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ORIGINAL RESEARCH ARTICLE

Estimating the Incremental Cost Per QALY Produced by the Spanish NHS: A Fixed-Effect Econometric Approach

Laura Vallejo-Torres[1]

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Abstract

Background Knowing the health opportunity costs of funding decisions is crucial to assess whether the health gains associated with new interventions are larger than the health losses imposed by the displacement of resources. Empirical estimates based on the effect of health spending on health outcomes have been proposed in several countries, including Spain, as a proxy to capture these opportunity costs. However, there is a need to regularly update existing health opportunity cost estimates and to explore the role of omitted variable bias in these estimations.

Objective The aim of this paper is to provide an updated and refined estimate of the causal impact of health spending on health in Spain that can be translated into an estimate of the incremental cost per quality-adjusted life-year produced by the Spanish national health system.

Methods We applied fixed-effect models using data for 17 Spanish regions from 2002 until 2022 to estimate the impact of public health spending on health outcomes and explored the extent of omitted variable bias. Changes in these estimates over time were assessed and alternative specifications were tested.

Results Based on fixed-effect models with control variables, the estimated spending elasticity was 0.061, which translated into an incremental cost per quality-adjusted life-year of approximately €34,000. The bias-corrected elasticity was 0.075, with a corresponding incremental cost per quality-adjusted life-year of €27,000. We found that the estimated impact of spending on health decreases when recent years of data are added, and that the extent of omitted variable bias appears to increase, particularly when adding the COVID-19 pandemic period.

Conclusions This study provides an updated estimation of the incremental cost per quality-adjusted life-year produced by the Spanish national health system. The estimates provided can be easily updatable as new data become accessible, and the methods applied might be transferable to other settings with similar available data.

1 Introduction

The health opportunity cost (HOC) is a measure of the forgone health that occurs when new costs fall into the health budget and patients, somewhere in the system, are affected by the displacement of resources. This information is key in health systems operating under constrained budgets because it allows a comparison of the expected health gains associated with new interventions that imposed costs into the health budget with the health likely to be forgone because of the displacement of resources required to fund the new interventions [1, 2]. Therefore, knowing the HOC allows the identification of health interventions which, if adopted, are likely to lead to overall improvements on population health.

In practice, measuring forgone health at each funding decision is not feasible for several reasons. Most often, it is unknown what services might get displaced if a new intervention is adopted and, within a country, different regions might displace different services. Furthermore, even after decisions are made, displacements might remain unidentifiable, particularly when these take the form of delaying other services or decreasing the quality of the services provided (e.g., increasing waiting lists). Therefore, a proposed alternative consists of proxying the HOC of funding decisions by the average change in population health because of changes in overall health expenditure [3]. This provides an estimate

✉ Laura Vallejo-Torres
Laura.vallejo@ulpgc.es

[1] Department of Quantitative Methods in Economics and Management, University of Las Palmas de Gran Canaria, Juan de Quesada, 30, 35001 Las Palmas de Gran Canaria, Canary Islands, Spain

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Key Points for Decision Makers

Empirical estimates of the incremental cost per quality-adjusted life-year produced by a health system are useful to assess whether the health gains of new interventions are larger than the health losses expected from the displacement of resources.

Current empirical estimates need to be updated and the extent of bias in these estimations needs to be explored.

This study provides an easily updatable and transferable framework to arrive at a bias-corrected value, which was estimated in Spain to be in the range of €27,000–€34,000 per quality-adjusted life-year.

of the system-wide HOCs that are expected when resources are displaced anywhere in the system. This value can be empirically estimated based on the marginal effect of health expenditure on population health. If population health is measured in terms of quality-adjusted life-years (QALYs), the HOC estimate can be translated into the incremental cost per QALY of current healthcare spending. This information can form the basis to set a threshold value in cost-effectiveness analyses taking the healthcare system perspective and using QALYs as the outcome measure. Interventions with an incremental cost per QALY lower than the estimated incremental cost per QALY of current health spending would be expected to yield improvements on population health and considered cost effective, and vice versa.

Following this approach, researchers in several countries have aimed at estimating the marginal cost per QALY produced by their health systems [4–15]. In Spain, using panel data from 2008 to 2012 across 17 Spanish regions, the cost per QALY produced by the Spanish National Health System (NHS) was estimated to lie between €22,000 and €25,000 [6]. These values are currently used widely to draw conclusions in the cost-effectiveness analysis literature conducted in Spain [16] and by some Spanish health technology assessment institutions that conduct cost-effectiveness analyses to inform funding decisions, such as the Spanish Network of health technology assessment agencies.[1]

There is a need though for these values to be regularly updated to account for changes in the budget and efficiency over time [6]. In addition, there are several remaining data availability and methodological issues in estimating the marginal effect of health spending on health that need to be addressed [17]. A major challenge consists of accounting for the large degree of endogeneity due to omitted variable bias in the relationship between health spending and health outcomes [18]. Therefore, for this evidence to play a major role in decision making, the methods used to arrive at such values need to be refined and the estimated values need to be up-to-date [19].

The aim of this paper was to provide an updated and refined estimate of the causal impact of health spending in Spain that can be translated into an estimate of the incremental cost per QALY produced by the Spanish NHS. To that end, in this study, we use the most comprehensive and recent evidence available on public health spending and health outcomes across Spanish regions.

In Spain, healthcare funding is provided through general taxes collected by both central and regional governments. The central government subsequently distributes a budget to the regions to support the provision of public services that autonomous communities (ACs) are responsible for: healthcare, education, social services, and other general services such as housing and infrastructure. An allocation system is used to calculate the portion of funds transferred from the central government to each region (except for Navarre and the Basque Country that have a specific financing system). This system is based on a set of weighting indicators classified into two groups: (i) one group is based on the population relevant for each of the four main service categories: the equivalent population under the coverage of NHS (for healthcare), the school-aged population (for education), the elderly population (for social services), and the total population (for other general services) and (ii) the other group is based on regional characteristics, given by the region's size, the dispersion of the population, and insularity [20]. The equivalent population under the coverage of the NHS is computed as the weighted sum of the population covered by the NHS across age groups, weighted according to the mean health spending for each age group. Based on these criteria, the central government assigns a total budget to the regions, which then decide how to allocate their total budget across the public services they oversee.

Exploiting variations in health spending and health outcomes across regions and over time, in this study, we apply fixed-effect methods on a 20-year panel dataset. We then formally assess the role of omitted variable bias in the estimations using the methods proposed by Oster [21]. In addition, in this study, the disaggregated effect of health spending on mortality and on quality of life (QoL) are explored separately, and we monitor how the effect of health spending changes as newer years of data become available, and its implications on the estimated value of the incremental cost per QALY produced by the health system over time.

