Quality of life and time to death: have the health gains of preventive interventions been underestimated?

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ABSTRACT

This paper explores the implications of the relation between quality of life (QoL) and time to death (TTD) for economic evaluations of preventive interventions that extend life. We argue that ignoring the relation between TTD and QoL results in an underestimation of the quality-adjusted life year (QALY) gains of these interventions if there is a positive relation between QoL and TTD. By using health survey data on QoL for the general Dutch population linked to the mortality registry, we quantify the magnitude of this mechanism. Our empirical results indicate that QoL decreases when approaching death suggesting that TTD is an important predictor of QoL. Moreover, the strength of the effect of TTD is higher when one is closer to death. Predictions of different regression models confirmed that ignoring the relation between TTD and QoL would result in an underestimation of the QALY gains for preventive interventions. This underestimation decreases with age and increases with the discount rate used. Our results indicate that, for preventive interventions, depending on age and discount rate, the underestimation ranges between 2% and 9%.

Key words: economic evaluations, time to death, life prolonging interventions, preventive interventions, quality of life, QALYs

1. Introduction

If a preventive intervention saves someone from a premature death, this person will live longer. Then, central questions are: how much longer and to what extent are additional years spent in good health? These questions need to be answered in any economic evaluation of a life-prolonging intervention. While much research has been performed on the estimation of short term effectiveness of preventive interventions on health (meta-analyses, indirect treatment comparisons etc.), less research has been done on how to translate these short term health effects into long term health consequences in terms of Quality Adjusted Life Years (QALYs). QALYs have been developed in order to capture the effects of both length of life and quality of life (QoL) and are widely used as a summary measure of health outcome for economic evaluation studies. In order to derive QALYs, health utilities or QoL weights are needed. These utilities are based on preferences for different states; more desirable health states will receive greater weight.
QoL utilities are measured on a cardinal scale ranging from 0 to 1, where 0 indicates the state ‘dead’ and 1 indicates full health. Sometimes, states can take negative values suggesting that values worse than dead are possible. Valuation functions have been developed for generic QoL instruments such as the EQ-5D (Dolan 1997), the SF-6D (Brazier, Roberts 2004) or the Health Utility Index mark 2 and 3 (HUI2 and HUI3, Feeny, Furlong et al. 2002).

Modeling techniques are frequently applied in economic evaluations of life prolonging interventions in order to estimate the effects of these interventions in terms of QALY gains. Examples of interventions in which models are used to estimate cost-effectiveness are: pharmaceuticals, smoking cessation, weight loss, screening, vaccination (de Kok, van Ballegooijen et al. 2009, van den Berg, Smit et al. 2011, Tariq, van den Berg et al. 2009, van Baal 2008). Finding appropriate QoL weights for the different states distinguished in these models is challenging in practice. However, the choice of QoL weights in a model can have high impact on the final outcome of economic evaluations. For example, a recently published modeling study, that estimated the effects of prostate cancer screening on health, showed that the number of QALYs gained was very sensitive to the utility estimate assumed for men who were cured from prostate cancer due to screening (Heijnsdijk et al. 2012).

Caution must be taken in calculating QALYs gained when preventive interventions extend length of life. In that case it is important to go beyond quality of life losses due to the disease of interest. If an intervention adds years to the life of a person then this person becomes exposed to other diseases that may also result in quality of losses (Fryback, Laurence 1997). However, in many economic evaluations only QoL losses due to the disease under study are taken into account. For example, in an economic evaluation on HPV vaccination in the Netherlands (de Kok, van Ballegooijen et al. 2009) all persons who received the HPV vaccination were assumed to have no QoL losses due to other diseases that might occur for the rest of their lives. Clearly, this approach overestimates QALYs gained since the absence of the diseases under study translates into perfect health. A better approach used in practice consists of assuming that QoL in life years gained equals the age-specific mean in the population (Mihaylova 2006). As QoL generally decreases with age, QALYs gained usually are much less than life years gained if one incorporates age specific mean QoL estimates. To our knowledge, up to date, this was the most accurate method used for estimating QoL in years gained due to a life prolonging intervention. In this paper, we argue that improvements to this method can be achieved by making use of the relation between QoL and mortality.

