., 2010](#)). Using consumer price indices from Statistics Netherlands we adjusted the data to 2017 prices.²

[Fig. 1](#) displays average non-medical household consumption by age, household size by age, log of non-medical consumption by survey year, and log of non-medical consumption by birth year. The average non-medical household consumption by age (top left) illustrates that consumption increases with age until the age of roughly 40–50, after which it decreases. This pattern is in line with previously published research on the relationship between age and non-medical consumption ([Alessie and Ree, 2009](#); [Fernández-Villaverde and Krueger, 2007](#)). Household size by age (top right) shows a plateau in the ages 35–35 and then decreases afterwards. The bottom part of the graph illustrates increasing trends of non-medical consumption both by year of survey and by birth year. For household size we see strong cohort patterns, with household sizes peaking for those born in the 1940's.

3.2. Model specification

Our aim is to estimate the costs of non-medical consumption if a death is prevented in an average household. Our approach consisted of two steps that deal with the two main empirical challenges: a) the accurate estimation of an age profile of consumption, correcting for calendar year and cohort effects, and b) the correction for household economies of scale which requires modeling household size and translating the consumption of households with different sizes into an equivalent measure. In the first step, we estimated consumption per household equivalent stratified by age. To compare consumption of multi-person households to that of singles, total household consumption is translated into the level of consumption each member of the household enjoys. To reflect economies of scale, weights smaller than one are used to divide total consumption over household members. We used the OECD-modified equivalence scale ([Hagenaars et al., 1994](#)). The scale assigns a weight of 1 to the first adult household member, 0.5 to each additional adult and 0.3 to each person under 14 years of age.

Our data set spans a large number of years, which allowed us to

¹ In the years 2003 and 2004 the survey methodology differed slightly in the way that the age of respondents above 80 years old was categorized as one category. We assumed an average age of 82.5 for these years based on the average age of those over 80 in the previous five surveys.

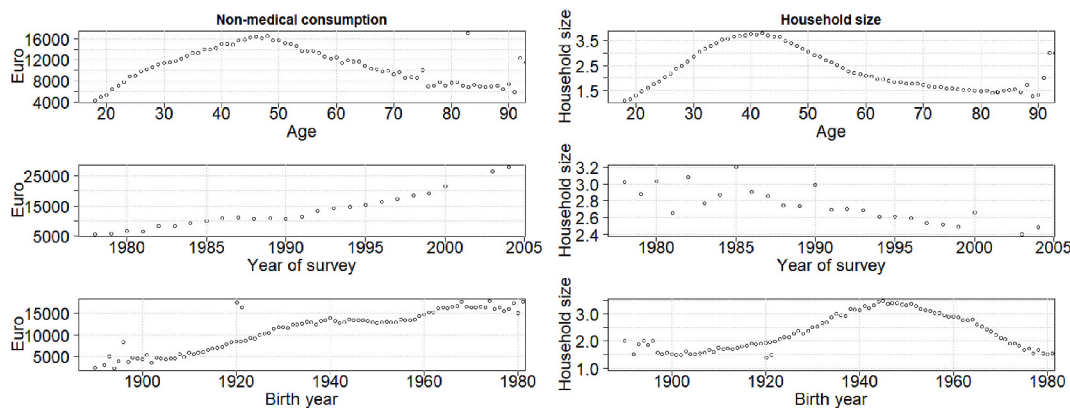


Fig. 1. Average annual household consumption in 2020 prices (upper left graph) and average household size (upper right graph) by age (average age of the adults in the household; age categorized in years as calculated from the Budget survey from the Netherlands for the years 1974–2004. Average annual household consumption by year of survey (lower left graph), and average household consumption by birth year (lower right graph).

separate cohort effects from age and period effects using an age-period-cohort (APC) model. We used cubic P-splines for age and birth year. P-splines are a combination of B-splines and penalized regression and offer a flexible alternative to both dummy variables and polynomial functions while not suffering their disadvantages (Eilers and Marx, 1996). Our model is:

$$\ln(hh\ equiv) = f(age) + f(birth\ year) + \gamma \cdot year + \epsilon, \tag{4}$$

where *hh equiv* denotes annual non-medical consumption per full household equivalent. $f(age)$ is the smooth function of age with modelled using P-splines; $f(birth\ year)$ the smooth function of birth year modelled using P-splines; γ a vector of coefficients that capture the differences between survey years; and ϵ is a normally distributed error term.

We used cubic P-splines for two reasons. First, we expected consumption to be a smooth function of age and of birth year. The disadvantage of dummy variables in such a case is that the age gradient would be irregular. On the other hand, a polynomial function might be too restrictive, and values for high ages can strongly influence the fit for lower ages (and vice versa). Because we did not necessarily expect macroeconomic shocks on consumption to be smooth functions of time, we included year dummies for the period effects. Second, a common problem with APC models estimated on repeated cross sectional data is that age, birth year, and period are not separately identified (as age is a linear function of period and cohort). Splines are nonlinear transformations of age and birth year, so that the variables are no longer perfectly collinear and the model can be identified. Age-period-cohort models, based on splines, have been estimated mostly in the context of mortality rates (Alkema and New, 2014; Clements et al., 2005; Jiang and Carriere, 2014).

