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## Cured Today, Ill Tomorrow: A Method for Including Future Unrelated Medical Costs in Economic Evaluation in England and Wales

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### ABSTRACT

**Objectives:** In many countries, future unrelated medical costs occurring during life-years gained are excluded from economic evaluation, and benefits of unrelated medical care are implicitly included, leading to life-extending interventions being disproportionately favored over quality of life-improving interventions. This article provides a standardized framework for the inclusion of future unrelated medical costs and demonstrates how this framework can be applied in England and Wales.

**Methods:** Data sources are combined to construct estimates of per-capita National Health Service spending by age, sex, and time to death, and a framework is developed for adjusting these estimates for costs of related diseases. Using survival curves from 3 empirical examples illustrates how our estimates for unrelated National Health Service spending can be used to include unrelated medical costs in cost-effectiveness analysis and the impact depending on age, life-years gained, and baseline costs of the target group.

**Results:** Our results show that including future unrelated medical costs is feasible and standardizable. Empirical examples show that this inclusion leads to an increase in the ICER of between 7% and 13%.

**Conclusions:** This article contributes to the methodology debate over unrelated costs and how to systematically include them in economic evaluation. Results show that it is both important and possible to include future unrelated medical costs.

**Keywords:** economic evaluation, future costs, NICE, unit costs.

VALUE HEALTH. 2020; ■(■):■-■

### Introduction

Population aging and its relationship with healthcare has not escaped attention in the research community.<sup>1</sup> A concern regarding the treatment of aging in economic evaluation is that extending life leads to additional consumption of healthcare.<sup>2</sup> A patient who receives a medical intervention providing them with additional life-years will continue consuming healthcare in the life-years gained (LYG). For example, a patient who is treated for a heart attack and survives may, during their LYG, get cancer. The costs in the LYG that are directly related to the disease being treated, for example, cardiovascular disease, are referred to as future *related* medical costs. Future *unrelated* medical costs, such as cancer treatment costs in the LYG, are a consequence of the life-extending nature of the treatment.<sup>3</sup> Studies show that increasing hospital survival leads to an increase in emergency admissions in patients whose lives were saved.<sup>4</sup> It is likely that this increase in admissions leads to an increase in medical costs.

The inclusion of future unrelated medical costs is a topic of debate in health technology assessment, with the United States and The Netherlands recommending<sup>5</sup> or requiring<sup>6</sup> the inclusion of future unrelated medical costs in economic evaluation. Furthermore, researchers have previously argued that future unrelated medical costs should be stipulated to be included in guidelines for England and Wales, provided by the National Institute for Clinical Excellence (NICE),<sup>7,8</sup> an amendment to NICE's current guidelines, which state that any costs considered unrelated to the condition or technology of interest should be excluded.<sup>9</sup>

There are several arguments for the inclusion of future unrelated medical costs. First, to the extent that unrelated treatments are a firm commitment made by the healthcare system (this may be less applicable in countries with less stable and comprehensive benefits packages, such as low- to middle-income countries)<sup>10</sup> and given a fixed healthcare budget, extending life and thereby increasing future unrelated medical costs leads to health opportunity costs by leaving less budget for others in added life-years.

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<https://doi.org/10.1016/j.jval.2020.05.006>

By excluding future unrelated medical costs, the opportunity cost of these life-extending interventions is underestimated.<sup>11</sup> Second, excluding future unrelated costs generated by life-extending interventions indirectly introduces a bias against quality-of-life improving interventions, which do not add future costs. Third, estimates of quality-of-life and life expectancy are typically obtained from people receiving unrelated care; excluding costs and including benefits of unrelated future medical care is inconsistent.<sup>3</sup>

There is a pragmatic argument against the inclusion of future costs worth discussing here: the argument that future costs for all diseases would need to be separately modeled, thus the estimation of these costs is too complex to be carried out for every economic evaluation.<sup>12–14</sup> Nevertheless, there are methods facilitating the estimation of future unrelated medical costs,<sup>2,15</sup> which have been applied in several countries including England and Wales.<sup>16–19</sup> What all these methods have in common is that rather than predicting the risk of all unrelated diseases and connecting these predictions to costs, they take per-capita costs by age and sex that comprise all medical spending as a starting point. Per-capita costs are then multiplied by survival curves to estimate incremental future unrelated medical costs. To avoid double-counting costs of related diseases, some studies have adjusted these per-capita costs for related diseases.<sup>17,20</sup> A further issue concerning aging and economic evaluation is that much of the increase in healthcare costs attributed to aging can be attributed to someone being in their last year of life. This is referred to as time to death (TTD)<sup>21</sup> and is most visible in hospital inpatient care, given the high cost of many inpatient treatments.<sup>22,23</sup> Previous studies have also considered that health spending is centered in the last phase of life, concluding that future unrelated medical costs are overestimated if one ignores TTD.<sup>15,18</sup>