[1] https://redets.sanidad.gob.es/.

Although the empirical analysis focuses on the Spanish case, this paper also aims to contribute to the international research on the incremental cost per QALY by providing a framework that might be relevant and transferable to other countries with regional data on health spending and health outcomes. To accomplish that, the analysis is conducted using data available in most settings and applies a relatively straightforward methodology. An additional purpose of this research is to provide an easily updatable estimation for Spain in the future. For this reason, the data collection and preparation were carefully managed with the underpinning aim of allowing these estimations to be routinely updatable as new data become accessible.

2 Methods

2.1 Econometric Approach

In order to estimate the causal impact of health spending on health outcomes, this study compiles a panel dataset of regional information over a 20-year period. The analyses exploit repeated observations on regions' health spending and health. Similar to the previous estimation [6], we use regional fixed-effect (FE) models including year-specific dummy variables as regressors. Data from 17 regions and for the period between 2002 and 2022 were compiled.

The 17 regions pertain to the 17 ACs that are responsible for planning and delivering health services to their populations in Spain and which hold over 92% of the overall national health budget. The only areas that are excluded are the two autonomous cities (Ceuta and Melilla) that are centrally managed and together represented under a 0.037% share of the Spanish population. Data were collected from 2002, when the decentralization process that assigned healthcare competencies to ACs was completed. Currently, the latest data published for regional health spending are those of 2021, while regional information on life expectancy (LE) is available until 2022.

The regression model takes the form:

$$log(H_{it}) = \alpha + \beta \log(HCE_{it-1}) + X'_{it}\theta + \gamma_t + \mu_i + u_{it}, \quad (1)$$

where H_{it} is population health observed for region i in time t, HCE_{it-1} is healthcare expenditure for region i in time $t-1$, X'_{it} is a vector of observed control variables for region i in time $t-1$, θ is the associated parameter vector of the vector of observed control variables X'_{it}, γ_t is the time fixed effect, μ_i is the regional fixed effect, and u_{it} is the idiosyncratic error term.

H and HCE are log transformed and so β can be interpreted as an elasticity: the expected percentage change in health given a 1% change in health spending. Health expenditure, along with the other explanatory variables, are lagged 1 year to allow for the expected delay in accruing a health benefit derived from variations in health spending.

Year and regional FEs account for both unobserved factors that may explain a common national trend in health spending and health as well as for unobserved time-invariant differences between regions. To explore any remaining biases that are not removed by the inclusion of FEs, we include a list of potential covariates, denoted by X'_{it}, that captures potential differences in demographic, socioeconomic, lifestyle, contextual, and health factors not amenable to health spending, similar to the approach taken in Siverskog and Henriksson [8]. The potential impact of omitted variable bias in the estimates is often assessed by exploring movements in the coefficients when incorporating additional controls, with limited movements generally being interpreted as a sign of limited omitted variable bias. However, as noted by Oster [20], the lack of coefficient movements alone when controls are added is not sufficient to disregard omitted variable bias. She proposes a method that scales coefficient movements by movements in R-squared, arguing that small coefficient movements could be due to the low explanatory power of these additional covariates. Based on assumptions regarding the importance of the unobservable variables relative to the observable variables in influencing spending (denoted by δ) and the share of variance of the dependent variable, which can be jointly explained by observed and unobserved variables (denoted by R_{max}), Oster proposes an approximation of the bias-corrected treatment effect that is derived as follows:

$$\beta^* \approx \widetilde{\beta} - \delta\left[\dot{\beta} - \widetilde{\beta}\right]\frac{R_{max} - \widetilde{R}}{\widetilde{R} - \dot{R}}, \quad (2)$$

where $\dot{\beta}$ is the estimate of β from the uncontrolled regression and $\widetilde{\beta}$ is the estimate of β from the regression including the control variables. $\dot{R}$ and $\widetilde{R}$ are the R-squared values from the uncontrolled and controlled regression, respectively. Oster argues that an appropriate upper bound of δ is that of equal selection (i.e., $\delta = 1$), which implies that the unobservable variables and observable variables are equally related to treatment and affect β in the same direction. The bound when $\delta = 0$ is $\widetilde{\beta}$, i.e., the estimate from the controlled regression. Therefore, the unbiased coefficient would lie within the bounds $\left[\beta^*, \widetilde{\beta}\right]$. The estimate of β^* also depends on the selected value of R_{max}, the maximum explained variation, which because of idiosyncratic measurement errors Oster assumes to be <1 and proposes a value $R_{max} = 1.3 * \widetilde{R}$ based on external evidence on randomized studies. This value suggests a bound where the unobservable variables explain somewhat less than the observable variables. This assumption has some intuitive appeal if observable variables are chosen to include the most important factors explaining the outcome [21]. This approach allows us to construct a set

of β with two bounds: $\widetilde{\beta}$, which is the estimate of β from the controlled regression, and β^*, which is the effect of health spending on health corrected for omitted variable bias, given a value of δ and R_{max}. β^* will be the upper bound if the effect of health spending on health is positive and omitted variables generate a downward bias, as it might be expected in the relationship between health and health expenditure. This is because health spending is partly determined by the level of healthcare needs, which in turn causes health outcomes, therefore, we expect models that do not account for omitted variable bias to show a downward bias in the relationship between expenditure and health. We used the Oster methods to estimate β^* using Eq. 1 as the controlled model, and we specify the uncontrolled models as:

$$log(H_{it}) = \alpha + \beta \log(HCE_{it-1}) + \gamma_t + \mu_i + u_{it}. \quad (3)$$

The uncontrolled regression includes only the key variable of interest (in our case, healthcare spending) and observed covariates whose correlation with the key explanatory variable of interest is not informative about selection bias; this is the case of the regions and year FEs, which are fully captured and do not have unobserved counterparts [22]. We calculate β^* using the formula in Eq. 2, where $\widetilde{\beta}$ and $\dot{\beta}$ are the β estimated from Eqs. 1 and 3, respectively, and $\widetilde{R}$ and $\dot{R}$ are the within R-squared values from Eqs. 1 and 3, respectively. Following Oster's suggestions, we use $\delta = 1$ and $R_{max} = 1.3 * \widetilde{R}$ to compute the upper bound estimate. In a supplementary analysis, we explored the assumption that $R_{max} = 1$ and applied the Stata command *psacalc* to estimate the Oster bias-corrected coefficients.