Cubic P-splines are estimated by first defining a large number of equally-spaced cubic B-spline functions over the age interval. B-splines are polynomial functions that have a non-zero value only within a

splines and put a penalty on the difference between the coefficients of adjacent B-spline functions. In our analyses, we used 10 evenly spaced cubic B-splines for each smooth. A smoothing parameter determines the influence of the penalty in the estimation: the stronger the penalty, the smoother the curve. The optimal smoothing parameters in our analysis were found by minimizing the Akaike Information Criterion (AIC). The model was fitted using the ‘mgcv’ package in R (Wood et al., 2016).

The second step in order to estimate the non-medical consumption caused by preventing the death of an adult for an average household in the general population, is modeling adult household composition. Since we used the OECD-modified equivalence scale we predicted the proportion of households with more than one adult, as additional consumption due to prolonging life differs whether life is prolonged in a multi-person household or in a single-person household. To estimate this proportion, we used the probability of a household having more than 1 adult as a dependent variable and estimated a binomial logistic regression model. The model specification followed a similar choice of covariates as equation (4); resulting in the following specification:

$$p(adults\ in\ hhs > 1) = \frac{\exp(f(age) + f(birth\ year) + \gamma \cdot year + \epsilon)}{1 + \exp(f(age) + f(birth\ year) + \gamma \cdot year + \epsilon)} \tag{5}$$

To account for the different effect a death has in a single-person household versus one in a multi-person household, we therefore need to scale back households into these two separate types when predicting for an average household. Here, we take advantage of the equivalence scale once again to address the impact of prolonging life on consumption in the two different types of households. In a single household the future annual consumption is the estimated full household equivalent consumption. In a multi-adult household, the consumption is, in accordance with the equivalence scale, half the full household equivalent consumption. After estimating (4) and (5), annual non-medical consumption by age caused by preventing a death an average household by combining equations (1) and (2), can be calculated as:

$$nmc(age) = p(adults\ in\ hhs > 1|age) \cdot hh\ equiv(age) \cdot 0.5 + (1 - p(adults\ in\ hhs > 1|age)) \cdot hh\ equiv(age) \tag{6}$$

specified range. Any linear combination of the basis cubic spline functions will result in a smooth function with a second-order derivative that is continuous at the joining points. The drawback of B-splines and other forms of local regression is that it is difficult to determine the number of knots and spacing of the basis cubic spline functions. As a solution to this problem, P-splines use a relatively large number of evenly spaced B-

As the budget survey is not entirely representative for the Dutch population of households we used sample weights provided by Statistics Netherlands. As the sample weights of Statistics Netherlands were partly determined by age we centered these weights to 1 for each age class

strata.

3.3. The impact of non-medical future costs on the ICER

We estimated $\frac{\Delta nmc}{\Delta Qalys}$ in the scenario where a death at a certain age is prevented due to a hypothetical intervention. $\frac{\Delta nmc}{\Delta Qalys}$ corresponds to $\frac{\beta^{nmc} C_2(i)}{\frac{\alpha Q_1}{\alpha} + \frac{\alpha Q_2}{\alpha} \beta S(i) + \frac{\alpha}{\alpha} \beta Q_2(i)}$ of our theoretical model and will be labeled as ‘partial ICERs’ that capture the increase in an ICER that already including all other costs as in equation (3). In that scenario QALYs gained can be calculated by estimating remaining quality adjusted life expectancy, and Δnmc can be estimated using remaining estimated lifetime non-medical costs using the following equation:

$$\frac{\Delta nmc}{\Delta Qalys} = \frac{\sum_a L(age = a) \times nmc(age = a)}{\sum_a L(age = a) \times Q(age = a)} \tag{7}$$

Where $L(age = a)$ is the number of years lived at age a and $Q(age = a)$ is the average quality of life at age a . Estimates of non-medical consumption by age were taken from predictions from the regression models as denoted in equation (6). Predictions for non-medical consumption were retransformed taking into account the fact that an OLS on the log scale underestimates the mean on the normal scale (Manning and Mullahy, 2001). Estimates of $L(age)$ and $Q(age)$ were taken from a recent study that estimated the quality of life and mortality in the Netherlands (Gheorghe et al., 2014). In accordance with Dutch guidelines, QALYs were discounted with 1.5% annually and costs with 4% annually (voor Zorgverzekerings, 2006). Costs were expressed in 2020 prices.

In our main prediction, we fixed the period effect to that estimated for the most recent year in the data (2004), and the birth year equal to the actual birth year of the individuals with age a in 2004 when predicting costs by age. Thus, if we predicted remaining lifetime non-medical consumption for 30-year olds in 2004, we set the birth year equal to 1974 in our predictions of the age profile. This may be viewed as relevant for an intervention that is targeted to a specific birth cohort in the current calendar year, for example screening programs at a certain age.

In sensitivity analyses, we relaxed various assumptions. First of all, using the estimated regression models from equations (4) and (5) we

ignored cohort effects by not fixing the birth-year but letting the birth-year increase as age increases when predicting the age profile. This way, we use the regression estimates to create a 2004 cross-section consisting of different birth cohorts. Second, we estimated equations (4) and (5) also without cohort effects and without period effects (results of regression models are displayed in the Appendix, Figs. 1 and 2) and recalculated the ICERs. Third, to explore the influence of household equivalence scales we also calculated partial ICERs by using results from a regression model in which household equivalent consumption was simply calculated by dividing household consumption by household size (thus not using equivalence scales and without predictions of household size). We also performed various sensitivity analyses with respect to discount rates used in other countries. Finally, in order to mimic previous studies, we made predictions from a regression model fitted using data from just one cross-section (2004 data only) where consumption was calculated by dividing household consumption by household size.

