



VOLY: The Monetary Value of a Life-Year at the End of Patients' Lives

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Abstract

Objective We explored the monetary value of the end-of-life (EoL) health gains, that is, the value of a life-year (VOLY) gained at the end of a patient's life in Croatia. We tested whether the nature of the illness under valuation (cancer and/or rare disease) is a factor in the valuation of EoL-VOLYs. The aim was for our results to contribute to the health and longevity valuation literature and more particularly to the debate on the appropriate cost-effectiveness threshold for EoL treatments as well as to provide input into the debate on the justifiability of a cancer and/or a rare disease premium when evaluating therapies.

Methods A contingent valuation was conducted in an online survey using a representative sample of the Croatian population ($n = 1500$) to calculate the willingness to pay for gains in the remaining life expectancy at the EoL, from the social-inclusive-individual perspective, using payment scales and an open-ended payment vehicle. Our approach mimics the actual decision-making problem of deciding whether to reimburse therapies targeting EoL conditions such as metastatic cancer whose main purpose is to extend life (and not add quality to life).

Results Average EoL-VOLY across all scenarios was estimated at €67,000 (median €40,000). In scenarios that offered respondents 1 full year of life extension, EoL-VOLY was estimated at €33,000 (median €22,000). Our results show that the type of illness is irrelevant for EoL-VOLY evaluations.

Conclusions The pressure to reimburse expensive therapies targeting EoL conditions will continue to increase. Delivering “value for money” in healthcare, both in countries with relatively higher and lower budget restrictions, requires the valuation of different types of health gains, which should, in turn, affect our ability to evaluate their cost effectiveness.

Key Points for Decision Makers

To deliver ‘value for money’ policymaking in healthcare requires the valuation of different types of health gains.

The monetary value of a life-year at the end of patient's life in Croatia averages at €67,000, about 5 times the gross domestic product per capita.

The monetary value of a life-year at the end of a patient's life is independent from the type of disease.

1 Introduction

The results of clinical studies of innovative therapies are presented in terms of direct outcomes such as overall survival and surrogate outcomes such as progression-free survival and quality of life. These results feed into the calculations of the incremental cost-effectiveness ratios (ICERs) that policy makers then compare to the cost-effectiveness (CE) thresholds to discern whether a particular therapy is relatively cost effective and hence whether it should be recommended for reimbursement. With regard to what might constitute a CE threshold and, consequently, how to estimate it, two broad concepts have emerged (e.g., [1–3]). The “supply-side” threshold would reflect the opportunity costs associated with using health system resources for a particular purpose, while the “demand-side” CE threshold refers to the willingness to pay (WTP) for a health gain. Ideally, the “demand-side” and “supply-side” thresholds would be equal, as this would imply an optimally set budget for healthcare [1]. However, given that the optimality of healthcare budgets

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is generally not established, and “supply-side” thresholds are not easily nor readily calculated, the information on both CE thresholds is useful for determining whether a new technology is too expensive for funding. While the reimbursement decision-making process is not linear and many other concerns in addition to relative CE play a role in the final reimbursement (and pricing) decisions, it is still regarded as one of the important “fourth hurdles” around Europe and elsewhere.

Policy makers worldwide are increasingly using more lenient CE thresholds to evaluate therapies targeting patients nearing life’s end. For instance, the National Institute for Health and Care Excellence until recently placed special consideration to life-extending end-of-life (EoL) treatments [4, 5] and applied a relatively higher threshold for technologies targeting EoL conditions (£50,000 per quality-adjusted life-year [QALY] [6]). This reflected the notion that our societies might be willing to pay relatively more for health gains achieved at the very EoL than for gains in previous periods of life. Although the evidence supporting this type of social preference was not uniform (e.g., [7]), which may have ultimately led to replacing EoL weights by severity weights in the UK context [5], in practice around Europe we see that therapies targeting near-death conditions such as metastatic oncological diseases still often receive reimbursement despite relatively high prices and despite with often only low life-extending and quality-improving properties (e.g., [8–10]).

