Estimating a cost-effectiveness threshold for the Spanish NHS

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ABSTRACT

The cost of generating a Quality-Adjusted Life Year (QALY) within a National Health Service (NHS)provides an approximation of the average opportunity cost of funding decisions. This information can be used to inform a cost-effectiveness threshold. The aim of this paper is to estimate the cost per QALY at the Spanish NHS. We exploit variation across 17 regional health services and the exogenous changes in expenditure that took place as a consequence of the economic crisis over five years of data. We conduct fixed effect models and use an instrumental variable approach to test for potential remaining endogeneity. Our results show that health expenditure has a positive and significant effect on population health, with an average spending elasticity of 0.07. This translates into a cost per QALYof between 21,000€ and 24,000€. These values are below the cost-effectiveness threshold figure of 30,000€ commonly cited in Spain.

1. INTRODUCTION

Cost-effectiveness analysis (CEA)results are usually summarised by the incremental cost-effectiveness ratio (ICER), defined as the incremental cost divided by the incremental effectiveness of two competing alternatives, using Quality-Adjusted Life Years (QALYs) as the measure of effectiveness. However, CEA evidence supplied as the incremental cost per QALY gained of competing health technologies is not enough

to ultimately make adoption or otherwise recommendations on the basis of cost-effectiveness. For decision-making, the ICER of a technology needs to be compared with a value that indicates the maximum amount considered acceptable to be paid for health gains in the health system, i.e. the cost-effectiveness threshold. This value is unknown in most health care systems.

A recent review of studies estimating a cost-effectiveness threshold identified 38 studies (Vallejo-Torres et al., 2016). The studies were driven by different views as to what the threshold ought to represent. The two main conceptual perspectives are that the threshold should reflect: i) society's monetary valuation of health gains, or ii) the opportunity cost resulting from the disinvestment required to adopt a new technology (Baker *et al.*,2011). A consultation among experts conducted in Spain concluded that both approaches should be explored in order to inform a cost-effectiveness threshold in Spain (García-Lorenzo *et al.*, 2015). Some authors have,however, emphasised that when facing a fixed health care budget, information on the opportunity cost of funding decisions is most relevant as it provides a basis to assess whether the health expected to be gained from the use of a new technology exceeds the health expected to be forgone as other services are necessarily displaced (Claxton *et al.*, 2015).

The aforementioned literature review (Vallejo-Torres *et al.*, 2016) and the consultation process (García-Lorenzo *et al.*, 2015)were part of a project commissioned by the Spanish Ministry of Healthto provide evidence on how to estimate a cost-effectiveness threshold for the Spanish National Health Service (SNHS). Following these, this paper focuses ona firstempirical estimation of the opportunity cost of health care funding decisions in Spain.

To do so,this study estimates the average cost per QALY at which the SNHS currently operates. The cost per QALY reveals how much health is lost when services currently

provided by the systemare displaced, and have been suggested as a proxy of the average opportunity cost value that can be used to inform a cost-effectiveness threshold (Claxton *et al.*, 2015).

We use data across the 17 regional health services that compose the SNHS over the period 2008-2012, whenthe health budgetexperienced considerable exogenous cuts due to the economic crisis. We exploit variations between regions and over time to estimate the impact of health spending on health outcomes, measured as Quality-Adjusted Life Expectancy (QALE). The estimated effect is then translated into the cost per QALY for the SNHS, providing a measure of the scale of theopportunity cost of health care funding decisions in Spain.

1.1.Previous studies

Measuring the average cost per QALY in a health care system involves estimating the impact of health care expenditure on health outcomes, i.e. the health spending elasticity of health. This has been the focus of severalprevious studies.

Gallet & Doucouliagos (2015)conducted a quantitative review of 65 studies estimating the relationship between health outcomes and health expenditure. The authors estimated meta-regressions on the health spending elasticityusing 885 estimates; 629 observations for mortality and 256 observations for life expectancy (LE). The results showed that "*spending elasticity for mortality is in the neighborhood of -0.10, whereas it is roughly equal to 0.02 for life expectancy*".

There are also a series of studies that have estimatedthe cost per Life Year (LY)basedon the estimated health spending elasticity. For example, Lichtenberg (2004) estimated a cost of $11,000 per LY in the USA using time series data from 1960-1997. In Spain, Puig-Junoy and Merino-Castello (2004) applied a similar methodology using health

spending and LE at birth from 1960-2001, and estimated a cost per LY of under13,000€.

Some studies have adjusted the estimated impact on mortality to account for Health Related Quality of Life (HRQoL) in order to approximate the estimation to the marginal cost of a QALY. For example,Martin *et al.*(2008; 2011) measured the cost per QALY for specific diseasesusing administrative data for Primary Care Trusts in England. The most recent of these papers used spending data from 2005/06 for five diseases.Their results ranged from £12,593 per QALY for cardiovascular diseases to£47,069 per QALY for diabetes. Claxton *et al.*(2015)useda similar approach but provided an estimate for each of the 23 disease programmes using expenditure data from 2008/09 and combined the disease-specific values to arrive at a central estimateof £12,936 per QALY in England.

1.2.Spanish health financing system

The SNHSexperienced a decentralisation process that started in the early 1980's and was completed in 2002, when all seventeen regions, named Autonomous Communities (ACs),that form the country were responsible for planning and delivery of their own health services. Therefore, the SNHS consists of 17 different regional health services that hold over 92% of the overall national health budget; the rest correspond to central government administration services.

Health care is financed through general taxation collectedby both the central and regional governments. The central government then allocates a budget across regions to meet the provisionof the following public services for which ACs are responsible: health, education, social services and other general services such as culture, housing and infrastructure. There is an allocation mechanism to compute the corresponding

sharestransferred from the central administration to each region[1]. The allocation mechanismis based on a set of weighting indicators that take into account demographic and geographical factors (de la Fuente, 2015). Based on these factors, the central government allocatesa total budget across regions, and each region then decides how to distribute their budget across the public services for which they are responsible.

Over the period of analysis, health spending was substantially reduced in Spain as a consequence of the economic crisis and subsequent health budget cutsand stringent requirement for ACs to meet deficit reduction goals. As a result, health spending decreased by nearly 10% between 2009 and 2012[2].

