NICE's end of life criteria: who gains, who loses?

Marissa Collins and **Nicholas Latimer** quantify the impact of raising the cost effectiveness threshold for end of life drugs and find that the effect on other NHS services could be substantial

In January 2009 the National Institute for Health and Clinical Excellence (NICE) introduced supplementary advice to improve NHS access to end of life treatments. The advice means that treatments for patients with short life expectancy can exceed NICE's cost effectiveness threshold of £30 000[1] (€35 000; $45 000) per quality adjusted life year (QALY) provided that they are for patients with a short life expectancy, they extend life by at least three months compared with current NHS treatment, and apply to small patient populations.[2]

The advice gives increased access to drugs for patients who need them, but, since the cost of the new treatments has to come from somewhere in a fixed NHS budget, funding of drugs under the end of life criteria has important implications for the NHS and patients. The applicability of the supplementary advice to cancer drugs refused by NICE before 2009 has been analysed.[3] However, the wider potential costs and benefits to the NHS have yet to be quantified. We estimate the effect of the end of life criteria on the NHS in England and Wales since they were introduced in 2009.

Funding decisions

NICE normally recommends a new intervention if its incremental cost effectiveness ratio (ICER) is below £20 000 per QALY gained.[1] The ratio is calculated by dividing the incremental costs of an intervention by its incremental QALY gain compared with standard treatment.

If the ratio is above £20 000/QALY the appraisal committee will take other factors into account. As the ratio increases from £20 000 to £30 000, there must be a stronger case for supporting the intervention based on the degree of certainty in the ICER, inadequately captured quality of life benefits, or innovation.[1]

When NICE recommends a new intervention that imposes additional costs on the NHS, the funds required must be found by disinvesting from other interventions. This will inevitably result in health losses for other patients. Thus ideally the threshold should represent the additional cost that has to be imposed on the system to forgo one QALY of health through disinvestment elsewhere.

However, NICE suggests that to calculate this ideal threshold accurately would require information on the costs and QALYs associated with all competing healthcare programmes.[4] As this information is not readily available NICE uses the

---

Assumptions made for analysis

- No additional social value to generating additional health in patients at end of life compared to patients not at the end of their lifetimes
- Comparators are those used in the cost effectiveness analysis of the NICE appraisal
- Newly recommended drugs are 100% taken up by the estimated patient population
- Cost effective treatments, for all disease areas, are displaced as a result of funding end of life treatments
- On average the NHS obtains 1 QALY for every £20 000-£30 000 spent
- QALYs gained and lost are of equal value regardless of who accrues or loses them

---

£20 000 to £30 000 threshold range as a guide to decision making.[1]

The end of life criteria adopted by NICE allow interventions with an (unweighted) ICER over £30 000 to be recommended if the appraisal committee judges that the QALY weighting required to reduce the ratio below £30 000 represents a plausible reflection of public preferences. The assumption behind the criteria is that society values QALYs obtained by patients at the end of life more highly than QALYs obtained by other patients. However, there is little evidence to support this assumption, and evidence is building against end of life weighting, most recently with the publication of a report by the NICE Decision Support Unit.[5]

If the assumption is wrong, and there is no additional social value to generating additional health in patients with a short life expectancy, patients with other diseases could unfairly suffer as a result of decisions to fund end of life treatments over the threshold. The losses will be greater than the gains from recommended end of life treatments if we assume that QALYs are of equal value regardless of who accrues them and if end of life treatments are less cost effective than the displaced services.

We have determined the number of QALYs forgone by the NHS as a result of funding new end of life treatments, under the premise that society does not give more value to end of life QALYs.

Impact of end of life criteria

We reviewed documents relating to appraisals completed between 2009 and December 2011 to identify the interventions that met the end of life criteria and determine which had been recom-

mended. From these documents we extracted the ICER, the incremental costs and QALYs and the number of patients in England and Wales who could benefit from the new treatment each year. We used the same comparator in our analyses as that used in NICE's cost effectiveness analyses. Occasionally this may represent only a proxy for the "real world" comparator, if several treatments are used in reality. However, as we are analysing interventions for end stage diseases, the comparators were often "best supportive care." In addition, we assumed that the newly recommended drugs are taken up by all of those eligible (box).