4. Results

Fig. 2 displays the included smooth functions describing the age and cohort effects and the estimated coefficients for the period dummies. The left column displays the parameter’s contribution to the non-medical consumption estimates and the right column displays the smooths and parametric variables used in the logistic model estimating the probability of a household having more than one adult. The age pattern for consumption shows a peak round about 55 and decreases thereafter, while for household size we see a decrease after the age of 40. Our estimates show cohort and period effects for both consumption and household size. Household size and consumption increase for cohorts births up until roughly 1945 and thereafter decrease. Period effects show an upward trend for consumption but generally a downward trend for household size.

In Fig. 3 we present the first steps of our main findings (equations (1) and (2)). We predict the age profile of annual non-medical consumption per household equivalent and the probability of a household having more than one adult in a hypothetical cohort with a birth year of 1974 and period effect fixed at 2004 (straight lines). To assess the effect of adjusting for cohort effects we also display age profiles fixing the period effect to 2004 but letting the birth year vary from 1974 (2004 minus 30) to 1919 (2004-85) parallel with age (the dotted lines).

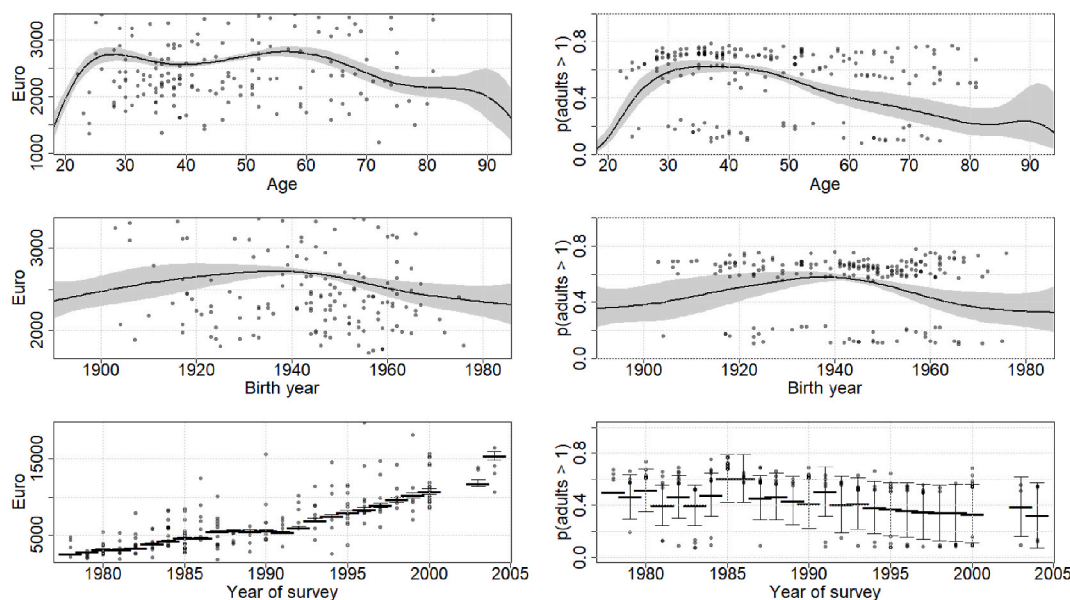


Fig. 2. Partial effects of fitted smooths and parameter estimates from the consumption model (left column) and the partial effect of the probability of having more than one adult in the household (right column) with 95% confidence intervals and a random sample of size 100 of partial residuals. Top row displays the of age on consumption, middle row displays the effect of birth year and the bottom row displays the effect of year of survey.

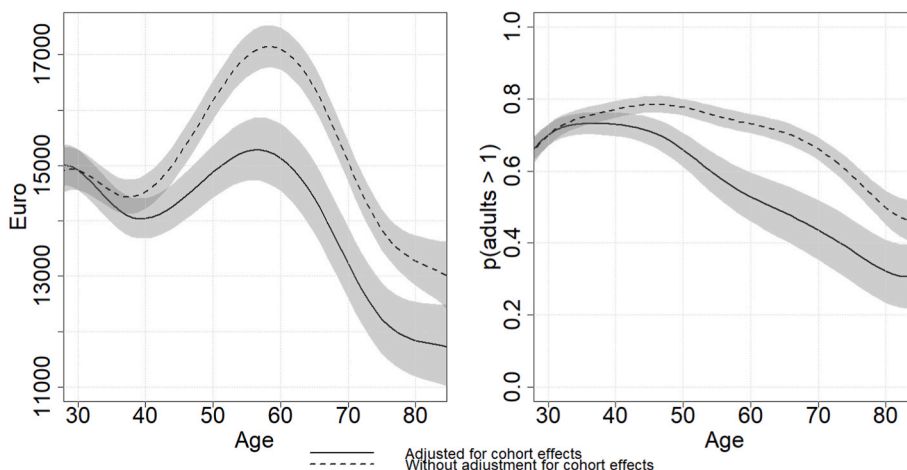


Fig. 3. Predictions of equivalence scaled consumption (left graph) with adjustment for cohort effects and without adjustment for cohort effects, and predicted probability of a household having more than one adult (right graph) with 95% prediction intervals. Lines indicates predictions with our main model specification accounting for cohort effects, dotted lines indicate predictions without accounting for cohort effects.