2. METHODS

2.1.Econometric approach

2.1.1. Fixed effect models

We create a longitudinal panelof 5 years of data (2008-2012) ofregion-level information across ACs in Spain.We run Ordinary Least Squares (OLS) models controlling for region and year fixed effects, and a comprehensive set of time- and region-variant indicators. The model takes the form:

$$log(H_{jt}) = \beta log(Exp_{jt-1}) + \delta X_{jt-1} + \gamma_t + \mu_j + \varepsilon_{jt} \quad \text{Eq. 1}$$

- H_{jt} is the population health variable observed for region *j* at time *t*,
- Exp_{t-1} is the lagged health expenditure variable of region *j* in year *t-1*,
- $X_{jt-1}$is a set of other lagged attributes of region *j* in year *t-1*,

[1]Except for the Basque Country and Navarre which account for a specific financing system, and for Ceuta and Melilla, which are centrally managed due to their small size.
[2]Available from http://www.msssi.gob.es/en/estadEstudios/estadisticas/inforRecopilaciones/gastoSanitario2005/home.htm

- γ_t is a fixed effect for year *t*,
- μ_j is a fixed effect for region *j*,
- ε_{it} is a disturbance term.

H and *Exp* have been log transformed, and therefore the β parameter estimate can be interpreted as an elasticity.The lag structure allow for the fact that the impact on health is not likely to occur contemporaneously with expenditure, as a delay in accruing a health benefit is expected.

2.1.2. IV models

Fixed effects are used as a means ofaddressingendogeneity. However, these modelsmay not capture all sources of variation within regions and years that correlate with expenditure and health outcomes; in that casesome degree of endogeneity might remain. We use an IV approach to test and address for this potential endogeneity problem. The performance of the IV estimators critically relies on the validity of the instruments, which have to satisfy two properties: they have to be highly correlated with the variables being instrumented (relevance of instruments); and, they must be uncorrelated with the error term of the healthoutcomes equation conditional on the other covariates in the model (orthogonalityrequirement). We test for the relevance property based on an F-test of the significance of the instruments in thefirst-stage equation. The orthogonality requirement cannot be formally tested and mainly relies on face validity arguments. If a larger number of instruments than endogenous variables are available, thena test of overidentifying restrictions can partly explore the validity of such set of instruments (e.g., Hansen-Sargan test).We test for exogeneity using auxiliary regressions (Davidson & MacKinnon, 1993). If we fail to reject the null hypothesis of exogeneity then, assuming the instrumentsare valid, OLSmodelsyield consistent parameter estimates.

We use the percentage of total public expenditure assigned to health as an instrument to test for the potential remaining endogeneity. This variable is expected to influence how much a region spends on health per capita, as the larger the percentage of total public expenditure that is allocated to health, the larger the per capita health expenditure a region would be able to incur, all else equal. Conditionally on the model covariates, the percentage of public expenditure allocated to health should not affect the health of the population, rather than via the impact that this variable has on variations in health expenditure per capita. For instance, it might be the case that spending proportionally more on health is correlated with lower/higher expenditures on other public services that also affect population health, such as education or social deprivation policies. However, our models include a comprehensive list of indicators (see below) controlling for this potential correlation, such as educational attainment, poverty risk, unemployment rates, GDP, etc. as well as regional and year effects.

2.2.*Data*

2.2.1. Health variable

Our measure of health is Quality-Adjusted Life Expectancy (QALE). QALE provides a comprehensive measure of health outcomes that is relevant for all SNHS activities, and allows the estimationof the impact of expenditure on mortality as well as on HRQoL. LE by region and year are computedby the Office of National Statistics (ONS) in Spainbased on mortality rates published in Life Tables[3].

We combine the information on LE with information on HRQoL to adjust LE by health status. The most widely used methodology to apply this adjustment is the Sullivan method (Sullivan, 1971) used to compute disability-free life expectancies applyinga

[3] Available from http://www.ine.es/jaxi/menu.do?type=pcaxis&path=%2Ft20%2Fp319a&file=inebase&L=0

dichotomous disability variable. We use a similar approach but applied data on EQ-5D weights to undertake this adjustment. This allows us to create a LE variable adjusted for HRQoL on a QALY scale. To do this we adjust the number of years lived in each age rangeaccording toLife Tables, multiplying them by the average EQ-5D scores by age and gender (Gaminde & Roset, 2001).

QALE values provide the expected number of healthy years that individuals of a certain age are expected to live. We conducted regressions of QALE at each age ($QALE_x$, x = at birth, 1 year , 5 years, 10 years,…, 95 years). In addition to estimating the impact of health expenditure on QALE at given ages, we also estimated the impact on the average QALE of the population. The latter is computed as follows, where w_x is the share of the population in age group x (Lichtenberg, 2004):

$$QALE_{pop} = \sum w_x \, QALE_x \qquad \text{Eq. 2}$$

2.2.2. Quality of life variable

The only source of Spanish nationally representative EQ-5D data is the SpanishHealth Survey (SHS) conducted in 2011/12. There are two other surveys, the SHS in2006/07 and the European Health Interview Survey (EHIS) conducted in Spain in 2009/10,which did not include EQ-5D but included a series of other health and socioeconomic indicators. We use these surveys[4] to generate predicted EQ-5D values that allow us to create a time-variant HRQoL indicator used to adjust LE information.

EQ-5D models are stratified by gender and age groups (15-44, 45-64 and 65 or more years). In each case we use generalised linear models (GLM) with log link function and gaussian variance on HRQoL decrements, i.e. on 1 minus reported EQ-5D values. The models take the form:

[4] Available from http://www.msssi.gob.es/estadisticas/microdatos.do

$$(1 - EQ5D_i) = \alpha + \rho H_i + \tau Soc_i + \varepsilon_i \quad \text{Eq. 3}$$

- $EQ5D_i$ is the EQ-5D score of individual *i*
- H_i is a set of health-related indicators of individual *i*
- Soc_i is a set of socioeconomic characteristics of individual *i*
- ε_i is a disturbance term.