Our study is designed to explore the monetary value of the EoL health gains. We do not aim to compare the value of EoL and non-EoL gains but instead focus on directly estimating the value of EoL longevity prolongment, at different quality-of-life (QoL) levels. Hence, we focus on estimating the monetary value of a life-year (VOLY) at the end of a patient’s life (EoL-VOLY). EoL-VOLY intends to provide further quantitative information on how people value changes in life expectancy. The aim of our results was to contribute to the health and longevity valuation literature and more particularly to the debate on the appropriate CE threshold for EoL treatments (such as metastatic diseases). Our study tests a related hypothesis, notably, whether the nature of the illness under valuation (cancer and rare disease) is a factor in the valuation of VOLYs. We intended our results to provide input into the debate on the justifiability of cancer and/or a rare disease premium (e.g., [11–14]) when evaluating therapies. This hypothesis might also be relevant for a broader discussion on the justifiability of cancer funds and rare disease funds as separate funding silos operating in different European jurisdictions. Finally, our study contributes to the literature by providing the first EoL-VOLY estimates for Croatia, among a few in South-East Europe more generally [15, 16].

2 EoL-VOLY: What Do We Know So Far?

Theoretically, policy makers can improve the health and safety of a population by reducing the risk of death, increasing life expectancy, and improving health-related QoL. These benefits can be monetarized in at least three alternative ways using: (i) the value of a prevented fatality or a value of statistical life, which respectively value small changes in fatality or mortality risks; (ii) the value of a life-year gained (EoL-VOLY, which values the extension to the length of life at the end of life); and (iii) QALYs (which value changes in health-related QoL and length of life in combination). The appropriateness of using either the value of statistical life or the EoL-VOLY as a means to calculate the cost of lives lost has been debated in the literature (e.g., [17–20] for the choice between the value of a prevented fatality or the value of a life-year).

The empirical health economics literature on EoL-VOLYs is generally less comprehensive than the literature exploring the monetary values of QALYs (for a systematic review of this literature, see e.g., [21, 22]). A recent systematic review of the demand-side methods of estimating the societal monetary value of health gain reveals that EoL-VOLY has typically been estimated as a part of the QALY gain valuations, with life extension as a QALY dimension of interest [23]. The review showed that across all studies that employed direct methods to estimate the monetary value of life-extending health gains, a median EoL-VOLY estimate was €28,488 (with a wide range of estimates, from €1942 to €572,557), which corresponds to a median ratio to gross domestic product [GDP] per capita of 0.57 (range 0.02–10.59). Eastern Europe [16] reports a considerably lower mean EoL-VOLY value of €5770 in Poland. The studies have employed mainly WTP methods when estimating EoL-VOLY, either from the healthcare payer or individual perspective. Most studies, however, employed the individual perspective, where the median EoL-VOLY was estimated at €41,364 (again, with a wide range of estimates) and the median ratio to GDP per capita was 0.82 (0.02–10.59) [24–30].

3 Methods

The EoL-VOLY estimated in this study is a VOLY achieved in a patient facing 100% risk of death and being close to the point of dying. The patient will die, no matter what, the question is only how long the patient has to live in a given health state. We asked a representative sample of the Croatian population about their WTP for a gain in life expectancy at a certain level of QoL (Table 1). This

Table 1 Scenario design

No.	Patients benefiting (I)	QoL at the end of life (0–1 scale) [II]	Additional months because of treatment (LYG) [III]	Total life expectancy (months) [IV]	Population-wide LYG (I*III)	Cancer	Rare disease
1	1000	0.20	48	54	4000	No	Yes
2	1000	0.2	48	54	4000	No	Yes
3	1000	0.6	48	54	4000	No	Yes
4	1000	0.4	48	54	4000	No	Yes
5	1000	0.4	48	54	4000	No	Yes
6	1000	0.2	48	54	4000	Yes	No
7	1000	0.2	48	54	4000	Yes	No
8	1000	0.6	48	54	4000	Yes	No
9	1000	0.4	48	54	4000	Yes	No
10	1000	0.4	48	54	4000	Yes	No
11	14,000	0.2	2	8	2333	No	No
12	14,000	0.2	6	12	7000	No	No
13	14,000	0.2	12	18	14,000	No	No
14	14,000	0.6	6	12	7000	No	No
15	14,000	0.6	12	18	14,000	No	No
16	14,000	0.2	2	8	2333	Yes	No
17	14,000	0.2	6	12	7000	Yes	No
18	14,000	0.2	12	18	14,000	Yes	No
19	14,000	0.6	6	12	7000	Yes	No
20	14,000	0.6	12	18	14,000	Yes	No
21	14,000	0.4	2	8	2333	Yes	No
22	14,000	0.6	2	8	2333	Yes	No
23	14,000	0.8	2	8	2333	Yes	No
24	14,000	0.8	6	12	7000	Yes	No
25	14,000	0.4	12	18	14,000	Yes	No
26	14,000	0.8	12	18	14,000	Yes	No
27	14,000	0.2	18	12	21,000	Yes	No
28	14,000	0.4	18	24	21,000	Yes	No
29	14,000	0.6	18	24	21,000	Yes	No
30	14,000	0.8	18	24	21,000	Yes	No
31	14,000	0.4	6	12	7000	Yes	No