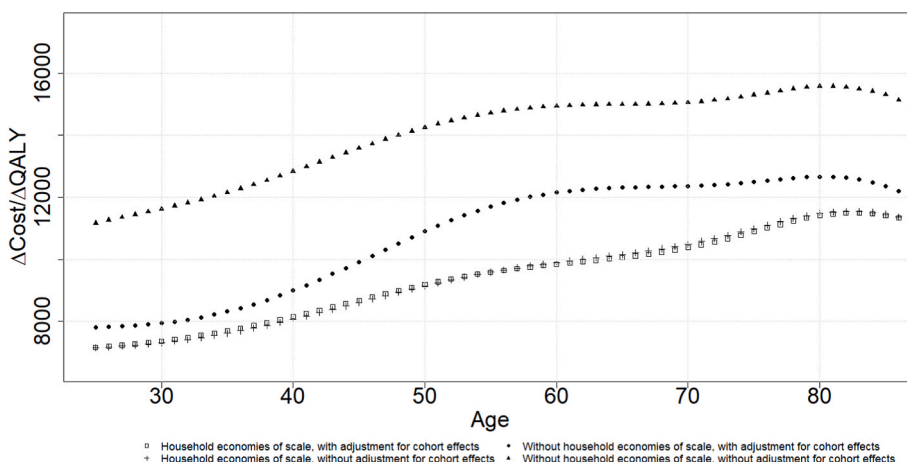


Fig. 4. The impact of non-medical consumption costs on the partial ICER of saving a life by age under different prediction specifications.

For consumption, the impact of adjusting for cohort effects is most noticeable around age 60 where consumption is lower when adjusting for cohort effects. For household size, the impact of cohort effects is most prominent at middle age where the probability that a household is comprised of more than one person is much lower when we take into account cohort effect.

In Fig. 4 we show the impact of including costs of non-medical consumption on the ICER. We show predictions for our main specification for an average household adjusting for cohort effects (the birth-year is fixed when we predict an age profile). The impact on the ICER is compared to predictions in which we do not control for cohort effects or ignore economies of scale within households (here we use predictions from a regression in which we define one household equivalent of consumption as household consumption divided by household size). In the main prediction, the impact of including non-medical consumption on the ICER increases by age even though household equivalent consumption decreases with age. This is due to the fact that at older age people are more often single and their quality of life is lower. When not accounting for economies of scale within the household the impact on the ICER is much larger. While adjusting for cohort effects results in lower consumption household equivalent age profiles it also results in more single-person households which increases the non-medical costs of life extension. On balance these effects more or less cancel each other out and thus adjusting for cohort effects only has a small impact on the

partial ICER.

In Table 1 we show results of the impact of including non-medical consumption on the partial ICER, by age and under different assumptions. The different sensitivity analyses do not alter the main conclusions and are in line with the results presented in Figs. 3 and 4. Even though household equivalent consumption decreases with age, the impact on the ICER increases by age which is due to the fact that both average household size and quality of life decrease at higher ages. Not adjusting for cohort effects only has a limited impact on the partial ICER. Not including period effects in our model specification also has a limited impact on the partial ICER for the same reason. However, not accounting for economies of scale within households, resulted in a (strong) over-estimation of consumption. This is also the main reason that our main predictions are much lower than those based on predictions using 2004 data only without adjusting for household economies of scale; as is currently done in economic evaluations. Finally, the effects of different discounting assumptions are shown, and compared to our main model, the effects are larger in the younger ages and converges with the main prediction model when the expected remaining life years decreases.

5. Conclusion and discussion

There is an ongoing theoretical debate on whether to include future non-medical costs in economic evaluations in health care. In this paper,

Table 1
Partial ICERs: the impact of including future costs under different assumptions and model specifications compared to our main prediction model. (Euros per QALY; 2020 price level; rounded to nearest hundreds').

Model specification Prediction settings	Age				
	30	45	65	75	85
Main model specification					
Average household	7000	8300	9600	10,400	10,900
Birth year fixed when predicting age profiles					
Discount rates: 4% cost and 1.5% QALYs					
Average household	7000	8200	9700	10,500	10,900
Ignoring cohort effects when predicting age profiles					
Discount rates: 4% cost and 1.5% QALYs					
Single household	10,400	12,300	14,000	14,200	14,100
Birth year fixed when predicting age profiles					
Discount rates: 4% cost and 1.5% QALYs					
Average household	11,400	12,100	12,000	12,100	11,800
Birth year fixed when predicting age profiles					
Discount rates: 3% cost and 3% QALYs					
Average household	11,700	12,100	11,900	12,000	11,700
Birth year fixed when predicting age profiles					
Discount rates: 0% cost and 0% QALYs					
W/o equivalence scale^a					
Birth year fixed when predicting age profiles					
Discount rates: 4% cost and 1.5% QALYs					
Average household	7600	9400	11,700	11,900	11,800
Alternative model w/o cohort variables^b					
Average household	6900	8200	9800	10,500	10,800
Discount rates: 4% cost and 1.5% QALYs					
Alternative model w/o period variables^c					
Average household	39,400	28,500	18,600	15,300	11,100
Birth year fixed when predicting age profiles					
Discount rates: 4% cost and 1.5% QALYs					
Predictions only using data from 2004^d					
Average household	6800	8000	9800	10,600	11,300
Discount rates: 4% cost and 1.5% QALYs					

Estimated smooth function and estimated parametric parameters for all alternate model specifications are available in the appendix.