The predictors included in the models are: age; self-assessed health; whether or not the individual has one of the 7 longstanding illnesses that were included across all surveys; and whether or not the respondent experienced no limitations, moderate or severe limitations on daily activities in the past 6 months.

Individuals might report different levels of EQ-5D due to differences in reporting behaviournot related to differences in their underlying health status but due to, for instance, their socioeconomic characteristics. Therefore, we also include in these models a series of socioeconomic indicators that consist of: nationality, marital status, educational attainment and economic activity. When predicting EQ-5D scores we fix the socioeconomic variables at the sample mean value with the aim of removing any socioeconomic-relatedreporting bias. As a result, our HRQoL indicator depends on the purged effect of health problems on HRQoL, and on the varying levels of these indicators across regions and across time.

We then compute the HRQoL indicator as the mean value of the predicted EQ-5D scores by region and year for each gender and age group. EQ-5D estimates constructed using SHS 2006/07 were used to adjust LE data in 2008, estimates using data from EHIS 2009/10 were linked to LE for 2009 and 2010 and the remaining years (2011-2013) were linked to SHS 2011/12 estimates.EQ-5D data on individuals younger than

15 years are not available in the SHS, thus the values estimated in the youngest available age group (15-44) were used for these individuals.

2.2.3. Expenditure data

Our measure of spending is health expenditure per person per year. We use total actual public health expenditure by region and by year as provided by the Ministry of Healthstatistics database[5]. We compute expenditure per capita by dividing total expenditure by the size of the population in the corresponding year according to the population statistics published by the ONS in Spain. Data were taken from 2008 to 2012 and adjusted for inflation using GDP deflator estimates for Spain provided by the World Bank[6]. Values are expressed in €2012.

2.2.4. Other indicators

We include a comprehensive list of variables capturing region- and time-variant differences in needs for health care resources. For this, we assemble a unique dataset of demographic, socioeconomic, health and environmental factors (seeAppendix 1).

Demographic variables include information on the size of the population; the proportion ofmales; and the proportion by age group. We also include a comprehensive list of health variables that aim to control for health spending needs over and above age and gender characteristics. These consist of prevalences of major diseases proxied by age/sex adjusted hospitalisation rates by ICD9 groups; individuals on incapacity benefits; individuals with disability; number of traffic accident victims; individuals on retirement benefits; and proportion of smokers. A series of regional socioeconomic indicators were also included that consist of GDP per capita; unemployment rate;

5 Available from http://www.msssi.gob.es/estadEstudios/estadisticas/inforRecopilaciones/gastoSanitario2005/home.htm
6 Available from http://data.worldbank.org/indicator/NY.GDP.DEFL.KD.ZG

poverty risk; individuals educational attainment; and number of immigrants by country of origin. We also aim to control for unavoidable variations in health spending such as differences on the cost of providing care proxied by the cost of floor space in squared metres and mean salaries. Finally, we take into account the number of individuals in each region who havehealth insurance cover provided by other public administrations.

3. RESULTS

3.1.Descriptive statistics

Table 1 provides the mean values of health expenditure per capita, LE and QALE at birth in each region and year. On average, health expenditure decreases over the period of analysis, particularly in 2012. The extent of these decreases varies by region, with a special case in Cantabria region where expenditure increased in 2012. This issue is explored in sensitivity analyses.

Both LE and QALE at birth have increased overtime, from over 81 years in 2009 to nearly 83 years of LE in 2013. The number of years that individuals are expected to live in good health has increased from 73 to 75 years in this period in Spain. Summary statistics of region- and time-variant control variables are presented in Appendix 2.

3.2.Quality of life models

The coefficients of the health and socioeconomic variables included in the regression models of EQ-5D decrementsstratified by age and gender using the SHS 2011/12 are presented in Table 2. Some covariates are excluded from the regression models due to small numbers or counter-intuitive signs due to collinearity. Mean values of the included covariates across the SHS 2006/07, EHIS 2009/10 and SHS 2011/12 used to derive out-of-sample predictions are also shown in Table 2.

3.3.Health expenditure models

Table 3 summarises the main model results. We run separate models for the average QALE of the population as well as for QALE at given ages. The effect of the control variables in the model of average QALE are presented in Appendix 2. The same covariates were included in every model.

The first row in Table 3 shows the results for the model of the average QALE of the population. The estimated elasticity of 0.0699 (second column) indicates that a 1% increase in per capita annual health expenditure increases average QALE in 0.0699%. This is a positive and statistically significant effect of health expenditure on population health. When evaluating this result at sample means, this finding implies that,on average,an increase in 1€ in health expenditure per person per year leads to a QALE increase of 0.0018 years or 0.65 days (third column). In other words, a 10€ extra spending per person per year in health would be related to, on average, an increased life expectancy of 6.5 days in perfect health.

When looking at QALE models at given ages, the estimated effects of health spending are positive in every case, and statistically significant at early ages as well as in the oldest age group. The results also show that while expenditure elasticity appears to increase with age, the marginal effects are lower at older ages, showing that the absolute impact of health spending on healthy years is lower as the individual ages (Figure 1).

3.4.Cost per QALY estimation

In order to transform the marginal effect of annual health expenditure on QALE into a cost per QALY we take into account the LE of the relevant group. For instance, the estimated effect on average QALE of 0.0018 healthy years will be accrued by increasing health expenditure in 1€ per year, and thus, considering the average life expectancy of this population of 44.31 years (fourth column), the cost per QALY is

estimated in 24,222€ (= 44.31/0.0018; fifth column). This calculation assumes that the estimated effect on QALE pertain to a permanent increase in spending per head of 1€ per year.