## Methods

### Conceptual Model

In economic evaluations for NICE, an ICER is calculated to provide a measure of an intervention's cost-effectiveness against the threshold,  $k$ . The ICER in its basic form is written as  $\frac{\Delta \text{Costs}}{\Delta \text{QALYs}}$ , where the change in costs refers to a change only in related medical costs. Nevertheless, as established in the introduction, interventions that extend survival implicitly generate future unrelated medical costs in the additional YG. Therefore, the decision rule for cost-effectiveness, from a healthcare perspective, can be written as:

$$\frac{\Delta[L \times (C_r + C_u)]}{\Delta[L \times Q]} < k \quad (1)$$

$L$  stands for life-years,  $Q$  for quality of life, and  $C_r$  and  $C_u$  for related medical costs and unrelated medical costs.  $k$  represents the cost-effectiveness threshold. Given that unrelated medical costs conditional on survival are independent of the intervention ( $\Delta C_u = 0$ ), equation 1 is rewritten as:

$$\frac{\Delta(L \times C_r) + \Delta L \times C_u}{\Delta[L \times Q]} < k \quad (2)$$

The difference in unrelated costs between intervention and comparator is solely dependent on the difference in life-years.

The variable of interest is the incremental future unrelated medical costs  $\Delta L \times C_u$ , which is denoted as  $\Delta lhc_u$ . The simplest way of estimating  $\Delta lhc_u$  is to use age-specific per-capita healthcare spending and to multiply these with survivor curves in the

treatment and comparator scenarios:

$$\Delta lhc_u = \sum_a l'(a) \times ac(a) - \sum_a l(a) \times ac(a) \quad (3)$$

Where  $l'(a)$  and  $l(a)$  denote the probability of surviving to age  $a$  in the treatment and comparator scenario, respectively.  $ac(a)$  indicates total annual health spending per capita at age  $a$ . This method has been proposed by Meltzer (1997)<sup>2</sup> and has the advantage that it is simple and data requirements are modest. Nevertheless, if lifetime related costs are already included, then using equation 3 leads to double-counting of related costs. To overcome this, per-capita health spending should be corrected so that only per-capita costs of unrelated diseases (denoted  $ac_u(a)$ ) are included (equation 4).

$$\Delta lhc_u = \sum_a l'(a) \times ac_u(a) - \sum_a l(a) \times ac_u(a) \quad (4)$$

### Standardizing estimates

To remove the double-counted related healthcare costs, per-capita unrelated costs can be calculated in a standardized manner using information on the related costs included in the original evaluation. To do this, total per-capita costs can be treated simply as the sum of per-capita related and unrelated costs:

$$ac_u(a) = ac(a) - ac_r(a) \quad (5)$$

Per-capita related costs are often not directly available. Nevertheless, they can be seen as the product of disease prevalence of disease  $r$  (denoted  $p(a, r)$ ), and per costs per patient for disease  $r$  related costs (denoted  $ac_r(a | r)$ ).

$$ac_r(a) = p(a, r) \times ac_r(a | r) \quad (6)$$

Equation 6 provides a framework to adjust average costs per capita for costs of usual care for related diseases that often are included in an economic evaluation but also are part of  $ac(a)$ .

Related costs are anticipated to be small when evaluating most interventions, given the relatively small number of people with each disease in a population. Exceptions are particularly likely in some public health interventions.<sup>17,24</sup> Note that when end-of-life costs are provided in an economic evaluation, these can also be used to adjust per-capita costs, because per patient costs for disease  $r$  are a weighted average of end-of-life costs and costs for those who are not in their last year of life:

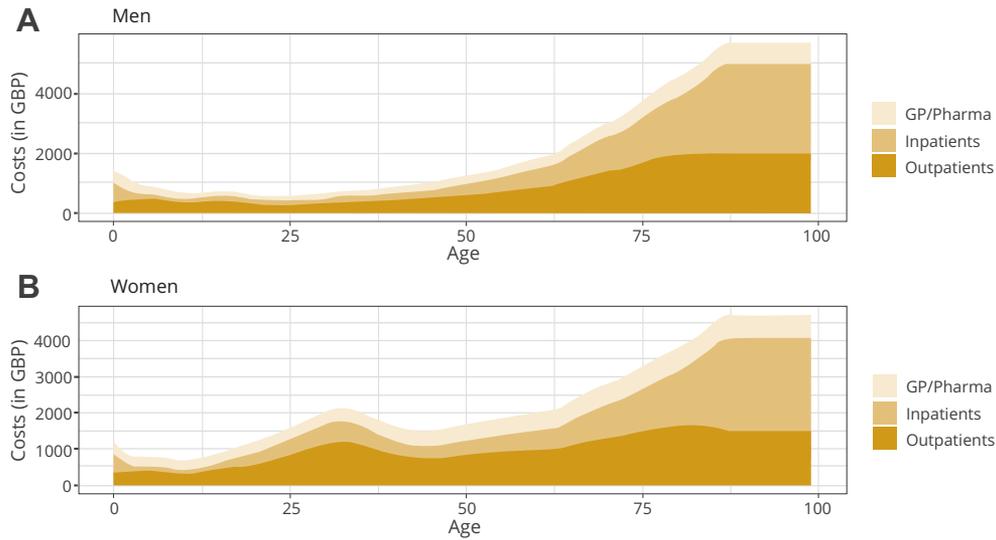
$$ac_r(a | r) = [1 - m(a | r)] \times sc_r(a | r) + m(a | r) \times dc_r(a | r) \quad (7)$$

Here,  $m(a | r)$  denotes the mortality rate at age  $a$  conditional on having disease  $r$ ,  $dc_r(a | r)$  denotes end-of-life/decedent costs for disease  $r$  conditional on having disease  $r$ , and  $sc_r(a | r)$  represents survivor costs, conditional on having the disease.