^a Same regression model specification as in equation (4) but the dependent variable is calculated as household consumption divided by household size. As household economies of scale are ignored there is no need to use predictions of household size.

^b Same regression model specification as in equations (4) and (5) but without parameters to model the cohort effects.

^c Same regression model specification as in equations (4) and (5) but without parameters to model the period effects.

^d The dependent variable is calculated as household consumption divided by household size. As household economies of scale are ignored there is no need to use predictions of household size. As data from only 1 cross-section is used, period and cohort effects are not modelled.

we provided empirical evidence regarding the impact of including such costs on the ICER. In doing so, we explicitly addressed two issues that thus far were ignored in the scarce empirical literature on future non-medical costs. First, we have used a very long series of repeated cross sections data, which allowed us to identify the age profile by correcting for period- and cohort effects. Second, we have accounted for the fact that saving a life can have a different impact on consumption depending on household size, because of economies of scale.

Our findings provide three important insights. First, we have confirmed the findings from previous studies that including the costs of future non-medical consumption can have a substantial impact on the ICER of life-prolonging interventions and the impact increases with age (Kruse et al., 2012; Manns et al., 2003; D Meltzer, 1997; Meltzer et al., 2000). This means that, regardless of whether the benefits of non-medical consumption are perfectly reflected in the QALY measure, non-medical consumption costs are important societal costs of medical interventions which should be part of a full welfare economic analysis, and about which policy makers should be informed. Here, it should be noted that ultimately the impact of including future costs on decisions depends both on all other costs that go into the ICER and the threshold that is being used. Second, accounting for economies of scale within households is important and lowers the impact of including future non-medical costs on the ICER because if life is prolonged in a multi-person household this results in lower additional consumption than in a single-person household. However, to be able to account for household economies of scale one also needs predictions of average household size by age. Although there are more single person households at old age, life prolonging interventions for old people are more likely to be cost-effective when accounting for household economies of scale. Third, the influence of correcting for possible cohort and period effects on consumption cost estimates was limited in our study. The reason for this is that cohort and period effects in consumption and household size had opposing effects on the ICER.

Some limitations of this study need noting. A first limitation is that, like most consumption studies (e.g. Alessie and Ree, 2009; Domeij and Johannesson, 2006; Fernández-Villaverde and Krueger, 2007), we had to rely on repeated cross section data of consumption. This means that, although we have used a very flexible approach based on splines, we still have had to make some implicit assumption to separately identify age, period and cohort effect. An important restriction might be that, in our empirical model, these effects are additive and separable. It could be that for instance macroeconomic events have a different impact on different age groups. An example is the financial crisis that seems to have had a different impact on the wealth holding of younger and older cohorts, which in turn affects consumption across the whole lifecycle. More flexible models, such as two-dimensional splines, could be used to capture such interactions. However, our current model provides a clear economic intuition of the age-, period- and cohort-effects and is comparable, both in approach as in outcomes, to previous empirical research (Alessie and Ree, 2009; Domeij and Johannesson, 2006; Fernández-Villaverde and Krueger, 2007). A limitation in this study is the use of relatively old data. This may have two implications: the economic growth since the data was published may have resulted in an underestimation of the estimates, and the consumption profiles by age may have changed. To address the first issue, we inflated the estimates to later years, however, we can observe an increase in consumption over time even after price adjustments and likely our estimates are therefore an underestimation of the actual consumption today. Regarding the second issue, the first paper describing an age pattern of consumption including the consumption hump at middle ages and a decrease at old age was first published in 1969 (Thurow, 1969). This age pattern has since been observed consistently in different time periods (Attanasio et al., 1999; Attanasio and Weber, 1995; Browning and Crossley, 2001; Fernández-Villaverde and Krueger, 2007; Gourinchas and Parker, 2002). Publications using data later than 2005 are sparse, but a similar consumption pattern was observed in 2010 for ages 45 to 75 in the UK (Banks et al., 2019). Given that the literature appears to suggest that consumption profiles by age are generally stable throughout time, we believe that our estimates of the age pattern results are still relevant.

Second, in this study, we have focused only on consumption, not on production or income. The partial ICERs as calculated using equation (7) can be interpreted as the cost effectiveness of a hypothetical intervention in which a death at a certain age is prevented at zero intervention costs. Previous research (e.g. Kellerborg et al., 2020; Meltzer, 1997) has

shown that such ICERs give a good indication of what the impact is of including future costs on the ICER of non-hypothetical interventions. We assumed that existing ICERs already include the effects on productivity, and showed how also including non-medical consumption would affect the ratio.