In many studies it has been showed that QoL is a good predictor for survival in persons with a chronic disease. Furthermore, in the general population it was found that a lower QoL is associated with a higher mortality risk (Kaplan 2007). If we turn this mechanism around, we can argue that QoL values decrease when persons approach death and are probably lowest in the period close to death. We hypothesize that a part of the decrease in QoL of the elderly is the result of higher mortality risks of the elderly accompanied by lower QoL values. Modeling QoL values exclusively depending on age suggests that life years gained by an intervention are primarily spent in poor health. However, if QoL values correlate with mortality and depend strongly on proximity to death or time to death (TTD), postponement of death will result in postponement of QoL losses and not all years gained will be spent in poor health. Not accounting for this mechanism when modeling the population of interest will result in an underestimation of QALY gains and consequently in an overestimation of the cost-effectiveness ratio compared
with the situation when the modeled population age-specific average QoL utilities would be used.

TTD has been investigated in relation to other measures of health such as health care expenditures (HCE, (HAKKINEN 2008, Polder 2006, Seshamani 2004, Seshamani 2004, Stearns 2004, Wanless 2004, Werblow 2007, Zweifel 1999, Zweifel 2004)) and disability (Klijs 2011). The first and probably most influential paper on TTD and HCE was published by (Zweifel 1999). This study analyzed the relationship between age and HCE using Swiss sick fund data, and found that the magnitude of HCE is explained to a greater extend by TTD rather than age. Therefore, higher average health care costs at higher ages are caused mainly by the fact that many elderly people die at those ages and the period before dying is associated with high healthcare use. This implies that, an increase in life expectancy postpones the expensive period of life suggesting that aging of the population might have a more limited impact on HCE than generally believed. The authors of this paper refer to age as to a “red herring” that diverts the attention from the real causes of HCE growth. It has been found that cost-effectiveness analyses overestimate the costs and consequently the incremental cost-effectiveness ratio (ICER) of life prolonging preventive interventions when the relation between TTD and HCE is not explicitly modeled (Gandjour 2005). We argue that not only estimates of costs can be improved by accounting for TTD but also those of QoL utilities.

The aim of this paper is to a) quantify the relation between QoL and TTD in the general population and b) show the relevance of this relation for the economic evaluation of preventive interventions. We will compare our proposed approach that is using age-specific QoL estimates stratified by TTD in life years gained (due to a life prolonging intervention) with the best used technique up to date in the practice of economic evaluations that is using age-specific QoL estimates in life years gained. By comparing the two methods, we argue that ignoring the relation between QoL and TTD results in an underestimation of QALYs gained for preventive interventions that extend life.

This paper will be organized as follows. Section 2 presents the data used in our study. Section 3 presents in more detail the methods employed to estimate QoL. Section 4 illustrates the main results and findings in our analyses. Finally, section 5 formulates conclusions.

2. Data

The present study was based on the Permanent Survey of Living Conditions (POLS: Permanent Onderzoek Leef Situatie) for years 2001-2008 that was linked to mortality registry. POLS is an on-going yearly cross-sectional survey, it started in 1981 and is coordinated by Statistics Netherlands. The survey is sampled on records from a centralized municipal registry, and does not include the institutionalized population. The POLS health survey monitors developments in lifestyle, health, medical consumption, preventive behavior, and well-being in the Netherlands and starting 2001 it includes the SF-12 questionnaire. The Health Module of the survey is collected both in a face-to-face interview and a written questionnaire. The interviewer visits the participants at home, asks for informed consent, conducts an interview and at the end leaves a written (drop-off) questionnaire that includes the SF-12 questionnaire. Not everyone that completed the interview returned the written questionnaire, so approximately 20-25% of the SF-
12 items were missing. We analyzed a complete data set obtained by deleting the records corresponding to the missing fields of the SF-12. The SF-6D was derived from the SF-12 using the algorithm developed by (Brazier, Roberts 2004).

Individuals from POLS for years 2001-2008 were linked to the mortality registry and were followed-up for approximately 10 years, i.e. for the period 2001-2010. In the POLS data, for each individual in 2001-2008 there is only one measurement of the SF-12. Within the POLS survey, for ages 50+, in 2001-2010, 1633 persons (952 men and 681 women) have deceased and 17664 individuals (8726 men and 8938 women) have survived. From the deceased aged 50+, approximately 116 (13%) men and 66 (9.6%) women have died within one year of the measurement. For the deceased, TTD will be the length of time from the SF-12 measurement until death.

Figure 2 shows the SF-6D distribution for the deceased men and women aged 50+. We notice that the SF-6D distribution is bounded between values 0.345 and 1 with an average QoL of 0.76 for men and of 0.7 for women. In addition, for both men and women the distribution is left (negative) skewed, slightly more skewed for men than for women.