It is always a possibility that the participants in the intervention trial are not average consumers of healthcare, for example owing to comorbidities. Some diseases are known to be causally related, and thus it is expected that average healthcare costs for those with comorbidities would be higher than those of an average individual. In these cases, unrelated costs can be updated by obtaining comorbidity-specific costs that are not defined as related costs, separately for survivors and decedents if possible, and then adding these comorbidity costs to the unrelated cost.

It can also be beneficial to adjust for TTD, by disaggregating individual future unrelated medical costs, which is labeled as  $lhc_u$ , into the sum of survivor,  $sc_u(a)$ , and decedent,  $dc_u(n)$ , unrelated medical costs, where survivor costs are costs at each age,  $a$ , excluding the age at which the individual dies and decedent costs

**Figure 1.** Average medical costs by sector. Costs are adjusted for 2018 price levels.



are costs incurred in the last year of life (equation 8).  $b$  is the age at which the intervention is implemented, and  $n$  is the age at which the individual dies.

$$lh_{cu} = \sum_{a=b}^{n-1} sc_u(a) + dc_u(n) \quad (8)$$

Average unrelated medical costs by age therefore need to be split into survival costs,  $sc(a)$ , and decedent costs,  $dc(a)$ . This is shown in equations 9 to 11. Average medical costs,  $ac(a)$ , are a weighted average of decedent and survivor costs in a certain year. Total survivor and decedent costs from the provided average costs are calculated using mortality rates,  $m$ , and the ratio of medical costs between those dying and surviving,  $\phi(a)m\phi(a)$ . This decedent-survivor cost ratio is taken from previous literature, in which healthcare expenditure panel data is combined with TTD and age information to estimate these ratios.<sup>23</sup> Given equations 9 and 10, which provide the decomposition of  $ac(a)$  and the definition of  $\phi$ , respectively, we can derive  $sc(a)$  (Eq. 11), thereby facilitating the calculation of the aforementioned weighted average.

$$ac(a) = (1 - m(a)) \times sc(a) + m(a) \times dc(a) \quad (9)$$

$$dc(a) = \phi(a) \times sc(a) \quad (10)$$

$$sc(a) = \frac{ac(a)}{1 + (\phi(a) - 1) \times m(a)} \quad (11)$$

## Data

For present purposes, this article takes a healthcare perspective, aligned with NICE's brief. NICE is charged with appraising cost-effective use, covering National Health Service procedures and Personal and Social Services.<sup>25</sup> Given that Personal and Social Services does not cover all long-term care options, long-term care data are not included. Average per-capita healthcare spending data estimated by Asaria et al (2017) are used<sup>26</sup>; they used administrative Hospital Episode Statistics data<sup>27</sup> from 2011 along with aggregate data on the number of general practitioner (GP) visits in a year. These per-capita data are available for sex and each age up until 85+—an average for all ages above 84. Costs are

available for 3 sectors: inpatient care, outpatient care, and GP and pharmaceutical spending (Fig. 1). The data are further smoothed using cubic splines. For mortality data, 2011 statistics from the Office of National Statistics are used,<sup>28</sup> which provides population and cause-of-death figures for England and Wales by age and sex.

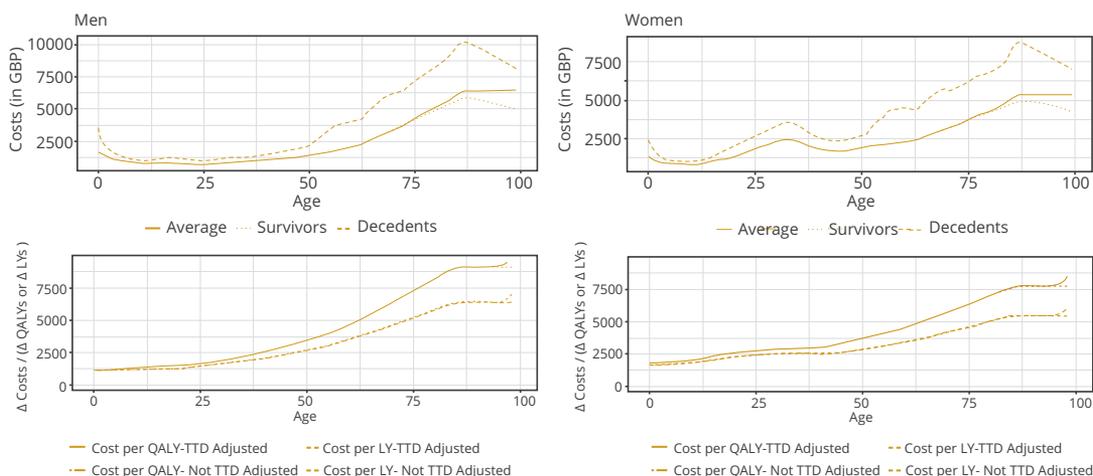
Decedent-survivor cost ratios estimated by Howdon et al (2018)<sup>23</sup> are used to adjust for TTD. The authors used Hospital Episode Statistics data from years 2005 to 2006 and 2011 to 2012. Ratios are available for inpatients age 50 onward. It is assumed that ages below 50 take the ratio provided for age 50. For outpatient and GP/pharmaceutical expenditure, the decedent-survivor ratio is assumed to be 1:1.