Third, when assessing the impact of including non-medical costs we used population averages for consumption as well as population averages for mortality and quality of life. As such, our estimates should be interpreted with caution whenever a target population of an actual intervention deviates from the average population. The impact of such deviations will probably be most influenced by differences (compared to population average) in mortality and quality of life because of the intervention. Hence, we believe our estimates of non-medical consumption are still informative for actual economic evaluations (and likely better than current zero estimates). Fourth, in our empirical application we assumed that health care interventions have no effect on lifetime consumption other than through increased survival. However, there are at least three additional channels through which the intervention might have an impact on consumption. First, the intervention might affect out-of-pocket spending on medical care. In our application, we have focused solely on the additional impact of including non-medical consumption to an evaluation, assuming the effects on medical consumption and productivity are already included. If the effect of the intervention on medical consumption is indeed included in the ICER, the effect of the out-of-pocket medical spending on non-medical consumption should be taken into account as well to prevent double counting (although in the Netherlands this is a minor issue, due to low out-of-pocket payments). Second, the intervention might have a positive effect on human capital (productivity) and thus increase the lifetime resources that can be used for consumption (although some of this might be mitigated by social insurance or other income transfers). Again, if the productivity gains are included, the income effects on consumption should be as well. The third channel through which the intervention might have an impact on consumption is through the relation between the utility of consumption and health. Health state dependence of the utility of consumption is often suggested as an explanation for the declining consumption pattern at older ages, such as the one we, like many other empirical studies, have found (Finkelstein et al., 2009). If the marginal utility of consumption is lower in poor health, that means that individuals tend to shift their lifetime consumption towards the younger years, where they can expect to be in better health. Likewise, if an intervention affects health in different life years, individuals might reallocate consumption across their remaining life or might increase overall consumption at the costs of lower bequests. Although theoretically appealing, actually identifying health state dependence is difficult and the direction of the effect has been found to be ambiguous and may likely depend on the type of health state change (Finkelstein et al., 2009; Gyrd-Hansen, 2016). Given this ambiguity, we have focused on the age pattern of consumption without adjusting for health status as we were interested in consumption patterns that conditional on age are not altered by the intervention under investigation. Future research could focus on the impact of healthcare interventions on non-medical consumption patterns conditional on being alive. Cost effectiveness studies might actually be able to provide valuable insights into the question of health-state dependence, as often interventions are randomly assigned to individuals with similar individual with the same health condition as control group. Extending the data collection in those studies to include consumption data could thus be valuable. Another, less data intensive, way to quantify the impact of health on non-medical consumption for the purpose of treatment evaluation could be to follow the approach already used for medical consumption and exploit the relation with time to death. As health losses and health care consumption are usually clustered at the end of life (Gheorghe et al., 2016; Payne et al., 2007), it might well be the case that non-medical consumption strongly decreases at the end of life to be shifted into medical consumption. Finally, although it is beyond the scope of this paper to provide a full discussion

of different discounting procedures (e.g. Attema et al., 2018), it is good to stress how that differences in discounting procedures also affect results as presented in this study (see Table 1). As we used the Dutch guidelines, prescribing differential discounting, countries applying other discount rates therefore need to be aware of this in interpreting our results.

Although it is common practice not to include costs of non-medical consumption in cost effectiveness analysis, a theoretical foundation for this practice is lacking, and the practice is not in line with what some have advocated (D Meltzer, 1997; Sanders et al., 2016). A possible explanation for this might be that guidelines for cost effectiveness analysis typically do not pay (much) attention to costs of non-medical consumption (possibly due to the lack of theoretical consensus on its inclusion), while they do often pay more attention to measuring and valuing production gains (Krol et al., 2013). Economic evaluations that do include future non-medical consumption often use data from a single cross-sectional survey and do not adjust for household economies of scale (Kruse et al., 2012; Manns et al., 2003; Meltzer, 2012). Such estimates are clearly different from our main estimates and likely constitute overestimations of real non-medical consumption due to life prolonging interventions. Important in the theoretical debate regarding the in- or exclusion of future non-medical costs is the extent to which the benefits of non-medical consumption are captured in the QALY gains of life-prolonging interventions. This can be captured in terms of functioning (i.e. being in a particular health state) or in the valuation of such states (see e.g. Tilling et al., 2010). If the benefits from non-medical consumption are not captured in QALYs, it could be considered inconsistent to include the related cost. While this inconsistency argument is valid and worth to be studied empirically, we note two things. First, current practice in economic evaluations taking a societal perspective is to include productivity gains, for which it is also unknown to what extent the costs and benefits (e.g. in terms of sacrificed leisure time) are fully captured in QALY gains (Nyman, 2011). Hence, excluding future non-medical costs on the same grounds could be seen as inconsistent in itself. Second, using our theoretical model we indicated that at least part of the utility of non-medical consumption is included in economic evaluations. More specifically, with regard to the theoretical debate it is important to empirically investigate whether benefits of non-medical consumption are considered when people value QALY gains using WTP exercises. More generally, if the current economic evaluation framework for health interventions does not fully capture the benefits of non-medical consumption, other ways of capturing them could be sought. This seems a more sensible response than leaving out real costs to account for a too narrow measurement of benefits. If these costs are to be included, then the estimates needs to be reliable.

The debate about the inclusion of non-medical consumption costs is still ongoing, but there are good reasons to argue that the inclusion of these costs is important. This also means that we need sound estimates of these costs, which are largely lacking. We have contributed by presenting estimates for The Netherlands, based on a longitudinal dataset and an analysis that takes age-period-cohort effects and the influence of household economies of scale into account. Our findings not only show that it is important to take the non-medical consumption costs of medical interventions into account, but also that without properly taking economies of scale into account these societal costs are misrepresented.

Credit

KK: Conceptualization, Methodology, Formal analysis, Data Curation, Writing - Original Draft, Writing - Review & Editing, Visualization. **BW:** Conceptualization, Methodology, Formal analysis, Writing - Original Draft, Writing - Review & Editing. **WB:** Conceptualization, Methodology, Writing - Original Draft, Writing - Review & Editing. **PVB:** Conceptualization, Methodology, Formal analysis, Writing - Original Draft, Writing - Review & Editing, Supervision.