All scenarios offer a default life extension of 6 months to which additional months are added because of treatment
 LYG life-years gained, QoL quality of life

gain in the remaining life expectancy constitutes a simple ‘add-on’ to survival time at the end of life. Paying for the new medicine would hence shift the individual’s survival curve outwardly¹. This mimics the actual decision-making problem of deciding whether to reimburse therapies targeting EoL conditions such as metastatic cancer whose main purpose is to extend life at the EoL, knowing that

the therapy does not offer a cure but adds weeks, months, or years of life.

3.1 Study Design

Our design consisted of 31 hypothetical scenarios where an unknown group of patients currently has 6 more months to live, after which they would die (a condition that might include the respondent herself). The new therapy under evaluation could extend their life for 2, 6, 12, 18, or 48 months (life-years gained [LYGs]) at 0.2, 0.4, 0.6, and 0.8 QoL levels (Table 1). Next to varying the size of the at-risk group, additional months of treatment, and QoL, the scenarios also varied the context in which the therapy is administered—in

¹ An alternative approach to calculating the VOLY would be, for instance, to value the reduction in the risk of dying in some future period or periods and to elicit the aggregate current WTP for marginal gains in individual life expectancy (and if those sum to 1 year, this would come close to the value of a statistical life [33]).

a risk group of patients with cancer, patients with a rare disease, or patients with a silent context regarding the type of illness (labeling it only as “severe illness” coded as “no-no” in Table 1). The size of the patient groups also varied to reflect the rarity of the condition under valuation (the European Union considers a disease as rare when it affects less than 1 in 2000 citizens, which would amount to more than 2000 patients in Croatia, while we use 1000 patients in the rare disease group). Respondents were asked how much they would pay for this new therapy once a month for 12 months through increased taxation (all residents above 18 years of age would also be obliged to pay the stated amount and the tax would be abolished after 12 months). Payment vehicles were two payment scales (the amount they would certainly pay and the amount they would certainly not pay) and an open-ended WTP question format (WTP(OE) in which the exact monetary amount was stated (example of wording in the Appendix). This social-inclusive-individual perspective imitates the real-world conditions of healthcare financing in Croatia (i.e., everyone contributes to healthcare without ever being sure whether, which, or when a particular healthcare service will be needed [31, 32]). Average EoL-VOLY was calculated on the bases of responses to all scenarios; additionally, some scenarios were repeated to directly test the difference in VOLYs obtained in patients with cancer versus patients with rare disease (scenarios 1–5 vs scenarios 6–10) and patients with severe illness versus patients with cancer (scenarios 11–15 vs scenarios 16–20) (Table 1).

3.2 Analysis

EoL-VOLYs were calculated using Eq. 1:

$$\text{EoL VOLY} = \frac{\text{WTP(OE)} \times 2,980,000 \times 12}{(\text{population} - \text{wide LYG}) / \frac{1}{(1+r)^n}} \quad (1)$$

where 2,980,000 represents the number of people paying for the new therapy (aged >18 years) and r is the discounting factor (UK discount rate for health of 3.5%) if the LYG duration was > 1 year. The WTP data were graphically inspected for distributional properties and outliers were identified using box and spike plots. Outliers were defined as data points above 200% of the interquartile range and trimmed from the data (replaced by missing values and not considered in the analysis). Mean and median EoL-VOLY estimates are presented as trimmed means and medians (zero WTP values were not excluded for the analysis). The EoL-VOLY estimates were stratified by QoL and LYGs. Multi-variable linear regression was used to test the associations between the main predictors of WTP-OE and hence test the theoretical validity of the results. A priori, WTP-OE should be positively and significantly associated with LYG, income, and the size of the patient group. With respect to the level

of QoL at which the LYG is achieved, we have no a priori expectations. On the one hand, *ceteris paribus*, a higher level of QoL within a QALY framework would yield a higher overall gain and hence would be expected to be associated with higher WTP-OE. On the other hand, *ceteris paribus*, a lower level of QoL could also be associated with higher WTP-OE if severity-related preferences would override preferences for health maximization. The EoL-VOLY estimates were compared using nonparametric tests. All analyses were performed using STATA SE16 (StataCorp LP, College Station, TX, USA).