The fifth column in Table 3 shows the cost per QALY for the average population as well as the cost per QALY at different ages. These results are shown graphically in Figure 1. The mean cost per QALY following from the age specific models, weighted to account for population sizes for different age groups in Spain (sixth column), is estimated in 22,314€. Alternatively, we estimated an overall cost per QALY of 21,023€ as the ratio between the sum of incremental permanent health expendituresacross age groups and the sum of the incremental health gains in each age group using the following formulae:

$$Cost\ per\ QALY = \frac{\sum_{x=1}^{j}(n_x * \Delta Exp_x * LE_x)}{\sum_{x=1}^{j}(n_x * \Delta QALE_x)} \quad \text{Eq.6}$$

- n_x is the population size of age group *x*
- ΔExp_x is the incremental annual expenditure in age group *x*
- $\Delta QALE_x$ is the incremental effect on QALE in age group *x*
- LE_x is life expectancy of age group *x*

3.5.IV Models

The last two columns of Table 3 show the results for the IV models. There is a strongly significant correlation between the instrument and the potentially endogenous variable (F-test 31.30; p-value<0.0001), indicating that the instrument meets the relevance requirement. We cannot empirically test for the orthogonality criterion; the partial test

of overidentification cannot be conducted as the number of instrumentsavailable is not higher than the potentially endogenous variables.

The IV results are very similar to the OLS modelestimates(elasticity = 0.0731; cost per QALY = 23,158 €). Assuming that the instrument is valid, the exogeneity tests fail to reject the exogeneity of health expenditure in every model. Therefore OLS estimates presented in the previous section are preferred to the 2SLS model estimates.

3.6.Additional analyses

Table 4 presents additional analyses that were conducted to explore a series of issues. For simplicity, we use the model of average QALE as the base case to allow comparisons across different model specifications.

Firstly, we tested for different functional forms of the health expenditure variable by including second- and third-order polynomial functions (without log transformation). The squared and cubic terms were non-significant.

Ministry of Health statistics on health expenditure included a note indicating that Cantabria health spending information included for the first time in 2012 payments made through the "extraordinary supplier payment" mechanism. Excluding this payment implies a reduction in health spending per capita from 1,766€ to 1,333€ in Cantabria in 2012, in line with the pattern observed in other regions. This, however, does not havea significant effect on the overall model results. The estimated marginalcost of a QALY using this adjusted figure for Cantabria is 24,841€.

We experimented with applying a 3% discount rate to QALE gains and to the corresponding lifetime health spending investment, assuming that health gains are proportional over time and linear with respect to increases in expenditure. The cost per QALY using this approach was estimated to be 23,868€.

In addition, Table 4 shows how the estimated impact of expenditure on QALE changes as increasingly more sets of covariates are included in the model. Controlling only for age and gender characteristics yields an observed negative relationship between expenditure and health outcomes. However, after controlling for differences in underlying health factors, the relationship between spending and QALE becomes positive. The estimated effect increases as controls for socioeconomic, environmental and population covered by insurance are added.

We estimated the impact of expenditure on QALE without allowing for a lag between spending and health outcomes. We found that in this case the effect of expenditure is considerably smaller and non-significant, suggesting that there is a delay in accruing health benefits related to higher spending. This might also reflect a larger degree of endogeneity between contemporaneous health and health spending.

Finally, we estimated a health spending elasticity for average LE of 0.0203 and for LE at birth in 0.0107 (Table 4). This was found to be in line with previous research (Gallet & Doucouliagos, 2015).

4. DISCUSSION

In this study we provide an estimate of the marginalcost of a QALY in theSNHS. This value approximatesthe average opportunity cost of incorporating health technologies in the SNHS when disinvestment is required to fund new interventions. The figure was estimated to liebetween 21,000€ and 24,000€ per QALY, depending on whether we consider the estimates provided by different age groups or the value derived from the average population model, respectively.

The methodology applied in this paper builds on previous work by Claxton *et al.*(2015). However, in this study we usedpanel data on expenditure and health outcomes for the

same regions over multiple time periods, which allows us to control for the effects of unobservable factorsbased on fixed effect specifications. Moreover, Claxton*et al.* (2015) estimated the effect of health spending on mortality alone and assumed that HRQoL improves in proportion to the estimated mortality improvement. In this paper we have used a health outcome variable capturing differences in mortality and morbidity in order to directly estimate the impact of health expenditure on mortality as well as on HRQoL.On the other hand, information on health spending across disease programmes is not available in Spain, and therefore disease-specific models as conducted in Claxton *et al.*(2015) were not feasible. While our approach does not allow for the flexibility of disease models,it provides us with an average estimateacross the overall SNHS,which is the ultimate aim of this research. It is also worth noting that our period of analysis, characterised by disinvestments across all regions, provides us with a potentially more accurate estimate of the amount of health displaced by disinvestment, i.e. the opportunity costs, than estimates based on periods of growing spending.

We acknowledge a series of limitations of this study. Firstly, there are data restrictions, especially with respect to HRQoL data collected only in 2011/12. We attempted to overcome this limitation by generating predicted values based on the impact that health problems have on HRQoL purged from reporting bias and the varying degree of these health problems over time and across regions. While this approachmight providemore appropriate HRQoL indicators than that from observed raw data, we had to rely on the estimated effects based on a single year of EQ-5D data. Routinely collecting EQ-5Dinformation in health surveys would help solving this limitation. Secondly, the exogeneity test indicating that spending is not endogenousrelies on the validity of the instrument we used. While the instrument met the relevance requirement, the orthogonality criterion could not be formally tested, yielding some uncertainty about the

validity of the instrument. However, variations in expenditure exploited in this study are mainly driven by exogenous changes in health spending due to the economic crisis and subsequently budget cuts. This might facilitate the identification of the causal effect of expenditure on health outcomes,and reinforces the finding of a lack of endogeneity bias in this analysis. Thirdly, the transformation we applied to translate the spending elasticity for QALE into a cost per QALY assumes that health gains estimated over the person life expectancy in our modelsare achieved when the corresponding extra annual health spending is sustained over the lifetime. The reason is that while the dependent variable is expressed as a life expectancy indicator, the health spending variable pertains to annual expenditure in health. This transformation imposes linearity between expenditure investment and QALY gains over time. Fourthly, while we have aimed in this study to provide a first empirical estimation of the cost per QALY in Spain, we acknowledgea degree of uncertainty around the magnitude of the health spending elasticity estimates that ought to be further explored and characterised.