Acknowledgments

This work was supported by the COMPARE project under the European Union's Horizon 2020 research and innovation programme (grant agreement No 643476). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.socscimed.2021.114414>.

References

- Alessie, R., Ree, J. De, 2009. Explaining the hump in life cycle consumption profiles. *Economist* 157, 107–120.
- Alkema, L., New, J.R., 2014. Global estimation of child mortality using a Bayesian B-spline Bias-reduction model. *Ann. Appl. Stat.* 8, 2122–2149.
- Attanasio, O.P., Banks, J., Meghir, C., Weber, G., 1999. Humps and bumps in lifetime consumption. *J. Bus. Econ. Stat.* 17, 22–35. <https://doi.org/10.2307/1392236>.
- Attanasio, O.P., Weber, G., 1995. Is consumption growth consistent with intertemporal optimization? Evidence from the consumer expenditure survey. *J. Polit. Econ.* 1121–1157.
- Attema, A.E., Brouwer, W.B.F., Claxton, K., 2018. Discounting in economic evaluations. *Pharmacoeconomics* 36, 745–758. <https://doi.org/10.1007/s40273-018-0672-z>.
- Banks, J., Blundell, R., Levell, P., Smith, J.P., 2019. Life-Cycle consumption patterns at older ages in the United States and the United Kingdom: can medical expenditures explain the difference? *Am. Econ. J. Econ. Pol.* 11, 27–54. <https://doi.org/10.1257/pol.20170182>.
- Bobinac, A., van Exel, N.J.A., Rutten, F.F.H., Brouwer, W.B.F., 2010. Willingness to pay for a quality-adjusted life-year: the individual perspective. *Value Health* 13, 1046–1055. <https://doi.org/10.1111/j.1524-4733.2010.00781.x>.
- Browning, M., Crossley, T.F., 2001. The life-cycle model of consumption and saving. *J. Econ. Perspect.* 15, 3–22. <https://doi.org/10.1257/jep.15.3.3>.
- Clements, M.S., Armstrong, B.K., Moolgavkar, S.H., 2005. Lung cancer rate predictions using generalized additive models. *Biostatistics* 6, 576–589. <https://doi.org/10.1093/biostatistics/kxi028>.
- Cutler, D., Deaton, A., Lleras-Muney, A., 2006. The determinants of mortality. *J. Econ. Perspect.* 20, 97–120.
- Dahlberg, S., Nahum, R.-A., 2003. Cohort Effects on Earnings Profiles: Evidence from Sweden. Uppsala University, Department of Economics, Uppsala.
- de Vries, L.M., van Baal, P.H., Brouwer, W.B.F., 2018. Future Costs in Cost-Effectiveness Analyses: Past, Present, Future. *Pharmacoeconomics*. <https://doi.org/10.1007/s40273-018-0749-8>.
- Deaton, A., 1997. The Analysis of Household Surveys: A Microeconomic Approach to Development Policy, A World Bank Publication. World Bank.
- Domeij, D., Johannesson, M., 2006. Consumption and health. *Contrib. Macroecon.* 6, 1–30.
- Eilers, P.H.C., Marx, B.D., 1996. Flexible smoothing with B-splines and penalties. *Stat. Sci.* 11, 89–102.
- Feenstra, T.L., van Baal, P.H., Gandjour, A., Brouwer, W.B., 2008. Future costs in economic evaluation. A comment on Lee. *J. Health Econ.* 27, 1641–1645. <https://doi.org/10.1016/j.jhealeco.2008.07.007>.
- Fernández-Villaverde, J., Krueger, D., 2007. Consumption over the life cycle: facts from consumer expenditure survey data. *Rev. Econ. Stat.* 89, 552–565.
- Finkelstein, A., Luttmer, E., Notowidigdo, M., 2009. Approaches to estimating the health state dependence of the utility function. *Am. Econ. Rev.* 99, 116–121.
- Gandjour, A., 2006. Consumption costs and earnings during added years of life—a reply to Nyman. *Health Econ.* 15, 315–317.
- Garber, A.M., Phelps, C.E., 2008. Future costs and the future of cost-effectiveness analysis. *J. Health Econ.* 27, 819–821. <https://doi.org/10.1016/j.jhealeco.2008.05.002>.
- Garber, A.M., Phelps, C.E., 1997. Economic foundations of cost-effectiveness analysis. *J. Health Econ.* 16, 1–31.
- Gheorghie, M., Brouwer, W.B.F., van Baal, P.H.M., 2014. Did the health of the Dutch population improve between 2001 and 2008? Investigating age-and gender-specific trends in quality of life. *Eur. J. Health Econ.* 1–11.
- Gheorghie, M., Picavet, S., Verschuren, M., Brouwer, W.B.F., Baal, P.H.M., 2016. Health losses at the end of life: a Bayesian mixed beta regression approach. *J. R. Stat. Soc. Ser. A (Statistics Soc.)*
- Gourinchas, P.-O., Parker, J.A., 2002. Consumption over the life cycle. *Econometrica* 70, 47–89. <https://doi.org/10.1111/1468-0262.00269>.
- Gyrd-Hansen, D., 2016. A stated preference approach to assess whether health status impacts on marginal utility of consumption. *Health Econ.*