## Cases

Before delving into disease-specific cases, future unrelated medical costs for the average person are estimated, using a hypothetical intervention for which there are no intervention costs and only future costs—for example, saving someone from a car accident. This is applied to all ages and demonstrates the cost-effectiveness ratio of saving a life. Here, saving someone's life has no future related medical costs. Average future unrelated medical costs are summed for each age and divide by quality-adjusted life-years (QALYs) gained. To calculate QALYs, we multiply survival by quality-of-life estimates, from Heijink et al (2011).<sup>29</sup> They predict EuroQol 5-dimension scores by sex and age using UK value sets. For all cases, discount rates of 3.5% for both outcomes and costs are used, as recommended by NICE.

The first case based on existing research is osimertinib, a medication used to treat non-small-cell lung carcinomas.<sup>30</sup> The study by Bertranou et al (2018) compares osimertinib to platinum-based doublet chemotherapy in patients age 62 and above. It was recommended by NICE in 2016, with a 1.54 QALY gain and a £41 705 per QALY ICER. The second case is the use of midostaurin, a multitargeted protein kinase. In the study by Tremblay et al (2018),<sup>31</sup> midostaurin with the standard of care (SOC) is compared to SOC for newly diagnosed acute myeloid leukemia adult patients aged 48 years and above. There were life-year gains of 1.67 and QALY gains of 1.47. It was recommended for reimbursement by NICE in 2018 with ICERs of £30 263 per life-year and £34 327 per QALY. The third case is the use of transcatheter aortic valve

**Figure 2.** Average, survivor, and decedent individual medical costs (top) and saving a life at age *a* (bottom). Costs and outcomes in the lower graphs were discounted according to NICE guidelines—3.5% discount rate for both costs and outcomes. Costs are adjusted for 2018 price levels.



NICE indicates National Institute for Health and Care Excellence.

implantation (TAVI) compared with medical management (MM). Van Baal et al (2016)<sup>11</sup> estimate survival curves from Watt et al (2012),<sup>32</sup> who found an ICER of £16 100. They look at patients over age 80 and find a QALY gain of 1.24. Transcatheter aortic valve implantation was also recommended by NICE in 2017.

For the aforementioned cases, the original studies' survival curves were extracted. Comparator future unrelated medical costs were subtracted from intervention future unrelated medical costs. Unrelated costs are combined with survival curves, assuming a starting age of 62 years for the osimertinib case,<sup>30</sup> 48 years for the midostaurin case, and 80 years for the TAVI case, adjusting for related costs (mentioned in the original literature) and TTD. By dividing this difference in costs by the difference in QALYs, we are left with the increase in the ICER.

In the osimertinib case, specific costs of end-of-life care are provided; equation 7 can be used to estimate average related costs. In the TAVI case, the comorbidity of diabetes mellitus (DM) is adjusted for. Fifty-seven percent of patients who cannot undergo surgery for aortic stenosis suffered from prohibitive comorbidities. Studies have found that approximately 36% of those who have received TAVI have DM,<sup>33</sup> and that average costs for DM in the United Kingdom are approximately £3500.<sup>34</sup> Using this information, DM-specific costs are calculated for this population (by multiplying average costs by prevalence) before adding them to unrelated medical costs. We assume that average UK costs are transferable to England and Wales.

Costs per patient provided in our cases<sup>30,31</sup> and prevalence data for England and Wales from the UK Prevalence Project (2015)<sup>35</sup> are used for cancer prevalence, while the National Health Service Health Survey for England 2017 is used for cardiovascular disease prevalence.<sup>36</sup> Population mortality rates for both of the cancers in our cases were accessed from Cancer Research UK (2016).<sup>37,38</sup> For cardiovascular disease, 2014 mortality rates from the British Heart Foundation Cardiovascular Mortality Statistics are used.<sup>39</sup>