![Figure 2: The distribution of the SF-6D for the deceased aged 50+](image)

For the ease of illustration, in figure 3 we divided the data in two groups, one group that includes the deceased individuals that died within 3 years of the SF-12 measurement and one group that contains the deceased that died in 3-10 years of the health measurement and the survivors. Approximately 426 (45%) men and 264 (38.7%) women died within three years of measurement. Indeed, figure 3 indicates that, in general, for most ages and both genders, the mean QoL is lower for the deceased that died within the first 3 years after filling in the health questionnaire than for the other group.
Methods

The relation between QoL and mortality is usually investigated with survival analysis with QoL entered as a predictor variable (Kaplan 2007). Since then the outcome is mortality, it would not be possible to produce QoL estimates stratified by TTD. Therefore, in this study regression models will be fitted using the SF-6D QoL as an outcome variable and age, gender, TTD and interactions between these variables as predictor variables. In the model specification we will deliberately exclude disease indicators. This is because just as age, TTD is a proxy variable that borrows its explanatory power in a statistical model based on the fact that it is closely related to varying processes of which diseases processes are the most important ones. The more would be adjusted for various diseases in the statistical analysis, the less will the variables age and TTD matter.

QoL utility scores are normally difficult to model as they are bounded (generally between 0 and 1), the distribution is left-skewed, and, for some of these instruments, the QoL distribution shows a strong ceiling effect at the values of one. An influential research paper indicated that for such bounded outcomes, the mean is a nonlinear function of the explanatory variables and the variance is heteroscedastic (Kieschnick, McCullough 2003).

Regression methods previously used in the literature for modeling QoL indexes include censored least absolute deviations (CLAD, (Austin 2002, RW.ERROR - Unable to find reference:62, RW.ERROR - Unable to find reference:61)), Tobit models (Austin 2002, RW.ERROR - Unable to find reference:62, RW.ERROR - Unable to find reference:61), latent class models (RW.ERROR - Unable to find reference:61), two-part models (RW.ERROR - Unable to find reference:61, Li, Fu 2009) and linear regression based on ordinary least squares (OLS, (Barton, Sach et al. 2008, Dan, Kallman et al. 2008, Wee, Cheung et al. 2008). Simulation studies found OLS to be superior to many of the above proposed approaches (Pullenayegum 2010). However, recently published studies showed that beta regression models outperform OLS when modeling QoL data. (Basu, Manca 2011, Hunger, Baumert & Holle 2011). To address the methodological challenges associated with modeling the SF-6D utility, in particular boundness,
skewness and heteroscedasticity, we employed Generalized Additive Models for Location, Scale and Shape (GAMLSS, (Stasinopoulos 2007)).

a. Generalized additive models for Location, Scale and Shape (GAMLSS)

GAMLSS\(^1\) are defined as *semi-parametric* regression-type models (Stasinopoulos, Rigby 2007). The adjective *parametric* refers to the required assumption of a parametric distribution for the response variable, whereas the prefix *semi-* refers to the possibility of modelling the relationship between covariates and the response variable as non-parametric smoothing functions. Indeed, GAMLSS can be regarded as an extension of the generalized additive models (GAM, (Hastie, Tibshirani 1990)). GAMLSS include probability distributions with a maximum of four parameters: i.e. location \(\mu\), scale \(\sigma\), skewness \(\nu\) and kurtosis \(\tau\). The model assumes independent observations \(y_i\) for \(i = 1, 2, \ldots, n\) conditional on a given set of explanatory variables, and in GAMLSS each of these distribution parameters is modelled separately through an additive model.

Because the SF-6D index is a continuous variable defined on the interval \((0, 1]\) we used the BEINF1 distribution assumption to model the QoL data in GAMLSS. BEINF1 is a special case of the class of inflated models. The word *inflation* is used to indicate that the probability mass is exceeded at the boundary of a certain parametric distribution; in this case, that of the beta distribution. Inflation can be associated with any parametric distribution. Therefore, BEINF1 is a mixture of a continuous beta distribution defined on the interval \((0,1)\) and a degenerate distribution, which gives non-negative probabilities at 1. BEINF1 has three parameters: the mean (or location) parameter denoted by \(\mu\), the so called precision (or scale) parameter denoted by \(\sigma\) and the parameter that models the probability at one denoted by \(\nu\). Note that, although we adopt the same notation for the parameters as shown above, the meaning of these parameters is not necessarily the same. We only have a distribution with three parameters where \(\nu\) does not model the skewness but the probability mass at 1. Generally, various shapes of the beta distribution can be obtained for various values of the parameters \(\mu\) and \(\sigma\). Using the GAMLSS parameterization, the probability density function of a \(BEINF1(\mu, \sigma, \nu)\) is:

\[
f(y|\mu, \sigma, \nu) = \begin{cases} 
(1 - p_1) f(y|\mu, \sigma), & 0 < y < 1 \\
p_1, & y = 1 
\end{cases}
\]

where \(p_1\) is the probability mass at 1 and represents the probability of observing 1 and \(f(y|\mu, \sigma)\) is the beta distribution defined by:

\(^1\) GAMLSS are implemented in the R package `gamlss`
\[
f(y|\mu, \sigma) = \frac{1}{B(\alpha, \beta)} y^{\alpha-1}(1-y)^{\beta-1},
\]

where the relation between the parameters \((\mu, \sigma)\) and \((\alpha, \beta)\) is given by \(\alpha = \frac{\mu(1-\sigma^2)}{\sigma^2}\), \(\beta = \frac{(1-\mu)(1-\sigma^2)}{\sigma^2}\) and \(B(\alpha, \beta)\) is the beta function. Details regarding the parameterization of the \textit{BEINF1} in GAMLSS can be found elsewhere (Rigby, Stasinopoulos 2010). The expectation of a random variable \(Y \sim \text{BEINF1}(\mu, \sigma, \nu)\), \(E[Y]\) is:

\[
E[Y] = \frac{\mu + \nu}{1 + \nu} = f(\mu, \nu)
\]

We modeled each \textit{BEINF1} distribution parameter by its own predictor and an associated link function. We used the default link functions logit, logit and log for modeling the parameters \(\mu\), \(\sigma\) and \(\nu\). Akaike information criterion indicated similar results when other link functions were used to model the parameters \(\mu\) and \(\sigma\). Each parameter was modeled as a function of explanatory variables age, gender, TTD and their interactions.

The goal of our analysis is to compare QoL estimates (and consequently to calculate QALY gains of life prolonging interventions) from a model containing variables age, gender and TTD with those from a model that contains only the variables age and gender. The former model will be called the TTD approach while the latter will be called the age-specific approach. The TTD approach is described by the following parameter equations:

\[
\begin{align*}
\text{logit}(\mu) &= \alpha_0 + \alpha_1\text{age} + \alpha_2\text{age}^2 + \alpha_3\text{gender} + \alpha_4\text{age*gender} + \alpha_6\text{TTD} + \alpha_7\text{TTD}^2 + \alpha_8\text{age*TTD} \\
\text{logit}(\sigma) &= \beta_0 + \beta_1\text{age} + \beta_2\text{age}^2 + \beta_3\text{gender} + \beta_4\text{age*gender} + \beta_6\text{TTD} + \beta_7\text{TTD}^2 + \beta_8\text{age*TTD} \\
\log(\nu) &= \delta_0 + \delta_1\text{age} + \delta_2\text{age}^2 + \delta_3\text{gender} + \delta_4\text{age*gender} + \delta_6\text{TTD} + \delta_7\text{TTD}^2 + \delta_8\text{age*TTD}
\end{align*}
\]

while the age-specific model includes the same equations excluding the terms that contain the variable TTD.

**b. Quality-adjusted life years (QALYs)**

QALYs are widely used in economic evaluations as a summary measure of health outcomes as they incorporate the impact of an intervention/treatment on both length of life and QoL. For example, assuming that a person has undergone an intervention at age \(x\) and gained \(n\) years of life, the QALY gains (\(QALY_{gains}\)) from the intervention are:

\[
QALY_{gains} = \sum_{j=0}^{n-1} QoL(x + j),
\]

where \(QoL(x + j)\) denotes the QoL at age \(x + j\).
QALY gains computed using QoL predictions from an age-specific model were compared with those using QoL predictions from a TTD model. Therefore, a relative percentage change of QALYs gained from the two models was calculated.

4. Results

For this section various situations will compare predictions from an age-specific model with those from a TTD model. Figure 4 shows the estimated mean QoL for all ages 50+ from: the age-specific model, the TTD model when TTD is fixed at 1 year before death and the TTD model when TTD is fixed at 10 years before death. As expected, for all ages 50+, the predicted mean QoL at 1 year before death is smaller than the one at 10 years before death and the predicted mean QoL from the age-specific model lies between the other two predictions from the TTD model. We notice that, for both genders, with advancing age, the difference between the mean QoL predictions in the three cases becomes smaller suggesting that the effect of TTD decreases with age. Hence at age 90, for both men and women, almost no difference is observed for the mean QoL in the three cases.