The main models are estimated using FE estimators. Population weighting[2] and adjustment of standard errors for clustering at the regional level are applied in all models. *P*-values lower than 0.1 are considered weakly significant, and *p*-values lower than 0.05 are considered strongly significant. A number of robustness checks are conducted including the use of different functional forms and lag structures. The impact of health spending on mortality and on QoL alone is also explored, as well as the changes on the estimated effect when recent years of data are added in the models. Analyses are conducted in Stata software v16.

2.2 Data

Population health is measured using average quality-adjusted LE (QALE). Quality-adjusted LE is derived by combining information on LE and QoL. Information on region-year-specific LE can be obtained from life tables [23], which provide information on the number of years a cohort is expected to live if exposed, from birth through death, to the mortality rates observed at year t. This information is generally routinely available in most settings.

To estimate the system-wide incremental cost per QALY, QoL data are required on a QALY scale at population level. Unfortunately, there is not routinely, nor regionally representative data collected on QoL in Spain, which might also be the case in other settings. In Spain, the only source of nationally and regionally representative data on a relevant QoL instrument is the Spanish Health Survey conducted in 2011/12, which collected EQ-5D data from a sample of over 21,000 Spanish residents aged 15 years and older. The Spanish Health Survey is conducted every 4–5 years (available in 2003/04, 2006/07, 2011/12, and 2016/17) [24]. The European Health Survey in Spain is an additional source of regionally representative health data, which is also conducted every 5 alternate years (i.e., in 2009/10, 2014/15, and 2019/2020) [25]. Using the same approach as in the previous estimation [6], we predict age-gender-region-specific EQ-5D values based on a common set of health and socioeconomic variables included in all these surveys (see Appendix 1 of the Electronic Supplementary Material [ESM]). EQ-5D models were stratified by gender and age groups (15–44, 45–64, and 65 or more years). Predicted EQ-5D scores by age-gender groups and by region and year were then applied to adjust LE, so that we obtain values of QALE using the approach described in Gaminde and Roset [26]. Predicted EQ-5D scores were assigned to each corresponding year when a health survey was conducted (either the Spanish Health Survey or the European Survey in Spain). For years in which predicted EQ-5D scores were not available (none of the surveys was conducted in 2005, 2008, 2013, 2018, and 2021), we used the values from the nearest year to adjust LE.

Quality-adjusted LE values provide the expected remaining number of healthy years individuals at a given age cohort *x* are expected to live (e.g., $QALE_x$ = at birth, 1 year, 5 years, 10 years, …, 95 years). The average QALE of a given population can be computed as the population-weighted mean QALE across age cohorts:

$$QALE_m = \sum w_x QALE_x, \quad (4)$$

where w_x is the share of the population in age group *x*. We use average QALE ($QALE_m$) as our main dependent variable.

The explanatory variable of interest is per capita annual public health expenditure. We have information on per capita region-year-specific annual health spending incurred annually by the ACs. This information is publicly available in Spain through the "key indicators of the NHS" website [27]. We used current expenditure for each year. The same coefficient estimates were obtained when using real values

[2] The population across regions in Spain varies from just above 300,000 individuals in La Rioja to over 8.4 million individuals in Andalusia.

computed using gross domestic product deflator estimates for Spain. We denote our explanatory variable of interest, annual healthcare expenditure per capita, by *HCE*.

Using primarily the "key indicators of the NHS" website [27], we also compiled a set of control variables based on routine sources from the Information System of the Spanish NHS and data sources managed by other official organizations. These indicators are published by the Spanish Ministry of Health in the "key indicators of the NHS" website immediately after the data are published in the original source. Some indicators are updated annually, while some others are updated according to the periodicity of the original source, for example, some indicators are retrieved from the health surveys conducted every 2–3 years. A series of indicators were also obtained from data published by the National Institute of Statistics (INE, Spanish acronym) of Spain, which offers a large amount of freely accessible statistical information from official sources [28–31].

The set of potential confounders was carefully chosen to incorporate factors falling into five predefined categories: demographic factors (age and gender profile, population size, population density); socioeconomic factors (gross domestic product per capita, unemployment rate, immigration rate, and out-of-pocket spending on healthcare), lifestyle factors (smoking, sedentarism, obesity prevalence), contextual factors (labor cost and floor space price), and health factors non-amenable to health spending (traffic accident victims and labor accident rates). The latest variables were selected following the conceptual model proposed by Siverskog et al. [7], which emphasises that "we should be careful when controlling for morbidity, since measures of morbidity that are affected by (amenable to) healthcare will block the path between expenditure and life expectancy". Table 1 summarizes the variables used in this study, their data sources, and their availability by year. When data were not available for a given year, information from the nearest year was used.

2.3 Deriving the Incremental Cost per QALY

As noted, the estimated β in Eqs. 1–3 measure the spending elasticity of health, interpreted in our case as the expected percentage change in the average remaining QALE of the population given a 1% increase in annual healthcare spending. To translate this into the incremental cost per QALY, we use the following formulae:

$$Cost\,per\,QALY = \frac{\overline{LE_m}}{\frac{\partial QALE_m}{\partial HCE}} = \frac{1}{\frac{\partial QALE_m}{\partial HCE}\frac{1}{LE_m}} = \frac{\overline{LE_m}}{\beta\frac{\overline{QALE_m}}{\overline{HCE}}} = \frac{1}{\beta\frac{\overline{QALE_m}}{\overline{HCE}}\frac{1}{LE_m}}, \quad (5)$$

where LE_m is the average remaining LE of the population, computed using the same formulae as for $QALE_m$ (Eq. 4). As noted by Siverskog and Henriksson [7], deriving the incremental cost per QALY based on these models that measure the impact of annual health spending on a measure of (quality-adjusted) LE, can be understood in two ways. First, as the average number of years left to live times the additional expenditure during each year (for a €1 increase in expenditure, this becomes simply the mean of LE_m), divided by the change in QALYs due to the increase in health expenditure (for a €1 increase in expenditure, this is the marginal effect of health spending on health denoted by $\frac{\partial QALE_m}{\partial HCE}$). Second, and shown next in Eq. 5, it can alternatively be computed and understood as the additional expenditure per year (i.e., €1 increase) divided by the change in QALYs owing to the increase in expenditure allocated equally across remaining life-years (for a €1 increase, this is the marginal effect of health spending on health divided by the remaining LE, i.e., $\frac{\partial QALE_m}{\partial HCE}\frac{1}{LE_m}$). The last two terms in Eq. 5 show how this is computed using the input from our regression models, where the β estimate is expressed as an elasticity rather than the marginal effect (i.e., $\beta = \frac{\partial QALE_m}{\partial HCE} \times \frac{\overline{HCE}}{\overline{QALE_m}}$). Using Eq. 5, we estimate the incremental costs per QALY corresponding to the estimated set of $\beta : \left[\beta^*, \tilde{\beta}\right]$.