## Results

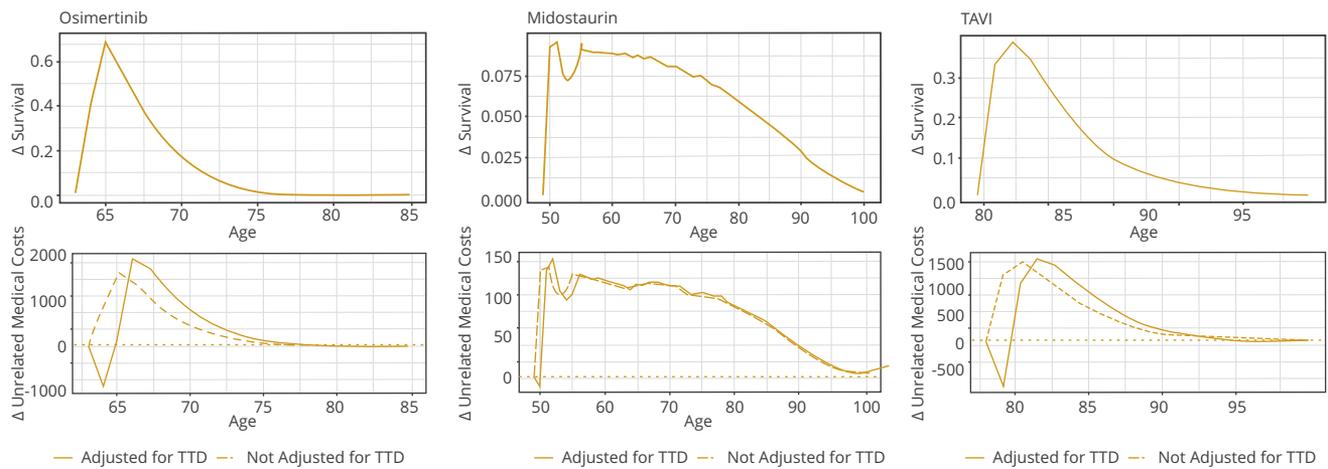
In this section, the case of saving a life is dealt with first. The upper graphs in Figure 2 show average future medical costs by age

and sex, independent of disease. Average costs and estimated decedent and survivor costs are displayed separately for men and women. The figure shows that decedent costs are higher than survivor costs at all ages, and that future medical costs increase with age. Furthermore, survivor future medical costs deviate from average future medical costs from age 80 onward, that is, when mortality rates substantially increase. The lower graphs show the change in future unrelated medical costs divided by the change in LYG and QALYs when a life is saved for free at age *a*, for both sexes. For example, saving a life at birth leads to an ICER of £1300 per QALY while saving a life at age 80 gives an ICER of £8000 per QALY. These graphs also show that adjusting for TTD has little impact on the ICERs.

The differences among all 3 cases' intervention and comparator for both survival rates (top) and future unrelated medical costs (bottom) are shown in Figure 3. For the osimertinib case, there is a dramatic difference in survival in the first years between patients who received the intervention and those who received the comparator, peaking at approximately 0.6. In the midostaurin case, the differences in survival are much smaller (~0.075) at the beginning between intervention and comparator and the decline in these differences is more drawn out. The difference in survival between TAVI and MM is still substantial, peaking at approximately 0.3 at age 83. Looking at the lower 2 graphs shows the difference in future unrelated medical costs between treatment and comparator, either adjusted or unadjusted for TTD. For all studies, the fact that survival in the treatment group is higher in the first years after treatment means that decedent costs are postponed by several years. This is shown clearly in Figure 3, where unrelated costs are larger for the comparator in the early years for TTD-adjusted estimates; lower survival means higher expected decedent costs in the early years after treatment.

Table 1 shows the difference between ICERs, including future medical costs where estimates are shown adjusted and unadjusted for TTD and double-counting (ie, excluding population average disease-specific costs from the estimate of unrelated costs), once again discounted according to NICE guidelines. The estimates are shown along with the reported change in LYG and QALYs and the ratio between these 2 variables because this is a further indicator of how large the impact of including future costs will be.<sup>2</sup> There is indeed an increase in all case ICERs. When

**Figure 3.** Difference in survival (top) and unrelated medical costs (bottom) for all 3 cases. Costs and outcomes were discounted according to NICE guidelines: 3.5% discount rate for both costs and outcomes. Costs are adjusted for 2018 price levels.



NICE indicates National Institute for Health and Care Excellence.

looking at the results when adjusted for TTD and double-counting, the ICER comparing osimertinib with PDC increased by £5112 (12%), the ICER for midostaurin and SOC versus SOC increased by £3167 (8%), and ICER for TAVI versus MM increased by £6345 (37%). In all cases, the difference in the ICERs resulting from adjusting for double counting is modest. Table 1 also shows that adjusting for TTD changes the ICER by between roughly £1000 and £2507 in our cases. Furthermore, by adjusting for comorbidities, TAVI costs increase by approximately an additional £1200 compared with only adjusting for TTD.

## Discussion

This article has a dual purpose: first, to show that the inclusion of unrelated healthcare costs can have potentially significant policy-relevant implications for healthcare systems requiring a systems perspective, and second, to demonstrate the feasibility of a method of including them. In addition, given that economic evaluations are conducted for a large variety of medical interventions, it is beneficial to have a standardized approach to including unrelated future medical costs. This article has provided