Using this information we calculated the total additional costs to the NHS of providing the new intervention rather than its most appropriate comparator (incremental cost of intervention×patient population) as well as the total change in QALYs gained (incremental QALYs×patient population).

Next, we estimated the number of QALYs displaced by the additional cost of the new treatment, assuming that on average the NHS obtains one QALY for every £30 000 spent on healthcare (additional cost/£30 000).[3] The QALYs displaced represent an estimate of the QALYs that would have been obtained if the funds spent on end of life interventions were instead spent on any alternative treatments. This figure can be used to calculate the net effect on QALYs associated with the adoption of the new treatment (QALYs displaced by the additional cost of the new treatment–QALYs gained by providing the new treatment).

We repeated the process using the lower cost effectiveness threshold value of £20 000 per QALY gained,[1] assuming that one QALY is obtained for every £20 000 spent on healthcare.

Between January 2009 and December 2011 NICE's appraisal committee discussed 24 interventions to determine if they met the end of life criteria. Fourteen interventions met the criteria, of which nine were approved for NHS use (table 1).[6-14]

Table 2 shows the total additional cost of providing these new interventions and their net effect on QALYs, using a cost per QALY gained threshold of £30 000 and £20 000. We estimate that 5933 QALYs are lost annually, assuming one QALY can be obtained for every £30 000 spent or 15 098 QALYs if the £20 000 threshold is used. The additional cost to the NHS of providing the new interventions analysed between 2009 and 2011 is over £549m a year based on the population figures presented in the appraisals (table 2).

Table 1 | Incremental costs and QALYs gained from end of life interventions approved by NICE, 2009-11

Year	Intervention	Indication	Incremental cost (£)	Incremental QALYs	Incremental cost effectiveness ratio* (£)
2009[6]	Sunitinib	Metastatic renal cell carcinoma	31 291	0.59	53 793
2009[7]		Gastrointestinal stromal tumours	15 928	0.50	31 856
2009[8]	Lenalidomide	Multiple myeloma after one previous therapy	54 291	1.24	43 783
2009[9]	Topotecan	Small cell lung cancer	6 194	0.18	33 847
2010[10]	Trabectedin	Advanced soft tissue sarcoma	18 458	0.54	34 501
2010[11]	Pemetrexed	Non-small cell lung cancer (maintenance)	13 379	0.28	46 993
2010[12]	Trastuzumab	Gastric cancer (HER2-positive metastatic)	12 332	0.25	49 061
2011[13]	Pazopanib	Renal cell carcinoma (first line metastatic)	27 900	0.72	38 912
2011[14]	Azacitidine	Myelodysplastic syndromes	75 975	1.57	48 392

*Figures may not be exact due to rounding.

Table 2 | Additional costs of new end of life treatments and net effect on QALYs assuming one QALY would have been obtained for every £30 000 or £20 000 spent*

Drug	No of eligible patients/year in England and Wales	Total change in costs (£)	Total QALYs gained	QALYs displaced by new treatment		Net effect on QALYs	
				£30 000/ QALY	£20 000/ QALY	£30 000/ QALY	£20 000/ QALY
Sunitinib (renal cell carcinoma)	3095	98 795 495	1 837	3 293	4 939	−1 457	−3 103
Lenalidomide	3562	193 384 542	4 417	6 446	9 669	−2 029	−5 252
Sunitinib (gastrointestinal stromal tumour)	240	3 822 720	120	127	191	−7	−71
Topotecan	1600	9 910 400	293	330	496	−38	−203
Trabectedin	600	11 074 800	321	369	554	−48	−233
Pemetrexed	4642	62 105 318	1 322	2 070	3 105	−749	−1 784
Trastuzumab	492	6 067 644	124	202	303	−79	−180
Pazopanib	4000	111 600 000	2 868	3 720	5 580	−852	−2 712
Azacitidine	700	53 182 500	1 099	1 773	2 659	−674	−1 560
Total	18 931	549 943 419	12 401	18 330	27 496	−5 933	−15 098

*Figures may not be exact due to rounding.