3 Results

3.1 Descriptive Statistics

Life expectancy at birth, QALE at birth, the average QALE of the population, and per capita public health spending for each region and for selected years of the period 2002–22 are presented in Table 2. Summary statistics for the full set of variables are shown in Table 1.

Overall, LE at birth in Spain increased from 79.7 years in 2002 to 83.05 years in 2022 (an increase of 4.2%), and QALE at birth increased from 73.3 to 75.8 years (an increase of 3.4%). All regions have followed similar trends: the lowest percentage change in LE in the period 2002–22 is a 3.3% increase in Aragon and the highest is a 4.9% increase in Madrid. However, the average QALE of the Spanish population has decreased from 39.9 to 37.3 years. The reason being that the latter is computed as the population-weighted mean QALE across age cohorts, taking into account the share of the population in each age group (see Eq. 4). In most regions, the shares of the oldest age groups have increased over time, and the expected remaining number of healthy years to live in these age groups is lower. This has led to a decrease in the average QALE of the population over the period of analysis. We come back to this issue and its implication for our estimates in the Discussion section. In contrast, public health spending per capita has doubled,

Table 1 Summary statistics for the period 2002–21

Variables	Source	Years available	Mean	St. Dev.	Min.	Max.
Dependent variables						
Average QALE	INE, MoH [23–25]	2002–22*	37.86	2.03	32.33	41.86
Average LE	INE [23]	2002–22	43.81	1.94	38.13	47.28
Explanatory variable of interest						
Health spending pc	MoH [27]	2002–21	1399.0 €	€261.5 €	€784.8	2025.6 €
Demographic variables						
Population size (weighting variable)	INE [28]	2002–21	2,667,869	2,373,228	310,322	8,153,907
Population density	INE [28]	2002-21	161.21	177.77	22.19	837.90
Proportion of women	INE [28]	2002–21	0.5065	0.0073	0.4927	0.5226
Proportion of under 5 years	INE [28]	2002–22	0.0470	0.0074	0.0284	0.0638
Proportion of population over 65 years	INE [28]	2002–23	0.1854	0.0320	0.1206	0.2655
Proportion of population over 85 years	INE [28]	2002–21	0.0266	0.0096	0.0107	0.0552
Socioeconomic variables						
GDP per capita	INE [29]	2002–21	22,511.9 €	4,782.0 €	11,592.0 €	36,206.0 €
Proportion unemployed	INE [30]	2002–21	0.1519	0.0680	0.0472	0.3622
Proportion secondary education or less	MoH [27]	2002–21	0.4611	0.0979	0.2310	0.6890
Proportion of immigrates	INE [28]	2002–21	0.0939	0.0496	0.0140	0.2235
Out of pocket spending on health	MoH [27]	2006–21	€363.3	€69.3	€229.9	€660.0
Lifestyle variables						
Smoking rate	MoH [27]	2001, 2003, 2006, 2009, 2011, 2014, 2017, 2020	0.2443	0.0333	0.1609	0.3134
Obesity prevalence	MoH [27]		0.1571	0.0293	0.0970	0.2222
Sedentarism rate	MoH [27]	2001, 2003, 2006, 2011, 2014, 2017, 2020	0.4245	0.1086	0.2087	0.6971
Contextual variables						
Price per urban squared metre of floor space	MoT [33]	2004–21	197.7 €	94.5 €	57.9 €	562.3 €
Labor cost per hour	INE [32]	2002–21	17.9 €	3.0 €	11.1 €	27.3 €
Health variables non-amenable to health spending						
Labor accidents per 100,000 workers	MoH [27]	2002–21	4341.09	1489.45	1863.50	9139.67
Mortal traffic accident victims	MoH [27]	2002–21	6.97	4.67	1.27	24.52
Non-mortal traffic accident victims	MoH [27]	2002–21	260.55	93.45	56.90	518.05

GDP gross domestic product, *INE* National Institute of Statistics, *LE* life expectancy, *Max.* maximum, *Min.* minimum, *MoH* Ministry of Health, *MoT* Ministry of Transport, *pc* per capita, *QALE* quality-adjusted life expectancy, *St. Dev.* standard deviation, *Average QALE is a variable constructed from LE data available from 2002 until 2022, and survey data available in 2003/04, 2006/07, 2009/10, 2011/12, 2014/15, 2016/17, and 2019/20

from €873 in 2002 to €1777 in 2021 (year with latest available data). The largest increase took place in the Balearic Islands (an increase of 120.6%), while the lowest increase was in La Rioja (an increase of 83.4%). In order to graphically compare the evolution between 2002 and 2021 of average QALE and per capita health spending, Fig. 1 shows the mean annual percentage change in public health spending versus the mean annual percentage change in average QALE for each region. The graph suggests a positive association between changes in health spending and changes in average QALE, but this observation by itself does not imply a causal relationship.

3.2 Econometric Results

3.2.1 Main Results

Table 3 shows the estimated coefficients from the regression analyses. For comparison purposes, the first two columns show the results of applying ordinary least square (OLS) to the pooled dataset without adjusting for regional FEs (we refer to these as pooled OLS models). We report estimates without controls (column 1) and with controls (column 2). The next two columns show the corresponding estimates for the uncontrolled (column 3) and controlled

Table 2 LE at birth, QALE at birth, the average QALE of the population, and per capita public health spending for each region and for selected years of the period 2002–2