**Table 1.** Difference in ICERs, adjusted for TTD and related costs.

Intervention	Osimertinib vs PDC	Midostaurin vs SOC	TAVI vs MM
Age at start of intervention	62 years	48 years	80 years
Change in L ( $\Delta L$ )	3.12	1.67	1.8
Change in QALY ( $\Delta[L \times Q]$ )	1.54	1.47	1.24
Change in L/change in QALY	2.03	1.14	1.45
$\left(\frac{\Delta L}{\Delta[L \times Q]}\right)$ Reported $\Delta\text{Cost}/\Delta\text{QALY}$ $\left(\frac{\Delta[L \times C_r]}{\Delta[L \times Q]}\right)$	£42 956	£38 033	£16 905
$\Delta\text{Cost}/\Delta\text{QALY}$ : including future costs	£48 442 (5486)	£41 434 (3401)	£24 736 (7831)
$\Delta\text{Cost}/\Delta\text{QALY}$ : including future costs, adjusted for TTD	£47 191 (4235)	£40 760 (2727)	£22 379 (5474)
$\Delta\text{Cost}/\Delta\text{QALY}$ : including future costs, adjusted for TTD and comorbidity*	~	~	£23 578 (6673)
$\Delta\text{Cost}/\Delta\text{QALY}$ : including future costs, adjusted for double counting	£48 418 (5463)	£41 270 (3237)	£24 076 (7171)
$\Delta\text{Cost}/\Delta\text{QALY}$ : including future costs, adjusted for double counting and TTD	£47 225 (4269)	£40 594 (2561)	£22 308 (5403)
$\Delta\text{Cost}/\Delta\text{QALY}$ : including future unrelated costs, adjusted for double counting, TTD, and comorbidity*	~	~	£23 507 (6602)

Note. Difference between actual and reported ICER shown in parentheses. Costs and outcomes were discounted according to NICE guidelines—3.5% discount rate for both costs and outcomes. Costs, including original ICERs, are adjusted for 2018 price levels.

ICER indicates incremental cost-effectiveness ratio; L, life-years; MM, medical management; PDC, platinum-based doublet chemotherapy; QALY, quality-adjusted life-year; SOC, standard of care; TAVI, transcatheter aortic valve implantation; TTD, time to death.

\*Only diabetes mellitus taken as a comorbidity.

such an approach, along with a complementary online tool (<http://imta.shinyapps.io/PAIDUK>). It shows the importance of future unrelated medical costs being included in economic evaluation, and the impact of adjusting the calculations to take TTD and double counting into account.

By estimating the change in the ICER owing to hypothetically saving a life at each age (Fig. 2), we see that including future unrelated medical costs in economic evaluation leads to increases in the ICER. For example, if we were to save the life of a man (or woman) at age 75, the increase in the ICER due to unrelated future costs would be around £7500 (£6250) per QALY, and these changes to the ICER increase with age. These results mitigate the worry that including future unrelated medical costs in economic evaluation is particularly disadvantageous for diseases in children because we find increases in the ICER resulting from including these costs are lowest at the younger ages.

The results show that adjusting for double counting has a modest impact on our results because the interventions examined affect relatively small subsets of the population. This adjustment will be more important for public health interventions affecting larger populations. Adjusting for TTD had a substantial impact on the ICER in our case studies, with the larger effects showing in older populations, where death is relatively more expensive.

When comparing the 3 cases, there are a few further results worth noting: First, it appears that the older the target group, the larger the impact of including future unrelated medical costs. Given that costs are highest at older ages, increased survival in older target groups leads to comparatively higher differences in future unrelated medical costs between treatment and intervention. Second, in interventions with a target group with higher future medical costs than the population average, adjusting for relevant comorbidities leads to substantial increases in the ICER. This is unsurprising given that additional (costly) comorbidities will cause unrelated medical costs to increase. Third, the ratio of change in LYG to change in QALYs is a further indicator of the impact of including future costs—the larger the ratio, the larger the impact. In other words, interventions where QALY gains were primarily driven by life extensions were more affected by including these costs than interventions where QALY gains were driven by quality-of-life improvements.

Overall, including future unrelated medical costs appears to have a considerable impact on the ICER. Given that reimbursement decisions are not based solely on cost-effectiveness but on myriad factors, we cannot say with certainty that increases in the ICER would influence specific reimbursement decisions. Nevertheless, an increase of between 7% and 30% in the ICER could be enough to change reimbursement decisions. The fact that increases in the ICER are not of the same magnitude among the cases used shows that including future unrelated medical costs may lead to a shift in the hierarchy of which interventions are viewed as most cost-effective, mitigating bias towards life-extending interventions. Our results are presented in an online tool, in which our estimates of future medical costs can be accessed and adjusted for specific interventions, with options to adjust for TTD and double counting of related costs.

There are limitations to our approach. First, average medical costs are assumed to be the same for every person within an age and sex group. Although this can be somewhat rectified by subtracting related costs, there is the possibility that some patient groups will have different unrelated future costs, for example, as a result of being too weak for certain treatments. Second, the data used have some restrictions, for example, decedent-survivor ratios only being available from age 50 onward. Furthermore, these are average ratios, covering all inpatient expenditure. Wong et al<sup>22</sup>