3.3 Survey

The online questionnaire was administered in June 2021 by a professional sampling agency to a representative sample of the Croatian population ($n = 1500$) in terms of age (> 18 years), sex, education level, and urban-rural as well as regional distribution. Prior to the implementation of the full-scale questionnaire, a pilot study was conducted on a smaller sample ($n = 100$) to test the survey design and its clarity. As the pilot study did not reveal any major issues,² we conducted the main survey.³ All respondents signed an informed consent agreeing to the data being used for research purposes (which includes the publication and dissemination of results). Anonymity and all General Data Protection Regulation (EU GDPR)-related rules were strictly adhered to.

4 Results

The time needed to complete the questionnaire was approximately 15 min.⁴ Each WTP scenario was solved 72–75 times; each respondent randomly solved either one or two scenarios. The characteristics of the sample, representative of the Croatian population,⁵ are presented in Table 2. Respondents assessed their health status as relatively good; most have at least a high school diploma and 33% have a university education. There were 132 VOLY data points treated as missing (above 200% of the interquartile range). The final data set hence included 2178 data rows. Zero WTP was indicated in 84 responses.

² In terms of the design or the respondents' comprehension of the tasks at hand.

³ Next to the questions presented here, the questionnaire also included a subset of unrelated questions.

⁴ Respondents who filled in the questionnaire in less than 10 minutes were considered to have clicked through the questionnaire and their responses were not delivered by the sampling agency.

⁵ Ensured by the professional sampling agency.

Table 2 Sample characteristics ($n = 1500$)

Variable	Mean	SD
Average household size	3.2 members	0.16
Average monthly household income (net)	€1519	€706
Average monthly personal income (net)	€676	€414
Female	51.6%	50.0%
Married	57.6%	49.4%
Having children	39.0%	48.8%
Education		
Elementary school	1.4%	11.7%
High school	65.8%	47.5%
University degree	32.8%	47.0%
Employment status		
Employed	69.5%	46.0%
Unemployed	9.6%	29.5%
Retired	9.7%	29.5%
Student	11.2%	31.5%
Self-reported well-being (on a scale from 0 to 10)	6.64	2.17
EQ5D visual analog scale ^a	75.27	3.04

SD standard deviation

^aVisual analog scale ranged from 0 (worst imaginable health) to 100 (best imaginable health)

4.1 EoL-VOLY

Average EoL-VOLY across all scenarios was estimated at €67,000 (median €40,000; Column I; Table 3). In scenarios that offered respondents 1 full year of life extension, EoL-VOLY was estimated at €33,000 (median €22,000). In the 1000 patients group, the EoL-VOLY in patients with cancer was about 10% higher than the EoL-VOLY in the rare disease group but the difference was statistically insignificant ($p > 0.05$). In a larger patient group (14,000), the average EoL-VOLY was equal between the generic “severe illness” group and the cancer group (both €57,000, $p > 0.05$). This signals no support for the cancer premium relative to other severe conditions, including rare diseases. Overall, we would argue that in this data set, the EoL-VOLYs are independent of the condition the patients are dying from.

We analyzed the EoL-VOLY variations both between QoL levels and LYG levels, for two different-sized patient groups and disease specifications (cancer, rare disease, severe disease). We first present the results of EoL-VOLY variations with respect to QoL variations, followed by

variations by LYG (scenarios were designed such that each QoL level contained the same LYG extensions).

