

Introduction

- In many countries, cost-effectiveness (CE) is a key factor in health technology assessment (HTA) and reimbursement decisions⁽¹⁻³⁾. Whether a new medical intervention is value for money or not is usually assessed based on its incremental cost per Quality-Adjusted Life Year (QALY) gained in relation to a predefined willingness-to-pay (WTP) threshold⁽⁴⁻⁵⁾. WTP threshold is a methodological tool that seeks to estimate the capacity to pay in a search to find out the intrinsic monetary value for acquiring the health benefit associated with the investigated medical intervention.
- Its wide application in CE assessments and in decision-making processes have made this tool one of the most requested and debatable in the area of health economics. Although several methods have been used to estimate WTP thresholds in different country-specific settings⁽³⁾, it is still inconclusive how to derive appropriate cut-offs⁽⁶⁾.
- In Greece, with the establishment of an HTA organization in Greek National Health System in 2018, CE evaluations brought officially to the surface as a necessary step for healthcare decision-making. Nevertheless, the role of these economic evaluations in the assessment and appraisal process is rather unclear.
- The lack of formal guidelines for good practice of economic evaluations and of an officially established WTP threshold that would help submission process and add clarity to the HTA committee verdict need to be addressed.
- In this context, the objective of present study was to systematically review the WTP threshold used in Greek CE studies over the last 10 years and investigate the methodology behind it.

Methods

This review was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria⁽⁶⁻⁷⁾.

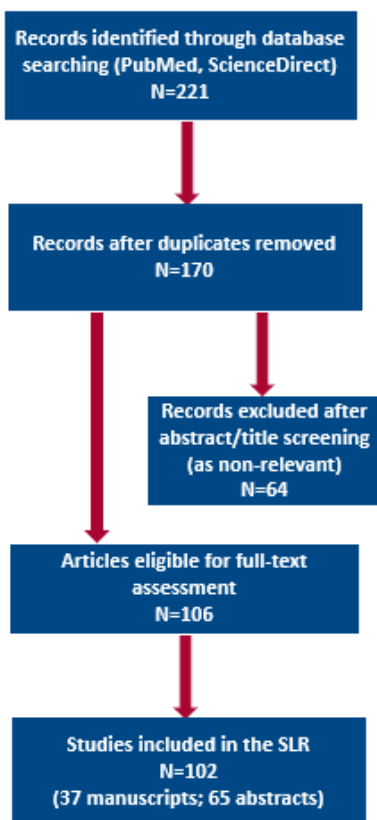
- Search strategy:** PubMed and ScienceDirect were searched using combinations of the relevant keywords. The search included studies in English.
- Study selection:** The identified studies were reviewed and assessed for inclusion by two independent researchers based on the predetermined inclusion criteria (Table 1). A third reviewer was involved to resolve potential discrepancies on extracted data between the two reviewers.
- Data extraction:** A standardized data extraction form, developed for the purpose of this review, was used by the same two reviewers to independently extract data.
- The extracted data from the selected studies were consequently synthesized and analyzed.
- Qualitative variables were presented with absolute (n) and relative frequencies (%) and quantitative variables with median and interquartile range (IQR). Mann-Whitney and Kruskal Wallis tests were performed where needed.

Table 1: Inclusion and exclusion criteria considered in the search strategy

Inclusion criteria	Exclusion criteria
Type of study: Cost-effectiveness and cost-utility only	Reviews or meta-analysis
Languages: Studies in English	Editorials
Time limit: Published in the last 10 years	Comments
Published full-paper or abstract of study	Letters to the Editor
Studies referring only to pharmacological interventions	

Results

Figure 1: Flowchart of systematic review



- From the 221 identified studies, 102 satisfied the inclusion criteria. Studies were categorized to oncology (26.5%) and a non-oncology related (73.5%) based on drug treatment (Figure 1 & Table 2).
- The WTP threshold was reported to 71.6% of the studies (oncology: 59.3%; non-oncology: 76%), whereas the most frequently reported outcome associated with threshold was the "per QALY gained" (oncology: 87.5%; non-oncology: 94.7%) (Table 2).
- A total of 34.3% of the studies with a reported threshold did not specify (NS) the origin of the threshold (oncology: 18.8%; non-oncology: 38.6%). From the rest of studies, the vast majority (91.7%) adopted thresholds equal to one-to-three times the gross domestic product (GDP) per capita (oncology: 100%; non-oncology: 88.6%), while the rest similar to NICE guidelines (Table 2).
- The median (IQR) WTP threshold was differentiated between oncology [€51,000 (€50,000 – 57,000)] and non-oncology studies [€34,000 (€30,000 – €35,000); p-value<0.001] (Table 2).
- When other than QALY outcomes were connected to a reported WTP threshold, the GDP methodology was again the most prominent (80%) across all relevant studies. (Table 2).
- In both type of studies, the median WTP thresholds were not statistically significantly different between GDP, NICE and NS methodologies

Table 2: Results of the included studies

	Overall N=102	Oncology N=27 (26.5%)	Non-oncology N=75 (73.5%)
Study Outcomes, n (%)			
QALY/LY	30 (29.4)	16 (59.3)	14 (18.7)
QALY	66 (64.7)	10 (37.0)	56 (74.7)
LY	2 (2.0)	0 (0)	2 (2.7)
LY/event avoided	1 (1.0)	0 (0)	1 (1.3)
PASI	2 (2.0)	0 (0)	2 (2.7)
Event avoided	1 (1.0)	1 (3.7)	0 (0)
No of studies with a reported threshold	N=73 (71.6)	N=16 (59.3)	N=57 (76)
Outcomes for WTP thresholds, n (%)			
LY	4 (5.5)	2 (12.5)	2 (3.5)
PASI	1 (1.4)	0 (0)	1 (1.8)
QALY	68 (93.2)	14 (87.5)	54 (94.7)
Method used, n (%)			
Not reported	29	11	18
From those reported:	N=73	N=16	N=57
1-3 GDP per capita	44 (60.3)	13 (81.3)	31 (54.4)
NICE	4 (5.5)	0 (0)	4 (7.0)
NS	25 (34.3)	3 (18.8)	22 (38.6)
WTP threshold, in €	N=73	N=16	N=57
Mean	37,194 (12,517)	50,375 (8,310)	33,494 (10,925)
Median (IQR)	34,000 (30,000 – 50,000)	51,000 (50,000 – 57,000)	34,000 (30,000 – 35,000)
Min – max	15,000 – 60,000	35,000 – 60,000	15,000 – 60,000
Mode (times)	30,000 (16)	51,000 (5)	30,000 (16)
p-value			<0.001

GDP: Gross domestic product, PASI: Psoriasis Area Severity Index, QALY: quality-adjusted life year, LY: life year, WTP: willingness to pay, NS: did not specify, NICE: National Institute for Health and Care Excellence
IQR: interquartile range

References

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Conclusion

To the best of our knowledge this is the first study which investigated the reported level and methodology of WTP threshold in Greece. Aligned with other countries where there is no standard WTP threshold to promote efficient use of healthcare resources, the most prominent practice in Greece was found to be that of one-to-three times the GDP per capita irrespective of type of treatment or outcome studied. Nonetheless, there was a meaningful portion of studies that did not specify the origin of their threshold used. To this end, it is a matter of great importance all relevant local stakeholders to initiate discussion around the most suitable level and methodology of WTP threshold that should be used here in Greece and enhance, as such, clarity of evidence-based decision-making.