show how drastically these ratios can differ from disease to disease in The Netherlands—for example, ratios at age 50 for lung cancer and diabetes are approximately 1000 and 7, respectively. The framework provided suggests adjusting for related costs before TTD, independent of whether related end-of-life costs are available, thereby assuming that the ratio of decedent-survivor costs is the same for both average and related costs. Third, medical expenditure data for England and Wales, compared with similar data for The Netherlands, are low. Given that England and Wales and The Netherlands spend comparable proportions of their gross domestic product on healthcare, it can be assumed that this is due to the collection of the data (bottom-up vs top-down) and long-term care not being included in our estimations. Our results for average unrelated future medical costs for England and Wales are in line with similar work by Briggs et al (2018), suggesting that these differences are country specific rather than solely attributable to our study. Fourth, 2011 data are used as a starting point for our costs, assuming that current spending patterns remain constant over time. Finally, we do not explicitly address the uncertainty around our estimates, which could stem from either survival gains or unit costs. Going back to the conceptual model presented in the Methods section, specifically equation 1, the addition of unrelated medical costs per QALY to the ICER can be written as  $\frac{\Delta[L \times C_U]}{\Delta[L \times Q]}$ . Owing to life-years ( $L$ ) being in both the numerator and denominator, uncertainty surrounding survival cancels out. Quality-adjusted life-years are provided by the cases used, and therefore our main source of uncertainty is in the unit costs themselves. As the original average costs are calculated from population-wide data, uncertainty is of relatively little concern here. Nevertheless, there are still sources of uncertainty, specifically the age pattern of costs and decedent-cost ratios. Estimating these ratios for England and Wales is beyond the scope of this article; however, these are relevant and interesting avenues for future research.

As this is the first work to present a standardized option for the inclusion of future unrelated costs for England and Wales, there is much future research to be considered. It may be beneficial to test the assumption that during LYG, unrelated medical costs are equal to per-capita average medical costs, using disease-specific patient data. Furthermore, previous literature<sup>40</sup> has provided an estimate of the NICE cost-effectiveness threshold, using supply-side data. They find marginal medical expenditure per QALY and suggest this as a threshold for NICE. It would be worth estimating the impact of the inclusion of future medical costs on this estimate because excluding them would lead to inconsistency between ICER and threshold estimates.

To conclude, this article provides an important methodological contribution outlining how future unrelated medical costs can be included in health technology assessment. It also demonstrates how these methods apply for England and Wales and provides an online tool for doing so in practice.

## Acknowledgments

We thank all discussants from the Health Economists' Study Group Winter 2019 and lowlands Health Economists' Study Group 2019 conferences for their useful comments on this article. Thanks go to Daniel Howdon for providing data on decedent-cost ratios. Furthermore, we would like to thank Matthijs Versteegh and the institute of Medical Technology Assessment for hosting the UK PAID tool and Klas Kellerborg for his input on building the tool itself.

Contributions to the paper are funded by the Horizon 2020 research and innovation program (grant agreement no. 754936) and part of the COMPAR project, work package 6 (<https://self-management.eu/compar-eu-project/work-packages/work-package-6/>).