Region		2002	2006	2010	2014	2018	2020	2021	2022
Andalucía	LE at birth	78.50	79.63	80.76	81.70	81.73	81.51	81.46	81.86
	QALE at birth	72.25	72.03	72.10	72.46	72.74	74.79	74.76	75.06
	Average QALE	40.13	39.50	38.41	37.82	37.03	37.95	37.68	37.69
	Health spending pc	839 €	1108 €	1262 €	1110 €	1265 €	1459 €	1548 €	
Aragon	LE at birth	80.38	81.41	82.18	82.85	83.44	82.38	83.25	83.06
	QALE at birth	74.68	74.98	75.48	75.81	75.63	76.21	76.88	76.71
	Average QALE	37.75	38.05	38.34	37.74	36.78	36.74	37.30	37.05 €
	Health spending pc	951 €	1319 €	1561 €	1478 €	1620 €	1794 €	1890 €	
Asturias	LE at birth	79.52	80.19	81.18	82.11	82.64	82.10	82.75	82.46
	QALE at birth	71.29	71.32	73.18	73.49	73.33	74.37	74.85	74.62
	Average QALE	34.05	33.59	34.27	33.35	32.48	32.45	32.70	32.33
	Health spending pc	946 €	1283 €	1588 €	1456 €	1684 €	1913 €	1984 €	
Baleares	LE at birth	79.47	80.85	81.56	82.60	82.97	83.11	83.00	82.90
	QALE at birth	72.44	73.54	74.52	74.77	76.15	76.84	76.75	76.67
	Average QALE	39.42	40.12	40.32	39.47	40.24	40.24	40.01	39.61
	Health spending pc	785 €	1115 €	1566 €	1290 €	1477 €	1679 €	1739 €	
Canarias	LE at birth	78.59	79.61	81.39	81.86	81.79	82.26	82.12	81.78
	QALE at birth	70.33	72.56	73.01	72.96	73.79	72.87	72.74	72.53
	Average QALE	39.59	40.39	39.67	37.84	37.44	36.09	35.71	35.10
	Health spending pc	904 €	1214 €	1402 €	1347 €	1530 €	1775 €	1888 €	
Cantabria	LE at birth	80.11	80.99	82.06	82.78	83.33	83.00	83.63	83.06
	QALE at birth	74.54	74.37	74.22	74.49	75.84	75.46	75.92	75.53
	Average QALE	38.57	37.98	37.19	36.24	36.63	35.75	35.99	35.24
	Health spending pc	1013 €	1403 €	1501 €	1417 €	1589 €	1856 €	1925 €	
Castilla la Mancha	LE at birth	80.37	81.68	82.71	83.28	83.42	81.22	83.02	83.33
	QALE at birth	73.93	74.94	74.37	75.53	74.72	74.00	75.34	75.56
	Average QALE	39.19	40.08	39.39	39.24	37.98	36.43	37.57	37.54
	Health spending pc	872 €	1299 €	1619 €	1298 €	1518 €	1797 €	1894 €	
Castilla y Leon	LE at birth	80.80	81.94	82.90	83.60	83.92	82.53	83.94	83.68
	QALE at birth	75.11	75.42	75.78	75.12	76.48	74.27	75.30	75.11
	Average QALE	37.78	37.36	36.86	35.63	35.59	33.25	34.06	33.72
	Health spending pc	893 €	1339 €	1503 €	1324 €	1629 €	1936 €	1946 €	
Cataluña	LE at birth	80.03	81.28	82.26	83.17	83.40	82.25	83.34	83.49
	QALE at birth	73.54	74.00	74.20	74.59	74.35	75.79	76.64	76.76
	Average QALE	38.67	39.20	38.92	38.48	37.45	38.42	39.07	39.01
	Health spending pc	873 €	1158 €	1455 €	1289 €	1492 €	1861 €	1886 €	
Extremadura	LE at birth	79.38	80.43	81.21	82.35	82.53	81.83	82.19	82.40
	QALE at birth	73.04	72.32	72.46	74.76	75.98	75.88	76.17	76.31
	Average QALE	38.77	37.81	37.07	37.68	37.39	36.54	36.62	36.57
	Health spending pc	945 €	1323 €	1659 €	1493 €	1663 €	1831 €	1953 €	
Galicia	LE at birth	80.00	80.81	81.93	82.91	83.09	83.33	83.41	83.23
	QALE at birth	71.68	71.42	72.08	72.73	73.68	74.89	74.96	74.83
	Average QALE	35.69	34.74	33.93	33.39	33.58	34.03	33.86	33.50
	Health spending pc	902 €	1229 €	1476 €	1338 €	1530 €	1755 €	1825 €	
La Rioja	LE at birth	80.48	81.88	82.95	83.78	83.63	82.50	83.27	83.20
	QALE at birth	75.33	75.21	75.30	75.72	76.86	75.36	75.93	75.87
	Average QALE	39.31	39.19	38.55	38.35	38.41	36.57	37.04	36.84
	Health spending pc	911 €	1553 €	1506 €	1352 €	1498 €	1626 €	1671 €	
Madrid	LE at birth	80.81	82.06	83.39	84.20	84.73	82.27	84.56	84.76

Table 2 (continued)

Region		2002	2006	2010	2014	2018	2020	2021	2022
	QALE at birth	74.61	75.15	75.58	76.82	76.36	76.15	77.96	78.11
	Average QALE	40.81	41.23	40.88	40.70	39.68	38.79	40.35	40.26
	Health spending pc	829 €	1089 €	1203 €	1187 €	1289 €	1522 €	1558 €	
Murcia	LE at birth	78.96	80.27	81.62	82.47	82.64	82.26	82.21	82.05
	QALE at birth	72.13	71.88	70.68	73.52	73.76	74.15	74.12	73.98
	Average QALE	40.73	40.21	38.15	39.55	38.92	38.69	38.44	38.22
	Health spending pc	880 €	1211 €	1612 €	1487 €	1612 €	1810 €	1946 €	
Navarra	LE at birth	80.83	82.02	83.68	83.45	84.14	83.33	84.26	83.85
	QALE at birth	74.87	74.75	76.55	75.31	75.41	76.75	77.46	77.14
	Average QALE	39.50	39.46	40.34	38.72	38.61	38.87	39.49	39.04
	Health spending pc	1011 €	1281 €	1601 €	1495 €	1688 €	1908 €	1985 €	
País Vasco	LE at birth	80.16	81.49	82.42	83.35	83.65	83.18	83.71	83.49
	QALE at birth	74.75	74.71	74.59	75.43	76.12	76.05	76.45	76.28
	Average QALE	38.41	38.06	37.03	37.09	36.81	36.20	36.37	36.04
	Health spending pc	976 €	1293 €	1685 €	1582 €	1735 €	1948 €	2026 €	
Valencia	LE at birth	79.01	80.44	81.55	82.39	82.53	82.32	82.21	82.47
	QALE at birth	73.44	72.00	72.74	74.83	75.22	74.45	74.37	74.56
	Average QALE	39.35	38.08	37.75	38.35	37.85	36.84	36.53	36.54
	Health spending pc	830 €	1106 €	1405 €	1284 €	1486 €	1692 €	1767 €	
Valencia	LE at birth	79.70	80.89	82.01	82.84	83.08	82.25	82.96	83.05
	QALE at birth	73.29	73.40	73.70	74.47	74.71	75.14	75.70	75.77
	Average QALE	39.09	38.93	38.36	38.00	37.37	37.15	37.49	37.34
	Health spending pc	873 €	1183 €	1421 €	1289 €	1466 €	1711 €	1777 €	