Having estimated each parameter of the BEINF1 distribution we can look at the entire QoL distribution for various ages and values of TTD. Figure 5 shows that both variables age and TTD play an important role in determining the shape of the QoL distribution. Therefore, for both men and women, the skewness decreases with advancing age while it increases when further away from death (for higher values of TTD). On the other hand, the variation increases with age while it decreases with TTD. In other words, older ages are associated with less skewed distribution and more variation and being closer to death is associated with less variation and more skewed distribution.

Figure 4: Mean QoL predictions form from the age-specific model and from the TTD model (predictions for 1 year before death and for 10 years before death)
Figure 5: The estimated QoL distribution for various ages using the age-specific approach (black continuous line), the TTD model at 1 year before death (dotted black line) and the TTD model at 10 years before death (dotted grey line). The vertical lines represent the estimated mean QoL corresponding to the 3 situations.

We have established that the effect of TTD decreases with age. Moreover, figure 6 shows that, for both genders, the effect of TTD is stronger when closer to death especially in the first 72 months before death. Interestingly, it seems that the effect of TTD tends to be slightly higher for women than for men.

Figure 6: The effect of TTD on QoL

For figure 7 let us assume that a hypothetical woman named Helen had a screening intervention at age 50 years and she was diagnosed with breast cancer. She received early treatment and she lived until the age of 65 years. Had she not undergone the screening, she
would have discovered the cancer later and she would have lived only until the age of 60 years. Therefore, due to the screening intervention she gained 5 more years of life. In figure 7 we show the estimated mean QoL using the age-specific approach (left) and the one using the TTD approach (right). QALYs gained using the age-specific approach were 3.7 and those gained using the TTD model were 3.9. The relative change suggests that QALYs gained were underestimated with 6.7% when the relation between TTD and QoL was left out. When computing these values we ignored the discounting rate. For example, a discount rate of 1.5% (as applied in the Netherlands) yields an underestimation of 7.6%. Furthermore, a discount rate of 3.5% (as applied in the UK) and of 4% results in an underestimation of 8.6% and of 9.3%, respectively. Therefore, if the relation between QoL and TTD is ignored, the higher the discount rate, the higher the underestimation of QALYs gained.

Figure 7: QALY gains for 5 extra years of life using the age-specific approach (left) and the TTD approach (right)

Figure 8: QALYs gain underestimation (%) for each age between 60 and 89 when 1 year of life was gained due to a life prolonging intervention
For quantifying the effect of discounting on the underestimation, for both genders, we looked at each age between 60 and 89 and assumed 1 year of life was gained due to a life prolonging intervention (as shown in figure 8). We assumed 3 situations: no discount, discount rate of 1.5% and of 3.5%, respectively. We notice that, as the effect of TTD decreases with age, the underestimation also decrease with age and, as expected, the impact of discounting is higher at younger ages. Accounting for discounting with rates of 1.5% and 3.5% can add approximately 1% and 2% to the QALY gains underestimation, respectively. It is worth noting that since the effect of TTD is stronger for women than for men (see figure 6), as expected, the underestimation tends to be slightly higher for women than for men (differences of approximately 1%).

Figure 9 shows that the QALY gains underestimation tends to diminish with the number of years gained due to a life prolonging intervention; however, the level of this decrease is small. For example, we observe differences of only 1% in the underestimation computed for an intervention that extends life with 1 year and one that extends life with 10 years, respectively.

**Figure 9:** QALYs gain underestimation (%) for an average man and an average woman of age 60 that gain from 1 to 10 years of life due to a life prolonging intervention

5. Conclusions and discussion

Modeling techniques are frequently applied in economic evaluations of life prolonging interventions in order to estimate the effects of these interventions in terms of QALYs. Because the choice of QoL weights in a model can have high impact on the final outcome of economic evaluations, it is important to derive appropriate QoL weights for the different states distinguished in a model. In this study we propose a method that estimates QoL in life years gained in preventive interventions.