The relationship between EoL-VOLYs and respective QoL levels in the 1000-patient group was weak (both cancer and rare disease; Table 3, Column II). In the 14,000-patient group (with no cancer and no rare disease, scenario number 11–15), the relationship between EoL-VOLY and QoL was negative; the mean EoL-VOLY was significantly lower at QoL = 0.6 than at QoL = 0.2 (€62,000 vs €50,000; $p < 0.05$). In scenarios 16–31 (also 14,000-patient group), which offered a broader span of QoL levels (0.2–0.8), we found an inverse U-shaped relationship between EoL-VOLYs and QoL (Table 3, Column II), initially, as the QoL level increased, so did the EoL-VOLY but then it decreased from QoL 0.6 to 0.8 QoL. Significant differences were found between QoL 0.2 and 0.6 and again between QoL 0.6 and 0.8 ($p < 0.05$), but no difference was found between 0.2 and 0.8 ($p > 0.05$). The same inverse U-shaped relationships were observed when scenarios offering equal LYG extensions were compared across QoL levels (Table 3, Column III). For instance, within the cancer group (14,000 patients), EoL-VOLY for LYG of 12 months at QoL = 0.2 equaled €28,000; QoL = 0.4 equaled €35,000; QoL = 0.6 equaled €37,000; and QoL = 0.8 equaled €25,000. Overall, the relationship between QoL and EoL-VOLY cannot be described as strictly positive or negative, in fact, it was relatively inconsistent across scenarios (Table 3, Column II). With respect to the EoL-VOLY variation by LYG, in the 14,000-patient group, when comparing average EoL-VOLYs within each particular QoL level, we found that EoL-VOLYs strictly decrease with LYGs (Table 3, Column III).

Considerably and significantly higher EoL-VOLYs were estimated in scenarios offering relatively shorter life extensions, for instance, EoL-VOLY at a 2-month extension averages at €124,000 while a VOLY at 18 months averages at €23,000. It could be argued that this signals the preference for more severe conditions, i.e., closeness to death, which inspires higher WTP-OE. However, this result might also be driven in part by the nonproportionality of WTP-OE estimates to the length of the gain on offer (in other words, higher WTP-OE estimates divided by similar LYGs results in ever lower EoL-VOLYs)⁶.

To test for this hypothesis, as well as to test for the theoretical validity of WTP-OE estimates and their relationship to the main variable of interest, LYG, we analyzed the

⁶ The same clear-cut conclusion could not be reached for QoL-related variation, possibly because respondents’ attention was more focused on LYG differences, owing to the properties of the design.

Table 3 Main results

Scenario no.	Patients benefiting	QoL at the end of life (0–1 scale)	Additional months because of treatment (LYG)	Cancer	Rare disease	Average EoL-VOLY (median)	EoL-VOLY by QoL level (median)	EoL-VOLY by additional months because of treatment
						Column I	Column II	Column III
1 & 2	1000	0.2	48	No	Yes	€90,000 (€66,000)	€92,000 (€66,000)	
3		0.4	48	No	Yes		€89,000 (€70,000)	
4 & 5		0.6	48	No	Yes		€88,000 (€66,000)	
6 & 7	1000	0.2	48	Yes	No	€99,000 (€72,000)	€98,000 (€66,000)	
8		0.4	48	Yes	No		€102,000 (€79,000)	
9 & 10		0.6	48	Yes	No		€93,000 (€72,000)	
11	14,000	0.2	2	No	No	€57,000 (€34,000)	€62,000 (€34,000)	€111,000 (€100,000)
12		0.2	6	No	No			€53,000 (€34,000)
13		0.2	12	No	No			€27,000 (€19,000)
14		0.6	6	No	No		€50,000 (€34,000)	€67,000 (€47,000)
15		0.6	12	No	No			€33,000 (€17,000)
16		0.2	2	Yes	No	€57,000 (€34,000)	€54,000 (€29,000)	€122,000 (€100,000)
17		0.2	6	Yes	No			€55,000 (€34,000)
18		0.2	12	Yes	No			€28,000 (€22,000)
19		0.2	18	Yes	No			€21,000 (€12,000)
20		0.4	2	Yes	No		€64,000 (€35,000)	€129,000 (€120,000)
21		0.4	6	Yes	No			€73,000 (€54,000)
22		0.4	12	Yes	No			€35,000 (€25,000)
23		0.4	18	Yes	No			€26,000 (€24,000)
24		0.6	2	Yes	No		€64,000 (€40,000)	€127,000 (€100,000)
25		0.6	6	Yes	No			€71,000 (€54,000)
26		0.6	12	Yes	No			€37,000 (€24,000)
27		0.6	18	Yes	No			€28,000 (€24,000)
28		0.8	2	Yes	No		€48,000 (€23,000)	€109,000 (€100,000)
29		0.8	6	Yes	No			€49,000 (€34,000)
30		0.8	12	Yes	No			€25,000 (€17,000)
31		0.8	18	Yes	No			€17,000 (€12,000)
Average						€67,000 (€40,000)		
Average VOLY at a 12-month life extension (14,000-patient group, across all QoL levels, in bold)								€31,000 (€22,000)