LE life expectancy, *QALE* quality-adjusted life expectancy, *pc* per capita

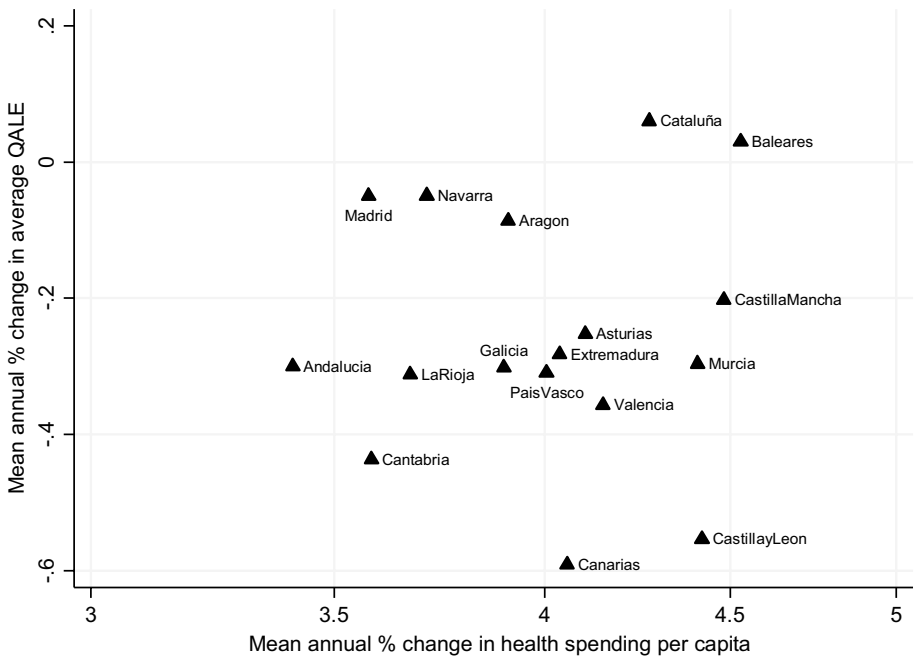

Fig. 1 Mean annual percentage change in average quality-adjusted life-years versus mean annual percentage change in health spending per capita per region in the period 2002–21. *QALE* quality-adjusted life expectancy

Table 3 Regression analysis results

Dependent variable: average QALE (in log)	(1) Pooled OLS: without controls	(2) Pooled OLS: with controls	(3) Fixed effects: without controls	(4) Fixed effects: with controls
Public health spending pc (in log)	−0.2194* [0.111]	−0.0592* [0.028]	0.0547 [0.040]	0.0610** [0.024]
Population density (in log)		−0.0098 [0.010]		0.2713** [0.100]
Prop. women (in log)		−0.7942* [0.378]		−0.3601 [0.627]
Prop. under 5 (in log)		0.1633*** [0.033]		0.0842 [0.053]
Prop. over 65 (in log)		−0.1445** [0.067]		−0.0409 [0.083]
Prop. over 85 (in log)		0.0061 [0.044]		−0.0372 [0.056]
GDP pc (in log)		0.0473 [0.035]		0.1675** [0.064]
Prop. unemployed (in log)		0.0094 [0.014]		0.0027 [0.011]
Prop. only secondary education (in log)		−0.1088*** [0.035]		−0.0287 [0.029]
Prop. immigrants (in log)		−0.0053 [0.013]		0.0088 [0.017]
Private health spending (in log)		−0.0406* [0.021]		0.0052 [0.017]
Smoking rate (in log)		−0.018 [0.019]		−0.0119 [0.016]
Sedentarism rate (in log)		−0.0026 [0.013]		−0.0029 [0.013]
Obesity rate (in log)		−0.0628*** [0.019]		−0.0138 [0.013]
Floor space cost (in log)		−0.0038 [0.005]		0.0037 [0.006]
Labor cost (in log)		−0.0518 [0.046]		−0.075 [0.095]
Labor accident rate (in log)		−0.0464* [0.024]		−0.0012 [0.019]
Mortal traffic victims (in log)		0.0033 [0.011]		−0.0025 [0.007]
Non-mortal traffic victims (in log)		0.0123 [0.007]		0.0067 [0.010]
Constant	5.1471*** [0.751]	3.8923*** [0.291]	3.2911*** [0.270]	0.1704 [1.330]
R-squared	0.268	0.888		
Within R-squared			0.601	0.692

Regressions based on 340 observations (N*T). All models include year dummies. Regressions (1) and (2) are OLS models without regional fixed effects; regressions (3) and (4) are regional fixed-effect models. Clustered standard errors by regions in brackets

GDP gross domestic product, *OLS* ordinary least square, *pc* per capita, *Prop.* Proportion

$*p < 0.10$; $**p < 0.05$; $***p < 0.01$

(column 4) regional FE models. All models include year dummies.

The pooled OLS model shows a negative relationship between health spending and average QALE of the population. When the controls are added, the absolute size of the effect decreases, but still shows a negative association. Incorporating regional FE changes the sign of the estimated effect, and adding the full set of control variables slightly increases the size of the coefficient and yields to an estimated significant and positive effect. In this preferred specification (column 4), the estimated effect indicates that a 1% increase in annual health spending increases population QALE by 0.061%. Over and above the impact of health spending, population density and gross domestic product per capita are the only additional statistically significant covariates in the model that account for regional FEs, both showing a positive effect.

Table 4 reports the bounds of the value of β from the FE models with controls. The bias-corrected elasticity (β^*) proposed by Oster under the assumptions that $\delta = 1$ and $R_{\max} = 1.3 \times \widetilde{R}$ is 0.075, which indicates that omitted variable bias generates a downward bias to the estimated effect.

The incremental costs per QALY corresponding to the estimated set $\left[\beta^*, \widetilde{\beta}\right]$ are presented in the last two columns of Table 4. These are computed by transforming the estimated elasticities into marginal effects at means (columns 3 and 4) and applying Eq. 5. The population-weighted mean values of average LE, average QALE, and average health spending per capita were 43.22, 37.49, and €1777 in 2021, respectively. Using these values, and based on the lower bound of the impact of health spending on QALE, the incremental cost per QALY is estimated in €33,578/QALY (= 43.22/(0.061*37.49/1777) or, equivalently, = 1/((0.061*37.49/1777)/43.22, see Eq. 5). This value decreases to €27,165/QALY when the upper bound β^*= 0.075 is used as the elasticity.