It is not clear that society would place a higher weight on extending life if the quality of that life was poor

Our analysis shows that use of NICE's end of life criteria has resulted in substantial QALY losses. We have assumed that the cost of end of life drugs is met entirely through displacement of other services or treatments in the NHS. Although we do not know whether this has been the case, as the NHS budget is under increasing strain, it seems reasonable to assume that disinvestment will be required. To put the losses into context, the £549m that we estimated has been spent on the nine end of life treatments each year is more than the £505m it cost to provide dialysis for the 21 544 patients with kidney failure in England in 2009.[15]

What does society want?

The reallocation of resources to end of life interventions may be acceptable if society truly values QALYs gained through an extension of life when a patient has a terminal illness more highly than those gained at any other time of life. In this case it would be valid to apply weights to QALYs for end of life treatments, and the QALY loss would represent societal preferences. This is explored by Linley et al,[16] who conducted a choice based experiment in the UK using web based surveys to explore societal preferences for several prioritisation criteria currently in place, including the end of life criteria. They found that only 34% of the 4118 respondents, with all else being equal, would prioritise patients with a reduced life expectancy. So far only cancer drugs have met the end of life criteria. Linley et al[16] found no evidence to support the claim that, all else being equal, society places a higher value on health benefits to patients with cancer.

In addition, it is not clear that society would place a higher weight on extending life if the quality of that life was poor. Instead, improvements in quality of life might be preferred. However, in a choice experiment Shah et al[5] showed that a gain in life expectancy without a gain in quality of life was preferred to an increase in quality of life with no gain in life expectancy, suggesting that focusing on extensions of life rather than improvements in the quality of life may be consistent with societal preferences.[5]

A further concern with the end of life criteria surrounds the "small patient population" criterion, which seems unlikely to reflect societal preferences. The inclusion of this criterion suggests concern about the budgetary impact of funding end of life interventions. However, even with this criterion in place we have shown that the estimated annual additional cost is high, and it is likely to grow as more research and development are invested in end of life interventions. Indeed, our analysis shows that the annual cost of funding drugs recommended on the basis of the end of life criteria (£549m) is substantially greater than the £200m ring fenced for the Cancer Drugs Fund. This fund was set up in England in 2011 to improve access to cancer drugs that had not been recommended or had been restricted by NICE on the basis of cost effectiveness.[17]

A key limitation of our analysis is that we assume that on average the NHS obtains one QALY for every £20 000-£30 000 spent, based on the traditionally accepted NICE cost effectiveness range.[1] Recently researchers have attempted to calculate an empirical estimate of the cost effectiveness threshold by analysing the benefits forgone as a result of marginal reductions in the effective budget generated by uptake of interventions recommended by NICE. This work estimates that the threshold is £18 317 per QALY.[18]

Regardless of the actual value, we have shown that the end of life criteria will result in QALY losses when the average cost per QALY gained obtained by the NHS is below the ICERs associated with the recommended end of life interventions, assuming that a QALY has the same value no matter who accrues it.

Our analysis has shown that if society does not place a higher value on QALYs obtained at the end of life, the application of the NICE end of life criteria is likely to have resulted in substantial QALY losses and budgetary pressures to the NHS and population in England and Wales, as cost effective interventions are displaced in favour of less cost effective interventions. If society does give more value to QALYs gained by people at the end of life the cost effectiveness threshold may need to change to reflect this.

Marissa Collins health economics researcher, Glasgow Caledonian University marissa.collins@gcu.ac.uk
Nicholas Latimer research fellow in health economics, ScHARR, University of Sheffield