Values in bold stand for a VOLY for a full LYG

EoL end of life, LYG life-year gained, QoL quality of life, VOLY value of a life-year

relationship between WTP-OE and LYG within a multivariable linear regression with logarithmic WTP-OE variable as the dependent variable (Table 4). We found that the LYG

is a significant positive predictor of WTP-OE, although the relationship between LYG and WTP-OE is non-proportional,

Table 4 Multivariable linear regression with log(WTP-OE) as the dependent variable

Log_WTP-OE	Coefficient	SE	$p > t $	95% confidence interval	
QoL	3.28	0.63	0.000	2.03	4.53
QoL squared	-3.57	0.67	0.000	-4.89	-2.25
LYG	0.25	0.064	0.000	0.12	0.38
h_income1	-0.07	0.069	0.320	-0.20	0.066
h_income2	-0.22	0.069	0.001	-0.35	-0.08
h_income3	(Omitted)				
h_income4	-0.18	0.077	0.022	-0.33	-0.02
Age	0.004	0.002	0.021	0.00	0.001
Patients benefiting	0.000074	0.00	0.000	0.00	0.00
Constant	2.1	0.31	0.000	1.49	2.71

h_income 1 – h_income4 refers to household income from the lowest (1) to the highest (4) level

LYG life-year gained, QoL quality of life, SE standard error, WTP-OE willingness to pay open-ended

ceteris paribus.⁷ The multivariable regression (adjusted R² = 0.026, $n = 2094$) shows that other significant predicting variables are the number of patients in the risk group as well as the level of their QoL (featured as a quadratic term to capture its U-shaped relationship to WTP-OE, as noted before). Household income does not behave in an expected manner, regardless of the specifications of the household income variable. This could be signalling that the income constraint has not been reached, that is, that respondents are willing to pay for the therapy up to the amount that is independent of their household income, or not restricted by it.

⁷ There is a positive and significant correlation between WTP-OE and LYG ($r = 0.05$, $p = 0.01$). In Table 4, we present the results of a linear regression with WTP-OE (not VOLY) as the dependent variable. In the linear regression, we test the theoretical validity of WTP-OE (raw estimates obtained from the survey). The results in Table 4 show that WTP-OE is sensitive to the length and the quality of life, when controlling for the other potential determinants (e.g., age, income). We tested whether other potentially important variables, such as the quadratic LYG and interaction between QoL and LYG should be included in the regression but this was dropped because of insignificance. The fact that the length of remaining life (variable LYG) has a positive coefficient, ceteris paribus, shows that across scenarios, a longer life expectancy (i.e., higher health gain) is associated with higher WTP-OE, as would be theoretically expected. However, when we recalculate WTP-OE into VOLYs by dividing raw WTP-OE values with the length of life in each row of data, the VOLY is on average lower for higher gains (i.e., longer life expectancy) than for smaller gains (i.e., shorter life expectancy). This is owing to the fact that raw WTP-OE values for a longer life expectancy (higher gains) are not proportionally higher than for a shorter life expectancy (lower gains), affecting the VOLY calculation's results. Simply put, dividing relatively similar raw WTP-OEs across scenarios by very different life expectancy gains leads to higher VOLYs for smaller gains than for larger gains.

5 Discussion and Conclusions

Policy makers around Europe typically focus on ICERs that use QALYs as the measure of health when conducting, assessing, or appraising the CE analysis. However, along with ICERs that present an additional cost per additional QALY gained, global CE models typically present another type of ICER—the ICER where the additional benefit of the intervention under evaluation is not expressed as a QALY but as a LYG. This ICER (additional cost per LYG) is often overlooked or ignored by policy makers and it rarely plays any role in the reimbursement of new technologies. The ICERs that use LYGs instead of QALYs stemming from the same study would be by default lower than the ICERs that employ QALYs as a measure of benefit. If the preferences over the duration and QoL within the QALY framework are not equal in strength, we could argue that the ICERs that use LYG could also be informative for efficient valuation and may warrant their own CE threshold. This additional threshold would provide additional quantitative information on how societies value changes in life expectancy at the end of life, supported by the debate on the appropriateness of QALYs as a measure of health benefits at the end of patients' lives (e.g., [34]). For LYG added to life expectancy at the end of patients' lives, a demand-side preference-based EoL-VOLY estimate could be informative in the virtually non-existent debate on the size of the cost per LYG threshold.