The lower part of Table 4 shows how the estimated effect, and the associated incremental cost per QALY, changes

Table 4 Oster bounds for fixed-effects models with controls: impact of public health spending on average quality-adjusted life expectancy

	Elasticity [within R^2]			Marginal effect at means		Incremental cost per QALY	
	$\dot{\beta}$	$\widetilde{\beta}$	β^*	Based on $\widetilde{\beta}$	Based on β^*	Based on $\widetilde{\beta}$	Based on β^*
Data until 2022	0.0547 [0.6012]	0.0610** [0.6920]	0.0754	0.00129	0.00159	€33,578	€27,165
Data until 2017	0.0714* [0.6537]	0.0713*** [0.7437]	0.0712	0.00195	0.00194	€22,753	€22,797
Data until 2018	0.0778* [0.6933]	0.0763*** [0.7694]	0.0717	0.00202	0.00190	€21,808	€23,188
Data until 2019	0.0637* [0.6267]	0.0651** [0.7064]	0.0689	0.00166	0.00176	€26,465	€25,008
Data until 2020	0.0569* [0.6275]	0.0686** [0.7048]	0.0998	0.00169	0.00246	€26,093	€17,926
Data until 2021	0.0576 [0.6116]	0.0643** [0.6914]	0.0819	0.00140	0.00178	€30,595	€24,046

$\dot{\beta}$ is the estimate of β from the uncontrolled fixed-effects regression, $\widetilde{\beta}$ is the estimate of β from the controlled fixed-effects regression; β^* is the bias-corrected coefficient estimated following the method proposed by Oster (assuming $\delta = 1$ and $R_{\max} = 1.3 * \widetilde{R}$). Clustered standard errors by regions were used

QALY quality-adjusted life-year

$*p < 0.10$; $**p < 0.05$; $***p < 0.01$

when increasingly incorporating one additional year of data over the past previous 5 years.[3] We observe that the estimated coefficients of health spending on health based on the uncontrolled and controlled FE models fall, which might suggest a decreasing spending elasticity over time. In addition, the results show that prior to 2020, the adjusted estimates and the bias-corrected estimates (i.e., the bounds $\widetilde{\beta}$ and β^*, respectively) were very close, indicating evidence of limited omitted variable bias prior to this year. However, this gap is larger after the COVID-19 pandemic. This result emphasizes that the bias exhibited in the relationship between health spending and health outcomes has increased because of the pandemic and the required response of the healthcare system to it. The largest gap is observed when data from 2020 are included in the analysis, but this gap is closing as newer years of data are introduced. As a result, while the uncontrolled and controlled estimates appear to decrease over time, there is not a clear trend on the bias-corrected coefficients. This is because the extent of the bias increased when including the years of the pandemic but has then decreased when including the post-pandemic period. Similar results were found when applying the assumption that $R_{max} = 1$ and using the Stata command *psacalc* (Appendix 2 of the ESM).

3.2.2 Additional Analyses

Table 5 shows the results of the controlled FE models when alternative specifications and lag structures are used. Including health spending in a quadratic form did not yield a significant non-linear effect (p value = 0.193; not shown in Table 5). Using a linear specification instead of a log-log model led to a similar impact in terms of the estimated marginal effect and the associated incremental cost per QALY. Estimating the impact without allowing for a lag on the relationship between health spending and health outcomes (i.e., health and spending data correspond to the same year) shows a smaller effect (and therefore, a higher incremental cost per QALY), and so does imposing a 2-year lag effect; in that case, the effect of health spending on average QALE is only weakly significant.

Table 5 also shows separately the impact of spending on mortality alone and on QoL alone. The former is conducted using as a dependent variable the average LE of the population, without adjusting for QoL, while the latter explores the impact of spending on the average QoL score value of the population using only the years when predicted QoL data were available. We observed that the estimated impact of health spending on mortality is slightly smaller than the impact on QoL, suggesting that health spending might have a larger impact on improving population QoL than on increasing LE. However, the impact on QoL is estimated to be only weakly significant, probably owing to the nature and lower quality and quantity of data, based on mean predicted EQ-5D scores by age groups derived from survey data.

Excluding the years of data most affected by the impact of the COVID-19 pandemic slightly increases the estimated impact of health spending on health outcomes and yields a lower estimated value of the incremental cost per QALY produced by the health system. These are estimated in €29,883/QALY when 2020 and 2021 data are excluded, and in €32,104/QALY when only data from 2020 are excluded. Including only the years when a health survey was conducted in Spain (i.e., excluding 2005, 2008, 2013, 2018, and 2021) yields very similar results to those obtained on the base case, which imputed QoL data on these years using the nearest year available.

[3] Excluding additional years of data decreases substantially the size of the dataset.

Table 5 Additional analyses: impact of public health spending on health outcomes based on controlled fixed-effect models

	Elasticity ($\widetilde{\beta}$)	Marginal effect (based on $\widetilde{\beta}$)	Incremental cost per QALY/LY
Base case	0.0610**	0.00129	€33,578
Linear model	–	0.00134**	€32,193
No lagged effect	0.0550**	0.00116	€37,230
Two-year lag effect	0.0523*	0.00110	€39,194
No QoL effect	0.0218**	0.00053	€81,483
No mortality effect[a]	0.0241*	0.00059	€73,863
Excluding 2020	0.0638**	0.00135	€32,104
Excluding 2020 and 2021	0.0686**	0.00145	€29,883
Excluding years without QoL data[a]	0.0590**	0.00124	€34,722

$\widetilde{\beta}$ is the estimate of β from the controlled fixed-effects regression. Clustered standard errors by regions were used

LY life-year, *QALY* quality-adjusted life-year, *QoL* quality of life

$*p < 0.10$; $**p < 0.05$; $***p < 0.01$

[a]These models exclude data for the years 2005, 2008, 2013, 2018, and 2021

4 Discussion

In this paper, we have illustrated the use of regional FE models and the Oster methods to estimate the impact of health spending on health outcomes in the Spanish NHS and to explore the role of omitted variable bias in this relationship. To do so, we have used a panel of 17 regions across 20 years of data and, based on the estimated effects, we derive the incremental cost per QALY produced by the health system. Data were compiled from freely accessible and routinely updated administrative and survey datasets available in Spain. Data collection was carefully managed through Stata programming so that estimates can be easily updated when new data become available.

According to the estimated figures, the lower and upper bounds of the health spending elasticity of QALE are 0.061 and 0.075, respectively, and the associated incremental cost values lie between €27,165 and €33,578 per QALY in Spain. These results suggest that there is some degree of omitted variable bias remaining after applying a controlled FE estimation, although the size of the gap is relatively small.

In addition, this study shows how the estimated impact, and the associated incremental cost per QALY, changes as new recent years of data are included in the analysis. Our results suggest that the spending elasticity might be decreasing over time, which translates into larger incremental cost per QALY values. However, the extent of omitted variable bias appears to increase, particularly when including data from 2020 and 2021. This finding indicates that, not surprisingly, the COVID-19 pandemic has increased the bias in the estimated relationship between health spending and health outcomes. Excluding these years of data yielded to slightly larger elasticities and lower incremental cost per QALY estimates.