Over and above the methodological complexities of estimating the actual cost per QALY, it is also worth noting that such information is only a proxy of the average opportunity cost of funding decisions. Leagues tables and the identification of the specific intervention(s) that would be displacedfor new interventions to be adopted arguably provide a better estimation of the true opportunity cost for each funding decision. However, league tables are generallynot feasible, and most often it is unknown what activities will be displaced when imposing new costs to the system. Moreover, disinvestment may not imply that specific services are fully removed, but instead that reductions in spending are imposedacross different health services within the system. Therefore, the use of the average cost per QALY across the system provides a useful approximation of the opportunity costs of health care funding decisions.

The estimate provided in this paper suggests that the most commonly cited threshold value of 30,000€ per LY/QALY used in Spain is higher than the estimated threshold derived from the opportunity cost approach. The 30,000€ figure was not based on an empirical estimation but simply reflected the findings from a review of the Spanish economic evaluation literature showing that authors of published papers were likely to recommend adoption of the intervention under study when the ICER was below this value(Sacristán *et al.*, 2004).

In this paper we have aimed to generate information on the cost per QALY of the SNHS on the basis that, under fixed budget constraints that characterise most health services, information on the opportunity cost is what matters to make allocation decisions. A serious danger with using such approach alone, however, is that it might perpetuate the belief that the opportunity cost threshold reflects the marginal benefits of health care, and decision makers would not be made aware of the series of technologies whose benefits offset their costs according to society's view. A society-value threshold allows for the identification of such interventions and this information might have implications for the size of the budget. Furthermore, budgets might not always be fixed, especially when new tax revenue becomes available for the health care system. The opportunity costs of allocating new funds to health would then not fall within the NHS, but across other alternativeuses of public spending. Therefore, the estimates provided in this paper will not be relevant to guide such decisions.Society's value of health gains would arguably better reflect the strengths of preferences across different alternatives of consumptions of the public, providing a more relevant threshold reference. There are some previous studies within the Spanish context that have used the WTP approach to inform a cost-effectiveness threshold (Pinto-Prades *et al.*, 2009; Donaldson *et al.*, 2011; Abellán-Perpiñán *et al.*, 2011; Martín-Fernández *et al.*, 2014).The finding of these

studies are characterised by the sensitivity of the WTP values to the assumptions and techniques applied in the analyses. Further work to overcome these limitations on the societal valuation of a QALY isrequired.

Furthermore, the threshold defined by the cost per QALY is a dynamic figure that needs to be frequently updated to account for changes in the budget and efficiency over time. The identification and/or development of new routinely collected data sources is required to refine and update the estimates currently provided, and further work is needed to account for any remaining source of endogeneity and to explicitly address uncertainties around the estimated values.

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Table 1. Mean values of health expenditure, life expectancy and quality-adjusted life expectancy at birth across regions and over time

	Health expenditure per capita (€)					LE at birth					QALE at birth				
Region / Year	**2008**	**2009**	**2010**	**2011**	**2012**	**2009**	**2010**	**2011**	**2012**	**2013**	**2009**	**2010**	**2011**	**2012**	**2013**
Andalucía	1,279	1,257	1,213	1,135	1,101	80.35	80.81	80.95	80.96	81.61	70.86	71.19	73.04	73.07	73.56
Aragón	1,442	1,535	1,485	1,528	1,521	82.02	82.25	82.39	82.74	83.16	75.02	75.20	76.11	76.42	76.75
Asturias	1,458	1,632	1,557	1,602	1,541	81.09	81.21	81.37	81.55	82.23	72.81	72.89	72.24	72.40	72.93
Baleares	1,267	1,339	1,553	1,453	1,175	81.16	81.63	82.00	81.92	82.69	74.02	74.39	74.82	74.76	75.38
Canarias	1,443	1,485	1,399	1,325	1,208	81.01	81.57	81.41	81.58	82.33	72.33	72.77	71.38	71.53	72.05
Cantabria	1,349	1,396	1,463	1,301	1,766	82.02	82.14	82.50	82.57	83.08	74.36	74.43	75.79	75.85	76.25
Castilla La Mancha	1,423	1,540	1,541	1,464	1,241	82.33	82.76	82.83	82.73	83.17	73.35	73.66	75.52	75.45	75.77
Castilla y León	1,435	1,395	1,423	1,311	1,362	82.73	82.98	83.24	83.20	83.57	75.45	75.63	76.67	76.65	76.95
Cataluña	1,360	1,420	1,438	1,350	1,261	81.94	82.33	82.61	82.53	83.08	74.26	74.57	75.71	75.64	76.09
Comunidad Valenciana	1,254	1,341	1,368	1,346	1,221	81.33	81.61	81.83	81.91	82.50	71.97	72.17	74.86	74.93	75.40
Extremadura	1,534	1,605	1,578	1,539	1,409	81.09	81.22	81.79	81.45	81.89	71.50	71.58	74.13	73.90	74.22
Galicia	1,391	1,475	1,424	1,325	1,274	81.51	82.02	82.19	82.29	82.69	71.38	71.74	74.34	74.42	74.74
Madrid	1,204	1,277	1,158	1,319	1,193	82.98	83.48	83.72	83.74	84.26	74.65	75.03	77.11	77.11	77.55
Murcia	1,513	1,573	1,546	1,556	1,444	80.92	81.63	81.73	81.73	82.35	69.87	70.35	74.21	74.21	74.68
Navarra	1,497	1,611	1,581	1,553	1,435	82.95	83.76	83.55	83.48	83.63	75.82	76.47	77.18	77.12	77.23
País Vasco	1,559	1,667	1,659	1,636	1,579	82.02	82.49	82.52	82.79	83.22	74.27	74.63	75.64	75.88	76.22
La Rioja	1,498	1,470	1,463	1,442	1,307	82.58	83.00	82.91	82.69	83.63	74.60	74.99	75.99	75.82	76.57
Total	1,406	1,472	1,462	1,423	1,355	81.77	82.17	82.33	82.34	82.89	73.32	73.63	74.98	75.01	75.43