The EoL-VOLYs are not an irrelevant notion. Therapies targeting EoL patients receive particularly favorable treatment and receive reimbursement often at very high prices. Cancer drugs, severe illness, and rare diseases are (explicitly or implicitly) evaluated against relatively higher CE thresholds (also in jurisdictions operating a relatively rudimentary value for money reimbursement frameworks, e.g., [35, 36]). The fact that we apply varying thresholds indicates that healthcare policy makers already accepted differential rules based on the properties of interventions under evaluation (or the characteristics of patients receiving those therapies). Should this framework be further extended? Instead of cost per QALY thresholds, in situations in which we have treatments targeting EoL patients whose main purpose is to extend life and not add quality to life, should a particular cost per LYG thresholds be also evaluated (instead of a fixed or varying cost per QALY threshold alone)? Additionally, as with the cost per QALY monetary thresholds, preference-based studies that estimate EoL-VOLYs might contribute to informing the reimbursement decision making in this particular context. This is what our study aimed to do.

The VOLY gained at the end of a patient's life in Croatia averaged at €67,000 (median €44,000), estimated from the social-inclusive-individual perspective (which is, in our view, the relevant perspective for this type of study).

In scenarios that offered respondents 1 full year of life extension, EoL-VOLY was estimated at €33,000 (median €22,000). This is about 2.5–5 times the GDP per capita in Croatia. Severe conditions (which a near-death condition certainly is) are in European jurisdictions often evaluated against higher thresholds (such as 3–5 times the GDP thresholds relative to 1 time the GDP per capita; for a review see [36]). A recent systematic review of the monetary value of health gains literature revealed that EoL-VOLYs have typically been estimated at €28,488 (with a wide range of estimates, from €1942 to €572,557 [23]). Croatian GDP per capita averaged at €14,500 in 2021, so our EoL-VOLY estimate is at this higher end of the cost per QALY threshold scale and in line with the UK HM Treasury's VOLY (2018). Finally, our results show that for EoL conditions, the type of illness is irrelevant for the EoL-VOLY evaluations. In other words, when people are dying, it makes no difference what they are dying from. This unsurprising result serves as an additional argument in the debate on the appropriateness of funding EoL therapies at relatively higher prices in any particular treatment domain.

Several limitations are important to discuss. First, we tried to keep the scenario design as simple as possible, to ease the understanding of the questionnaire. As with all stated preference studies, we cannot be certain whether all respondents understood the hypothetical scenarios or provided a WTP value that they would actually commit to. However, because the variables behave in an expected manner (except income, but this is likely due to the low WTP values relative to household income, Table 4), we believe that misunderstanding the hypothetical scenarios is not a major source of concern. Second, we did not include patients' (beneficiaries') age in our study design, that is, the study was silent with respect to the age of the EoL patients. Likely, EoL-VOLYs in children would be relatively more valuable than those in elderly patients. However, given that age is not a formal priority-setting criteria in any of the European CE guidelines [37], we opted for not including age as a differentiating factor in our study. The third point worth raising is the non-proportionality of our results to the scale of the good under evaluation. This is, however, in line with various WTP studies that have previously explored the monetary value of health gains (e.g., [38, 39]). Finally, our results are not intended to provide an empirical justification for introducing the cost per LYG threshold but to explore