The values provided in this study (using data from 2002 until 2022) are not directly comparable to the previously published values for Spain that used data from 2008 to 2012 [6]. Nonetheless, we note, with caution, that the spending elasticity was estimated in 0.068 in Vallejo-Torres et al., while the estimate from a similar controlled FE model yielded a value of 0.061 in this study. As a result of this, and also because of the changes in the mean values of health spending, average QALE and average LE of the population, the estimated cost per QALY figures have increased from an upper value of €25,000/QALY in 2012 to an upper value of €34,000/QALY in 2022. This is an increase of 34%, which is larger than the inflation rate over this 10-year period (estimated at 14% in Spain [33]). When considering the lower bound of €22,000/QALY in Vallejo-Torres et al. and the bias-corrected estimate of €27,000/QALY in this study, the observed change is also larger than the inflation rate (a 23% increase). Notwithstanding the caution needed in these comparisons, this suggests that applying inflation rates to update estimates of the incremental cost per QALY produced by a healthcare system is unlikely to provide reliable values. Instead, when new data become available, the approach used in this study can be easily replicated, by enlarging the panel of data used to estimate the effects of interest.

Comparing empirical cost per QALY estimates published in the literature for different countries is not straightforward because of the diversity of methods and data sources used across studies [17], as well as the large disparities in the performance of health systems. The cost per QALY/DALY produced/averted by a health system have been estimated in AUS$28,033 (~€17,000) in Australia [4], in SEK180,000 (~€19,000) [7] and SEK400,000 (~€35,000) [8] in Sweden, in €41,000 [9] and €73,626 [10] in The Netherlands, in R38,500 (~€200) in South Africa [11], in ¥37,446 (~€5000)

in China [12], in £12,936 (~ €15,000) [3] and, more recently, in £5000–£10,000 (~ €6000–€12,000) in the UK [13], in US$100,000 (~ €90,000) in the USA [14], and in 17 million COP (~ €5000) in Colombia [15]. Most of these studies did not make use of longitudinal data, with some relying on the use of instrumental variables to address potential endogeneity bias likely to affect cross-sectional analyses, and/or were not capable of estimating the impact of healthcare spending on QoL, over and above the impact on mortality/LE. However, a common finding among most of these studies is that the estimated figures were below the policy relevant threshold used in that jurisdiction, and, particularly, below the rule of thumb of setting a cost-effectiveness threshold in the range of one to three times the country gross domestic product per capita.

The transferability of the approach proposed in this study to other settings with regional data on health spending and QALE is straightforward. However, while information on health spending and LE might be available at some regional level in most health systems, we acknowledge that information on a QoL instrument measured on a QALY scale might not always exist at a regionally representative level. That was also the case in Spain, and therefore our approach of predicting EQ-5D scores by age-gender-region groups using health survey data might also serve as an alternative to settings lacking this information. Even when data to predict QALY weights are not available, analysts might consider aiming to estimate the effect of health spending on mortality alone, similarly to our approach using average LE as a dependent variable. As mentioned above, this has been the approach taken in other studies, which have then assumed the effect of spending on morbidity to be the same, in proportionate terms, to the estimated effect on mortality [3, 13], i.e., the surrogacy assumption. Our study provides some support to such an assumption: according to our estimations, the spending elasticity of LE is less than the spending elasticity of QoL, and thus suggests that the impact of spending on morbidity is, at least, proportionate to the impact of spending on mortality.

There are several issues affecting this analysis that deserved to be acknowledged. First of all, as already mentioned, nationally representative information on health-related QoL in Spain is poor. The only national survey including the EQ-5D instrument was conducted in 2011/12. Although the methods applied in this study make the best use of the evidence available, it is strongly advisable to incorporate this instrument in future waves of the Spanish Health Survey and the European Health Survey in Spain. That information could then be used when updating these estimates in the future. Second, this study has gone one step further in assessing the role of omitted variable bias in the relationship between health spending and health outcomes. However, the conclusions drawn in this sense depend on the assumptions applied when using the Oster methods regarding the importance of the unobservable variables relative to the observable variables and the share of variance of health outcomes, which can be jointly explained by observed and unobserved variables. Even when applying the bound of $\delta = 1$ and assuming that unobserved controls could increase the explained variance of health outcomes by 30% (i.e., using $R_{\max} = 1.3 * \widetilde{R}$), the results show that FE models deliver estimates of the effect of health spending that are fairly robust. Using the extreme assumption that $R_{\max}$ equals to one yielded similar results. It is also worth noting that as shown in Table 2, LE and QALE at birth have increased over the period of analysis, but the average QALE of the population, our main dependent, has decreased. As explained, the reason is that the shares of groups with lower QALE values are increasing over time as the population ages. This common trend as well as time-invariant differences in the demographic structures between regions are nonetheless removed from the estimation by applying region and year FEs and adding demographic control variables to account for changes in the share of age groups that might vary both across regions and over time. These adjustments ensure that the estimated effect of health spending on health outcomes measures its impact on the overall health of the population and not on their regional demographic structure.

5 Conclusions

In summary, the analysis conducted in this study is based on a simple and transferable approach that allows measuring the incremental cost of producing a QALY from a system-wide perspective. In the case of Spain, this value was found to be between €27,000 and €34,000 per QALY. This information allows us to proxy the health likely to be forgone if resources from the health system are displaced, and thus allows the approximation of the health opportunity costs of health funding decisions. While there might still remain a debate about the appropriateness of having an explicit and fixed cost-effectiveness threshold to inform adoption and reimbursement decisions [34], the relevance of this information to support decision makers in assessing whether funding decisions are expected to lead to improvements in population health is undoubtable. In addition, monitoring the impact of health spending on health outcomes provides further insights regarding the changes of the efficiency of the health system over time.

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Declarations

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Conflict of interest Laura Vallejo-Torres has no conflicts of interest that are directly relevant to the content of this article.

Ethics approval Not applicable.

Consent to participate Not applicable.

Availability of data and material All data used in this study were taken from open sources of publicly available repositories including the Spanish Ministry of Health key indicators website (https://inclasns.sanidad.gob.es/main.html), the Spanish National Institute of Statistics website (www.ine.es), and the Spanish Ministry of Transport website (https://www.transportes.gob.es/). In addition, survey data were downloaded from https://www.sanidad.gob.es/estadEstudios/estadisticas/sisInfSanSNS/nivelSalud.htm.

Code availability Not applicable.

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