Note: LE = Life expectancy; QALE = Quality-adjusted life expectancy

Table 2. Coefficients on EQ-5D decrements across gender and age groups models

		Females			Males		
	Mean	**15-44**	**45-64**	**65+**	**15-44**	**45-64**	**65+**
Health indicators							
Age	51.13	0.025***	0.007***	0.021***	0.012***	0.024***	0.018***
Self-assessed general health							
Very good	0.158	-1.660***	-1.876***	-0.868***	-1.959***	-1.850***	-1.552***
Good	0.493	-0.836***	-1.143***	-0.658***	-1.735***	-0.548***	-0.869***
Fair	0.247	-0.532***	-0.580***	-0.328***	-0.981***	-0.098***	-0.351***
Bad	0.078	-	-0.356***	-0.158***	-0.263***	-	-0.233***
Very bad	0.024	Omitted category					
Longstanding illnesses							
Hypertension	0.249	0.350***	0.028	-	0.062	-	0.051*
Myocardial infarction	0.025	0.670***	-	-	0.444***	-	-
Chronic cervical pain	0.201	-	0.301***	0.085***	0.100**	0.194***	-
Chronic back pain	0.220	0.430***	0.010	0.093***	0.250***	-	0.152***
Chronic bronchitis	0.057	-	0.067**	-	0.034	-	-
Diabetes	0.080	-	-	0.077***	0.546***	0.008**	0.107***
Ulcer stomach / duodenum	0.055	-	-	-	-	-	-
Incontinence	0.050	0.147*	0.008	0.111***	0.102	-	0.069**
Depression/anxiety	0.149	0.534***	0.419***	0.134***	0.244***	0.225***	0.241***
Stroke	0.016	0.252***	0.268***	0.191***	0.436***	0.397***	0.203***
Migraine	0.116	-	0.036	-	-	-	0.056
Osteoporosis	0.068	0.224***	-	-	-	0.054	-
Limitation on daily activities							
Severe limitations	0.053	1.671***	1.091***	2.180***	2.583***	2.004***	1.535***
Moderate limitations	0.206	0.951***	0.692***	1.092***	1.183***	1.334***	0.852***
No limitations	0.741	Omitted category					
Socioeconomic variables							
Nationality							
Non-Spanish	0.066	0.012	0.106	-0.185**	0.489***	0.785***	-0.113
Spanish	0.934	Omitted category					

Marital status							
Single	0.263	0.068**	0.207***	-0.113**	0.173***	0.221***	-0.119*
Widowed	0.128	0.093**	-0.284***	-0.024	-0.529	-0.938***	-0.100**
Separated	0.027	0.074	-0.194***	-0.108	0.641***	0.503***	0.547***
Divorced	0.032	-0.079	0.014	-0.294	-0.579	-0.096	-0.355*
Married	0.548	Omitted category					
Educational attainment							
No primary education	0.128	0.627***	-0.108**	-0.078***	-1.214***	-0.146*	0.073
Primary education	0.253	0.576***	-0.201***	-0.151***	-1.429***	-0.211**	0.143*
Lower secondary	0.186	0.636***	-0.026	-0.099***	-1.098***	-0.123*	0.037
Upper secondary	0.095	0.860***	-0.393***	-0.111*	-0.716***	-0.324***	0.111
Post-secondary non-tertiary	0.098	0.329***	-0.352***	-0.243***	-0.779***	-0.020	0.281**
Short-cycle tertiary	0.059	0.660***	-0.358***	-0.124	-1.447***	-0.326**	-0.139
Tertiary high education	0.155	0.164	-0.249***	-0.290***	-1.274***	-0.717***	0.102
Illiterate	0.024	Omitted category					
Employment status							
Unable to work	0.020	0.609***	0.430***	0.500**	0.382***	0.658***	0.728
Unemployed	0.094	0.134***	0.122***	-0.372	-0.548***	0.129**	
Retired	0.270	0.148	0.187***	0.131***	-0.321	0.259***	0.442
Student	0.048	-0.112	0.445	-4.280	0.333***	-7.140	
Taking care of home and family	0.158	-0.028	0.100***	0.031	-0.422	-0.202	0.030
Other activity	0.006	0.117	-0.218***	0.354**	0.589***	0.094	-5.726
Working	0.439	Omitted category					
Sample size	72,524	4,100	3,529	3,663	4,137	3,216	2,211

Note: *p-value<0.10. **p-value<0.05. ***p-value<0.01. Negative coefficients mean the variable increases HRQoL and viceversa.

Table 3. Main model results: elasticities, marginal effects and costs per QALY estimates

Dependent variable (1)	Elasticity (2)	ME (3)	LE (4)	Cost/QALY (5)	Population (6)	Elasticity IV models	Durbin-Wu-Hausman (p-value)
$QALE_{pop}$	0.0699**	0.0018**	44.31	24,222 €	46,512,199	0.0731**	(0.8739)
QALE at 0	0.0527**	0.0029**	82.29	28,044 €	424,881	0.0407**	(0.3530)
QALE at 1	0.0577**	0.0032**	81.53	25,635 €	1,895,731	0.0488**	(0.4822)
QALE at 5	0.0586**	0.0031**	77.58	25,321 €	2,478,498	0.0515**	(0.5931)
QALE at 10	0.0588**	0.0029**	72.62	25,350 €	2,267,843	0.0522**	(0.6365)
QALE at 15	0.0618**	0.0028**	67.65	24,235 €	2,140,570	0.0569**	(0.7425)
QALE at 20	0.0654**	0.0027**	62.71	23,036 €	2,374,617	0.0609**	(0.7793)
QALE at 25	0.0662**	0.0025**	57.79	22,915 €	2,749,308	0.0625**	(0.8331)
QALE at 30	0.0679**	0.0023**	52.88	22,531 €	3,456,208	0.0653**	(0.8950)
QALE at 35	0.0727**	0.0023**	47.98	21,236 €	4,032,770	0.0696**	(0.8841)
QALE at 40	0.0775*	0.0021*	43.13	20,179 €	3,858,819	0.0752*	(0.9235)
QALE at 45	0.0857*	0.0021*	38.35	18,549 €	3,689,866	0.0855*	(0.9947)
QALE at 50	0.0891*	0.0019*	33.69	18,058 €	3,333,372	0.0856*	(0.9059)
QALE at 55	0.0830	0.0015	29.18	19,717 €	2,877,803	0.0721	(0.7448)
QALE at 60	0.0936	0.0014	24.81	17,895 €	2,491,892	0.0630	(0.4456)
QALE at 65	0.0904	0.0011	20.61	19,186 €	2,327,434	0.0387	(0.3047)
QALE at 70	0.0825	0.0008	16.58	20,935 €	1,809,958	0.0185	(0.2110)
QALE at 75	0.0944	0.0007	12.79	18,195 €	1,652,238	0.0194	(0.1486)
QALE at 80	0.0677	0.0004	9.42	25,169 €	1,403,260	0.0055	(0.2527)
QALE at 85	0.0700	0.0003	6.63	24,128 €	825,182	0.0149	(0.3326)
QALE at 90	0.0826	0.0002	4.58	20,189 €	333,079	0.0648	(0.7614)
QALE at 95	0.3023**	0.0006**	3.31	5,452 €	88,871	0.2022	(0.1969)
Average cost per QALY				21,023 €[1]	22,314 €[2]		
F-test of relevance of instrument (p-value)						31.30 (<0.0001)	