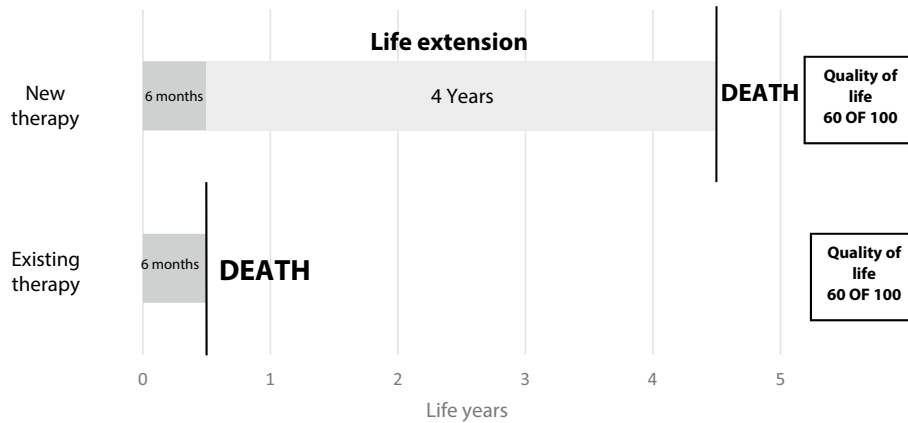
the preferences regarding VOLYs as well as to highlight the need to further explore whether monetary valuations of health gains that are underpinned by QoL improvements versus longevity improvements (within a QALY framework) differ significantly and would lead to a different CE threshold.

Estimates of the value of a life-year that are used in the policy-making arena need to be up-to-date and informed by appropriate revealed or stated preference/behavioral data elicited from studies valuing changes in longevity in representative samples, in particular jurisdictions, to better reflect the preferences therein (e.g., [40]). Appropriate revealed preference data, which would be the basis for estimating an EoL-VOLY, do not exist in Croatia or in any other jurisdiction and hence the stated preference survey drawing on the most up-to-date methodological approaches is the only viable option. Our approach has a clear conceptual link to the QALY framework and adds to the longevity valuation literature by improving our understanding of the complex issue of valuing life. Applying VOLYs in pricing and reimbursement might lead to more informed decisions and could have major implications not only for efficiency but also for equity in government healthcare spending. As the pressure to reimburse increasingly expensive therapies targeting EoL conditions increases, so does the necessity to adjust and improve our ability to evaluate their CE.

Appendix

An example of the wording:

Imagine a person who went to a medical examination during this week due to the appearance of certain health problems. After the examinations, the doctor informs her that she is suffering from a **SERIOUS DISEASE** (advanced form of cancer) and that with **USUAL TREATMENT** she can live another 6 months. Assume that this happens to 1,000 patients in Croatia annually (3 people per 10,000 inhabitants), among whom might be you. However, in addition to the usual treatment, there is also a new drug that can extend the life of affected people for an additional 4 years (4 and a half years in total), while keeping the quality of life at the same level, as shown in the graph below. After 4.5 years the patients will die.



Assume that the healthcare system does not have enough money to pay for this medicine, and that is why a new tax is being introduced in Croatia, which will be paid by all people over the age of 18 (regardless of whether they belong to the risk group), once a month for 12 months. The tax will be abolished after 12 months.

On the scale, mark the highest tax that you would certainly pay/certainly not pay for the new drug every month for the next year.

0 kn	1 kn	3 kn	5 kn	7 kn	10 kn	13 kn	15 kn	17 kn	20 kn	23 kn	25 kn	30 kn	35 kn	40 kn	45 kn	50 kn	60 kn	70 kn	80 kn	100 kn	300 kn
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Note: 1€=7.5345 Croatian kuna (kn)

In the previous answers, you stated that you would certainly pay x kuna every month for the next year, while you would certainly not pay y kuna.

Indicate the exact amount of tax (in the range of x to y kuna) that you would surely pay every month for the next year, in order to prolong the life of the persons in the risk group, among whom you might be. When answering, take into account the total monthly income of your household!

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Declarations

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Conflict of interest Elizabeta Ribarić, Ismar Velić, and Ana Bobinac have no conflicts of interest that are directly relevant to the content of this article.

Ethics approval See the Electronic Supplementary Material.

Consent to participate Before starting the survey, each respondents agreed to participate in the study.

Consent for publication Before starting the survey, each respondent consented to the survey data being used for research, publication, and dissemination purposes.

Availability of data and material The dataset is available from the corresponding author on reasonable request.

Code availability The code used for the data analysis is available from the corresponding author on reasonable request.

Author contributions Each author has made a substantial contribution to the concept and the design of the article; the acquisition, analysis, and interpretation of the data for the article, and has participated in drafting the article and revising it critically for important intellectual content. Finally, each author has approved the version to be published.

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