Our findings illustrate that the relation between QoL and TTD has important consequences when estimating QoL weights in life years gained due to preventive interventions. We proposed to estimate QoL in life years gained by using the average age-specific QoL weights stratified by TTD for the target population. These estimates were compared with those derived using the best method applied in practice that is with the average age-specific QoL estimates of the modeled population. We argue that ignoring the relation between TTD and QoL results in an underestimation of QALYs gained due to a preventive intervention.
Although the method proposed can be applied to any life prolonging intervention, we empirically applied and compared the two methods for preventive interventions by using survey data for the general Dutch population linked to mortality registry. Our empirical results indicate that the effect of TTD is stronger when one is closer to death; for both men and women, this effect is higher especially in the first 72 months before death. Indeed, ignoring the relation between TTD and QoL results in QALYs underestimation in life years gained due to a preventive intervention compared with the case in which age-specific QoL weights would be used. This underestimation decreases with advancing age and increases with the discount rate used. Similar results were observed for both genders with a slight tendency of a higher underestimation for women than for men (differences of 1%). Moreover, our results show that the number of life years gained from a life prolonging intervention has a small impact on the underestimation. Only differences of 1% were observed between an intervention that extends life with 1 year and one that prolongs life with 10 years, respectively. Hence, the results reveal that, depending on age and the discount rate, QALY gains underestimation in economic evaluations of preventive interventions ranges between approximately 2% and approximately 9%, respectively. It is worth mentioning that discount rates for the health effects larger than 3.5% (the UK rate) would yield even higher underestimations than the ones mentioned above.

This study has a number of strengths. First, all models used in economic evaluations of life prolonging interventions predict survival; therefore, this method could be easily applied to other interventions and populations of interest. Importantly, the empirical results presented in this study can be used in the practice of economic evaluations of preventive interventions.

Second, in order to address the methodological challenges associated with modeling the QoL utility, we used GAMLSS with \textit{BEINFI} assumption for the response variable. In particular, GAMLSS accounted for specific features of the QoL distribution such as boundness, skewness and heteroskedasticity. One advantage of GAMLSS is that they allow modeling not only the parameter of the mean, but all other parameters of the conditional response variable distribution. For example, the parameters involving the variability and the shape of the SF-6D index were explicitly modeled as functions of the explanatory variables age, gender and TTD. A similar modeling approach would have not been possible with more traditional regression models like GAM or OLS.

This study has also a number of limitations especially related to our empirical experiment. First, in our empirical analysis we used a cross-sectional data; therefore, for each individual, in the period 2001-2008 there is only one measurement of the SF-12. The underlying assumption was that QoL did not change from the measurement until death. This might have influenced our results as QoL may change in time. Further research using longitudinal data would be helpful in order to clarify this aspect.

Second, we only used the complete case data by deleting the records corresponding to the missing items of the SF-12. This could have biased our results; however, previous research that employed the same data set for both survivors and deceased indicated that QoL in the imputed data was similar with that from the complete case data (Gheorghe, Van Baal 2011).

Third, a limitation of the POLS data is that it does not include the institutionalized population. However, probably, persons that are very close to death and have a low QoL would not be in a survey whether they are institutionalized or not. Nevertheless, because the percentage of the institutionalized Dutch population is not very high, it varies from approximately 0.5% at age 80 years to 9% at age 90 years, we would not expect dramatic changes in our estimates.
Finally, we used in this study the SF-6D derived from the SF-12; recall that the observed range of the SF-6D was from 0.345 to 1. In (Fryback 2007) the authors showed that for a national survey sample of non-institutionalized adults, both the range and the mean of a number of QoL indices (e.g. HUI2, HUI3, EQ-5D, SF-6D derived from the SF-36) differ significantly. For example, the minimum observed value for the EQ-5D was $-0.11$ while for the HUI3 was $-0.34$ and for the SF-6D (derived from SF-36) was 0.3. The range discrepancies between various QoL indices suggest that our results may be sensitive to the QoL instrument used. For example, given the larger range of EQ-5D and of HUI compared to SF-6D, we suspect that the QALYs gain underestimation would be higher when the former instruments would be used compared to the SF-6D.

This research indicates that using age-specific QoL utilities stratified by TTD instead of age-specific QoL weights in life years gained due to preventive interventions results in improved estimates of QALY gains in these interventions. This conceptual idea can be applied to any population of interest for which there is a relation between QoL and TTD. Because we used survey data for the general Dutch population linked to mortality registry, we applied this theoretical idea for preventive interventions. Our empirical findings confirm that, if the relation between TTD and QoL is ignored, QALY gains in modeling studies of economic evaluations of preventive interventions are underestimated; this implies that the cost-effectiveness is overestimated.


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