Note: *p-value<0.10. **p-value<0.05. ***p-value<0.001. LE = Life expectancy; ME = Marginal effect.

1 Based on the population-weighted mean of the cost per QALY across age groups

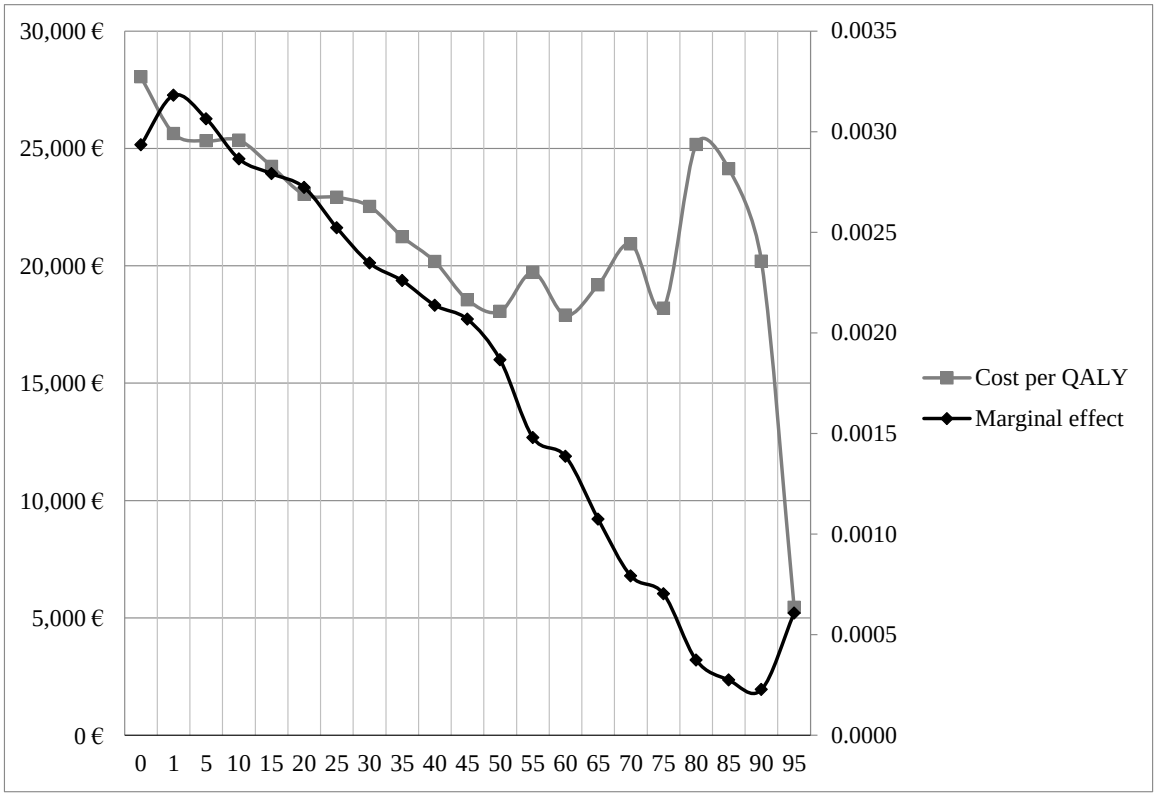
2 Based on the ratio between the sum of incremental annual health expenditures across age groups and the sum of the incremental annual health gains in each age group (Equation 6).

Table 4. Additional analyses results

Expenditure functional form	**Coefficient**	**(p-value)**	
Expenditure per capita	-0.05344	(0.551)	
Expenditure per capita squared	0.00003	(0.590)	
Expenditure per capita cubic	0.000000	(0.645)	
	Elasticity	**ME**	**Cost/QALY**
Base case ($QALE_{pop}$ model)	**0.0699****	**0.0018**	**24,222 €**
Adjusted Cantabria expenditure	0.0682*	0.0018	24,841 €
Applying 3% discount rate	-	-	23,868 €
Set of control variables			
Only demographic controls	-0.0004	-0.00001	-
Plus health indicators controls	0.0323	0.0008	52,425 €
Plus socioeconomic controls	0.0576	0.0015	29,427 €
Plus environmental controls	0.0650*	0.0017	26,052 €
Plus insurance controls (base case)	0.0699**	0.0018	24,222 €
Not allowing for lagged effect	0.0328	0.0009	41,298 €
Not adjusting for HRQoL (LE_{pop})	0.0203	0.0006	66,743 €
Not adjusting for HRQoL (LE at birth)	0.0107	0.0006	126,800 €