## REFERENCES

1. de Meijer C, Wouterse B, Polder J, Koopmanschap M. The effect of population ageing on health expenditure growth: a critical review. *Eur J Ageing*. 2013;10(4):353–361.
2. Meltzer D. Accounting for future costs in medical cost-effectiveness analysis. *J Health Econ*. 1997;16(1):33–64.
3. de Vries LM, van Baal PHM, Brouwer WBF. Future costs in cost-effectiveness analyses: past, present, future. *Pharmacoeconomics*. 2019;37:119–130.
4. Laudicella M, Martin S, Li Donni P, Smith PC. Do reduced hospital mortality rates lead to increased utilization of inpatient emergency care? A population-based cohort study. *Health Serv Res*. 2018;53(4):2324–2345.
5. Sanders GD, Neumann PJ, Basu A, et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. *JAMA*. 2016;316(10):1093–1103.
6. Versteegh M, Knies S, Brouwer W. From good to better: new Dutch guidelines for economic evaluations in healthcare. *Pharmacoeconomics*. 2016;34:1071–1074.
7. van Baal P, Morton A, Brouwer W, Meltzer D, Davis S. Should cost effectiveness analyses for NICE always consider future unrelated medical costs? *Br Med J*. 2017;359:j5096.
8. van Baal P, Morton A, Meltzer D, Brouwer W. Future unrelated medical costs need to be considered in cost effectiveness analysis. *Eur J Health Econ*. 2019;20(1):1–5.
9. Morton A, Adler AI, Bell D, et al. Unrelated future costs and unrelated future benefits: reflections on NICE guide to the methods of technology appraisal. *Health Econ*. 2016;25(8):933–938.
10. Culyer AJ. Cost, context, and decisions in health economics and health technology assessment. *Int J Technol Assess Health Care*. 2018;34(5):434–441.
11. van Baal P, Meltzer D, Brouwer W. Future costs, fixed healthcare budgets, and the decision rules of cost-effectiveness analysis. *Health Econ*. 2016;25(2):237–248.
12. van Lier LI, Bosmans JE, van Hout HP, et al. Consensus-based cross-European recommendations for the identification, measurement and valuation of costs in health economic evaluations: a European Delphi study. *Eur J Health Econ*. 2018;19(7):993–1008.
13. Morris S, Devlin N, Parkin D. *Economic Analysis in Health Care*. John Wiley & Sons; 2007.
14. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the panel on cost-effectiveness in health and medicine. *JAMA*. 1996;276(15):1253–1258.
15. van Baal PHM, Wong A, Slobbe LCJ, Polder JJ, Brouwer WBF, de Wit GA. Standardizing the inclusion of indirect medical costs in economic evaluations. *Pharmacoeconomics*. 2011;29(3):175–187.
16. Briggs ADM, Scarborough P, Wolstenholme J. Estimating comparable English healthcare costs for multiple diseases and unrelated future costs for use in health and public health economic modelling. *PLoS One*. 2018;13(5):e0197257.
17. van Baal PHM, Hoogendoorn M, Fischer A. Preventing dementia by promoting physical activity and the long-term impact on health and social care expenditures. *Prev Med*. 2016;85:78–83.
18. Gandjour A, Lauterbach KW. Does prevention save costs?: considering deferral of the expensive last year of life. *J Health Econ*. 2005;24(4):715–724.
19. Blakely T, Atkinson J, Kvizhinadze G, Nghiem N, McLeod H, Wilson N. Health system costs by sex, age and proximity to death, and implications for estimation of future expenditure. *N Z Med J*. 2014;127(1393):12–25.
20. van Baal P, Perry-Duxbury M, Bakx P, Versteegh M, van Doorslaer E, Brouwer W. A cost-effectiveness threshold based on the marginal returns of cardiovascular hospital spending. *Health Econ*. 2019;28(1):87–100.
21. Zweifel P, Felder S, Meiers M. Ageing of population and health care expenditure: a red herring? *Health Econ*. 1999;8(6):485–496.
22. Wong A, van Baal PHM, Boshuizen HC, Polder JJ. Exploring the influence of proximity to death on disease-specific hospital expenditures: a carpaccio of red herrings. *Health Econ*. 2011;20(4):379–400.
23. Howdon D, Rice N. Health care expenditures, age, proximity to death and morbidity: implications for an ageing population. *J Health Econ*. 2018;57:60–74.
24. van Baal PH, Feenstra TL, Polder JJ, Hoogenveen RT, Brouwer WB. Economic evaluation and the postponement of health care costs. *Health Econ*. 2011;20(4):432–445.
25. McCabe C, Claxton K, Culyer AJ. The NICE cost effectiveness threshold: what it is and what it means. *Pharmacoeconomics*. 2008;2(9):733–744.
26. Asaria M. Health care costs in the English NHS: reference tables for average annual NHS spend by age, sex and deprivation group 2017;1–19
27. Asaria M, Grasic K, Walker S. Using linked electronic health records to estimate healthcare costs: key challenges and opportunities. *Pharmacoeconomics*. 2016;34(2):155–160.
28. Office for National Statistics (United Kingdom). Deaths by single year of age tables - UK; 2018.
29. Heijink R, van Baal P, Oppe M, Koolman X, Westert G. Decomposing cross-country differences in quality adjusted life expectancy: the impact of value sets. *Population Health Metrics*. 2011;9(1):17.
30. Bertranou E, Bodnar C, Dansk V, Greystoke A, Large S, Dyer M. Cost-effectiveness of osimertinib in the UK for advanced EGFR-T790M non-small cell lung cancer. *J Med Econ*. 2018;21(2):113–121.
31. Tremblay G, Dolph M, Patel S, Brandt P, Forsythe A. Cost-effectiveness analysis for midostaurin versus standard of care in acute myeloid leukemia in the United Kingdom. *Cost Eff Resour Alloc*. 2018;16:33.
32. Watt M, Mealing S, Eaton J, et al. Cost-effectiveness of transcatheter aortic valve replacement in patients ineligible for conventional aortic valve replacement. *Heart*. 2012;98(5):370–376.
33. Puls M, Bleckmann A, Jacobshagen C, et al. Diabetes increases short- and long-term mortality after transcatheter aortic valve implantation (TAVI). *Dtsch Med Wochenschr*. 2014;139(16):822–828.
34. Kanavos P, van den Aardweg S, Schurer W. *Diabetes expenditure, burden of disease and management in 5 EU countries*. LSE Health. London School of Economics; 2012.
35. 20-year cancer prevalence in the UK. Public Health & Macmillan. [http://www.ncin.org.uk/about\\_ncin/segmentation](http://www.ncin.org.uk/about_ncin/segmentation). Accessed September 1, 2019.
36. Health survey for England 2017. National Health Service. <https://digital.nhs.uk/data-and-information/publications/statistical/health-survey-for-england/2017>. Accessed September 1, 2019.
37. Acute myeloid leukaemia (AML) statistics. Cancer Research UK. <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/leukaemia-aml#heading-Zero>. Accessed September 1, 2019.
38. Lung cancer statistics. Cancer Research UK. <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer>. Accessed September 1, 2019.
39. Cardiovascular disease statistics 2014. British Heart Foundation. <https://www.bhf.org.uk/informationsupport/publications/statistics/cardiovascular-disease-statistics-2014>. Accessed September 1, 2019.
40. Claxton K, Martin S, Soares M, et al. Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. *Health Technol Assess*. 2015;19(14):1–503. v-vi.