- Hagenaars, A.J.M., Vos, K. de, Zaidi, M.A., Communities., S.O. of the E., 1994. Poverty Statistics in the Late 1980s : Research Based on Micro-data. Office for Official Publications of the European Communities, Luxembourg.
- Jiang, B., Carriere, K.C., 2014. Age-period-cohort models using smoothing splines: a generalized additive model approach. *Stat. Med.* 33, 595–606. <https://doi.org/10.1002/sim.5970>.
- Kellerborg, K., Perry-Duxbury, M., de Vries, L., van Baal, P.H., 2020. Practical Guidance for Including Future Costs in Economic Evaluations in the Netherlands: Introducing and Applying PAID 3.0, Value in Health. <https://doi.org/10.1016/j.jval.2020.07.004>.
- Krol, M., Brouwer, W., Rutten, F., 2013. Productivity costs in economic evaluations: past, present, future. *Pharmacoeconomics* 31, 537–549.
- Kruse, M., Sørensen, J., Gyrd-Hansen, D., 2012. Future costs in cost-effectiveness analysis: an empirical assessment. *Eur. J. Health Econ.* 13, 63–70.
- Lee, R.H., 2008. Future costs in cost effectiveness analysis. *J. Health Econ.* 27, 809–818. <https://doi.org/10.1016/j.jhealeco.2007.09.011>.
- Lundin, D., Ramsberg, J., 2008. On survival consumption costs—a reply to Nyman. *Health Econ.* 17, 293–297.
- Manning, W.G., Mullahy, J., 2001. Estimating log models: to transform or not to transform? *J. Health Econ.* 20, 461–494.
- Manns, B., Meltzer, D., Taub, K., Donaldson, C., 2003. Illustrating the impact of including future costs in economic evaluations: an application to end-stage renal disease care. *Health Econ.* 12, 949–958. <https://doi.org/10.1002/heec.790>.
- Meltzer, D., 2012. 42 Future Costs in Medical Cost-Effectiveness Analysis, vol. 447. Elgar companion to Heal. Econ.
- Meltzer, D., 2008. Response to “Future costs and the future of cost-effectiveness analysis. *J. Health Econ.* 27, 822–825. <https://doi.org/10.1016/j.jhealeco.2008.05.001>.
- Meltzer, D., 1997a. Accounting for future costs in medical cost-effectiveness analysis. *J. Health Econ.* 16, 33–64.
- Meltzer, David, 1997b. Accounting for future costs in medical cost-effectiveness analysis. *J. Health Econ.* 16, 33–64. [https://doi.org/10.1016/S0167-6296\(96\)00507-3](https://doi.org/10.1016/S0167-6296(96)00507-3).
- Meltzer, D., Egleston, B., Stoffel, D., Dasbach, E., 2000. Effect of future costs on cost-effectiveness of medical interventions among young adults: the example of intensive therapy for type 1 diabetes mellitus. *Med. Care* 38, 679–685.
- Nelson, J.A., 1988. Household economies of scale in consumption: theory and evidence. *Econom. J. Econom. Soc.* 1301–1314.
- Nyman, J.A., 2011. Measurement of QALYs and the welfare implications of survivor consumption and leisure forgone. *Health Econ.* 20, 56–67.
- Nyman, J.A., 2004. Should the consumption of survivors be included as a cost in cost-utility analysis? *Health Econ.* 13, 417–427. <https://doi.org/10.1002/heec.850>.
- Payne, G., Laporte, A., Deber, R., Coyte, P.C., 2007. Counting backward to health care's future: using time-to-death modeling to identify changes in end-of-life morbidity and the impact of aging on health care expenditures. *Milbank Q.* 213–257.
- Richardson, J.R.J., Olsen, J.A., 2006. In defence of societal sovereignty: a comment on Nyman's inclusion of survivor consumption in CUA. *Health Econ.* 15, 311–314.
- Sanders, G.D., Neumann, P.J., Basu, A., Brock, D.W., Feeny, D., Krahn, M., Kuntz, K.M., Meltzer, D.O., Owens, D.K., Prosser, L.A., Salomon, J.A., Sculpher, M.J., Trikalinos, T.A., Russell, L.B., Siegel, J.E., Ganiats, T.G., 2016. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. *J. Am. Med. Assoc.* 316, 1093–1103. <https://doi.org/10.1001/jama.2016.12195>.
- Schäfer, W., Kroneman, M., Boerma, W., Berg, M.V.D., Westert, G., Devillé, W., van Ginneken, E., 2010. The Netherlands: health system review. *Health Syst. Transit* 12 (xxvii), 1–228.
- Thurow, L.C., 1969. The optimum lifetime distribution of consumption expenditures. *Am. Econ. Rev.* 59, 324–330.
- Tilling, C., Krol, M., Tsuchiya, A., Brazier, J., Brouwer, W., 2010. In or out? Income losses in health state valuations: a review. *Value Health* 13, 298–305.
- voor Zorgverzekerings, C., 2006. Rapport Richtlijnen voor farmaco-economisch onderzoek; evaluatie en actualisatie.
- Wood, S.N., Pya, N., Säfken, B., 2016. Smoothing parameter and model selection for general smooth models. *J. Am. Stat. Assoc.* 111, 1548–1563. <https://doi.org/10.1080/01621459.2016.1180986>.