Note: *p-value<0.10. **p-value<0.05. ***p-value<0.001. ME = Marginal effect

Figure 1. Cost per QALY and marginal effect at given ages



Appendix 1. List of control variables and sources

Variable	Source
Demographic characteristics	
Size of the population	ONS statistics
Proportion of males	ONS statistics
Proportion of individuals by age group (0-14, 15-44, 45-64, 65-84, 85+)	ONS statistics
Health indicators	
Prevalence of major diseases (proxied by adjusted hospitalisation rates by ICD9 groups)	Ministry of Health statistics
Individuals on incapacity benefits	IMSERSO
Individuals with disability	BEDPD
Traffic accident victims	DGT
Individuals on retirement benefits	Ministry of Labour and Social Security statistics
Proportion of smokers	SHS 2006/07, EHIS 2009/10 and SHS 2011/12
Deprivation indicators	
GDP per capita	ONS statistics
Unemployment rates	Economically Active Population Survey, ONS
Poverty risk	Quality of Life Survey, ONS
Educational attainment	Economically Active Population Survey, ONS
Immigrants by country of origin	ONS statistics
Environmental indicators	
Price per floor squared metre	Ministry of Development statistics
Labour cost	Quarterly Labour Cost Survey
Health insurance coverage	
Number of individuals on ISFAS health insurance	Ministry of Defence
Number of individuals on MUGEJU health insurance	Ministry of Justice
Number of individuals on MUFACE health insurance	Ministry of the Finance and Public Administrations

Note: ONS = Office of National Statistics; IMSERSO = Institute for the elderly and social services; BEDPD = National database of persons with disability; DGT = General Department of Traffic; SHS = Spanish Health Survey; EHIS = European Health Survey Interview

Appendix 2. Mean values and coefficients of covariates

Variable	Mean	SD	Minimu	Maximum	Coefficient
$QALE_{pop}$(Dependent variable)	35.13	1.92	38.62	30.22	-
Expenditure per capita	1,423	139	1,766	1,101	0.0699**
Size of the population	2,718,847	2,424,730	316,192	8,377,809	-0.0000***
Males (%)	49.538	0.7574	47.9622	50.6947	-0.1291**
Individuals aged 0-14 (%)	14.414	1.7623	10.2846	17.6587	-13.2188*
Individuals aged 15-44 (%)	42.316	2.8555	36.5234	48.1285	-13.1944*
Individuals aged 45-64 (%)	25.505	1.7458	21.4179	29.7670	-13.1791*
Individuals aged 65-84 (%)	15.294	2.2783	11.4876	19.4273	-13.1308*
Individuals aged 85 or more (%)	49.538	0.7574	47.9622	50.6947	-13.2784*
Individuals on incapacity benefits (%)	17.2865	2.3452	10.9400	23.7700	0.0021
Individuals with disability (%)	71.9345	8.8989	52.3000	86.5700	0.0050**
Traffic accident victims (%)	14.2942	2.1491	10.9100	21.2200	-0.0048
Individuals on retirement benefits (%)	7.6756	1.4499	4.8900	12.9900	-0.0016
Hospitalisation rates ICD-1	18.0931	4.2469	10.6900	28.8300	0.0024
Hospitalisation rates ICD-2	28.0434	5.5599	18.3000	44.8400	0.0017
Hospitalisation rates ICD-3	85.6839	8.8983	65.7600	108.6800	-0.0022**
Hospitalisation rates ICD-4	90.2626	14.1187	54.5000	117.0500	-0.0013
Hospitalisation rates ICD-5	95.8742	13.8312	58.8800	116.6000	-0.0019
Hospitalisation rates ICD-6	47.6111	8.6283	30.1700	62.5000	0.0030
Hospitalisation rates ICD-7	105.5381	13.3298	79.6100	136.6700	-0.0009
Hospitalisation rates ICD-8	8.5531	1.7140	4.8900	11.7100	0.0013
Hospitalisation rates ICD-9	55.5948	17.6231	26.3300	104.7600	0.0001
Hospitalisation rates ICD-10	11.2044	1.7278	7.5700	15.1200	-0.0048
Hospitalisation rates ICD-11	21.7442	5.1583	13.1900	33.5600	0.0033*
Hospitalisation rates ICD-12	34.1458	8.0871	14.1100	54.5900	0.0011
Hospitalisation rates ICD-13	67.3052	9.0706	43.5100	89.3000	-0.0008
Hospitalisation rates ICD-14	5.6652	7.0636	0.0400	39.7600	-0.0003
Hospitalisation rates ICD-15	0.0227	0.0085	0.0047	0.0390	3.0394***
Hospitalisation rates ICD-16	0.0574	0.0185	0.0298	0.1126	-0.5663
Hospitalisation rates ICD-17	0.0023	0.0008	0.0007	0.0045	-24.0641*
Hospitalisation rates ICD-18	15,038	14,782	989	60,182	0.0000***
Proportion of smokers	0.2798	0.0303	0.2142	0.3378	-0.2739**
GDP per capita	22,790	4,353	15,133	30,947	0.0000
Unemployment rates (%)	0.1774	0.0659	0.0662	0.3435	-0.2569
Poverty index	0.2538	0.0833	0.0880	0.4210	0.0236
Individuals with university degree (%)	0.2002	0.0437	0.1345	0.3046	0.4397
Individual illiterate (%)	0.0819	0.0404	0.0189	0.1635	0.1378
Immigrants Africa (%)	0.0013	0.0009	0.0002	0.0050	7.6490
Immigrants America (%)	0.0029	0.0017	0.0007	0.0105	-8.1533**
Immigrants Asia (%)	0.0006	0.0005	0.0001	0.0027	-21.4360**
Immigrants no EU (%)	0.0004	0.0002	0.0000	0.0011	13.2507
Labour cost (€)	2,421	239	2,030	2,987	-0.0001
Price floor square meter (€)	227.6	95.1	67.0	523.6	0.0000
ISFAS	36,002	38,911	4,767	151,692	0.0000
MUGEJU	4,450	4,332	345	17,043	0.0000
MUFACE	90,370	85,003	10,018	317,901	0.0000
Year 2009	0.2000	0.4024	0.0000	1.0000	-0.0072
Year 2010	0.2000	0.4024	0.0000	1.0000	-0.0153
Year 2011	0.2000	0.4024	0.0000	1.0000	-0.0470
Year 2012	0.2000	0.4024	0.0000	1.0000	-0.0790
N	85	85	85	85	85

Note: *p-value<0.10. **p-value<0.05. ***p-value<0.001