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Systematic Literature Review

Utility Values of Health Status in Gastric Cancer: A Systematic Review

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ABSTRACT

Objectives: Gastric cancer (GC) imposes a significant burden of disease globally. Multiple treatments are available but are associated with high costs and potentially detrimental effects on quality of life. The utility values of health status are measures of patient preference over quality of life, which are increasingly used for health and economic decision-making. Currently, there is little systematized information on the utility values for different stages of GC. This systematic review synthesizes and meta-analyses the literature on GC utilities.

Methods: A search was conducted in PubMed, Embase, MEDLINE, and Cochrane Library for studies reporting utility values calculated using direct and indirect methods. Information from the selected studies was extracted and appraised, and meta-analyses of utility values based on GC health states were performed.

Results: Twelve studies involving 4585 patients were included. Random-effects meta-analysis estimates showed a mean utility of 0.77 (95% CI 0.7–0.85) for stage I, 0.75 (95% CI 0.65–0.85) for stage II, 0.70 (95% CI 0.63–0.96) for stage III, and 0.64 (95% CI 0.56–0.32) for stage IV. All estimates showed considerable heterogeneity.

Conclusions: Our study provides an updated overview of the literature on utility values in GC and presents a discussion of the relevance of GC stages for its analysis. Decision-makers should consider patients' preferences in the proposal of policies and clinical decisions.

Keywords: economic evaluation, EQ-5D, gastric cancer, health-state utility values.

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Introduction

Every year, 984 000 new cases of gastric cancer are diagnosed worldwide, generating 841 000 deaths globally, making it the second leading cause of cancer mortality.[1] In 2019, 22.2 million disability-adjusted life-years were attributed to gastric cancer worldwide, positioning as one of the 3 main causes of disability-adjusted life-years among men.[2]

Treatment of gastric cancer consists of multiple interventions that are generally associated with high costs, adverse effects on the patient, and a significant impact on health-related quality of life (QOL).[3] Despite notable strides in both treatment and diagnosis, individuals diagnosed with gastric cancer continue to face a challenging prognosis. The 5-year survival rate remains low, ranging from 10% to 20%; for those who do not undergo chemotherapy, results are even grimmer: the median survival rate is only 3 to 4 months.[4]

In this context, decision makers are increasingly considering health and economic evidence to shape public policies to prevent and treat gastric cancer. The use of quality-adjusted life-years (QALYs) as a measure of benefits from health interventions is widely accepted.[5]

QALYs are essential for cost-utility analysis, which incorporates the QOL (morbidity) and length of life (mortality) into a single measure. This measure is based on utilities that reflect a population"s preference for certain health status.[6]

Utility (or health-state utility value [HSUV]) is the relative value that patients place on different health conditions in terms of their impact on health-related QOL, ranging on a scale of 1 to 0, in which 1 represents perfect health, and 0 represents death. However, there may be negative values for statuses valued worse than death.[7] There are 2 main methods for calculating utility, direct and indirect methods. Direct methods map preferences directly from utility scales using techniques such as standard gamble and time trade-off. Indirect methods map preferences using a generic health-related quality-of-life questionnaire (such as the EQ-5D, the most frequently used, and the 6-dimensional abbreviated form [SF-6D], among others).

The standard gamble method assesses the risk threshold a patient is willing to accept to avoid a negative outcome, such as death, or severe long-term neurological consequences, such as a stroke. In contrast, the time trade-off technique involves sacrificing future years of life in a less-than-optimal state of health, in exchange for shorter life expectancy and better health. However, the application of these methods to the evaluation of temporary health states poses inherent challenges.[8]

In the case of indirect measurements of utility, it is preferable to use the results obtained from the EQ-5D as a generic measure. This is because it is a short and simple instrument with a positive impact on data quantity and quality. In addition, it is a questionnaire validated for several pathologies and different population groups, which gives it better validity.[9] The EQ-5D is structured around 5 key attributes: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each attribute comprises 3 levels, indicating the absence of problems, presence of some problems, or experience of severe problems. This configuration results in 243 potential health states. To quantify these states, each is assigned an index score using preference weights, also known as tariffs. These tariffs can be derived from 2 primary sources: (1) individuals currently experiencing a health state, providing an experience-based valuation, and (2) a sample from the general population offering a hypothetically based valuation.[10]

However, limitations of the EQ-5D have been described, including a possible ceiling effect. This effect occurred when a large proportion of participants achieved the highest test score. In other words, when the scores of the values are clustered within the ceiling of the measurement or the highest score, the measurement loses its value. This is common, for example, in the measurement of the QOL in patients with advanced-stage cancer.[11]

In some situations, such as in a specific health state for an illness, it is not possible to find primary studies with information on their utility. In this situation, mapping algorithms are a solution accepted by the National Institute for Health and Care Excellence.[5] Mapping is a technique that allows transforming values from health-state perceptions to preference-based measures, such as utilities calculated using the EQ-5D. In the case of cancer-related conditions, the European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire Core 30 (EORTC QLQ-C30)[12] is one of the most widely used instruments for measuring QOL. For example, the mapping allows the conversion of EORTC QLQ-30 values to EQ-5D utilities.

Although several studies have evaluated the cost-effectiveness of different interventions for the prevention and treatment of gastric cancer, few updated systematic reviews[13] have provided an overview of the different measures of utility, which tend to be heterogeneous in terms of the population group studied or the level of gastric cancer development. The scarcity of systematic reviews has the effect that, for cost-utility studies, simple averages of QALYs are used without further justification or single-study estimates. This generates conflicts with the recommendations of the National Institute for Health and Care Excellence,[5] which recommends using all available evidence in a systematic manner.

Healthcare utilities are essential from the perspectives of patients, healthcare professionals, and decision-makers. Research has shown that the weight of utilities from a population perspective may be more valid in terms of economic decisions regarding the allocation of limited resources to different treatments.[14]

In the context of a greater need for information on preference for decision-making in health, the objective of this study was to carry out a systematic review of studies that report utilities for gastric cancer for its different disease stages, both using direct and indirect methods, to provide useful and updated information for decision-makers, health professionals, and researchers.

Methods

Search and Selection

General and specific health and economics literature databases were searched, including PubMed, MEDLINE, Embase, and Cochrane Library.

A broad search strategy was developed by incorporating criteria related to cost-utility studies. Specifically, we considered terms incorporated in a systematic review of Canakis[15] regarding decision models for performing gastric cancer endoscopy. The search strategy for each database is described in Box 1 (see Appendix Box 1 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2024.101063).

Titles and abstracts were searched for articles published between 2000 and January 25, 2024. Articles written in languages other than English were excluded from this study. The main search inclusion criteria were that the studies reported utilities in a gastric cancer population, were estimated using direct or indirect methods of utilities, and were described according to the stage of gastric cancer.

The utilities of different health states are usually secondary outcomes in studies, specifically, in cost-utility studies. Therefore, it is necessary to adapt the classical methods of systematic reviews in such a way as to include various types of studies and designs. For this reason, studies that directly reported the utilities of gastric cancer were included, and cost-utility studies, in which the referenced studies that reported the utilities were identified.

We excluded studies in populations with 2 or more types of cancer, such as gastric and esophageal cancers, to avoid an extra source of heterogeneity in the results. In addition, we excluded those that did not present assessments according to the stage, because we were interested in obtaining stage-specific utilities. Finally, we excluded studies using an indirect evaluation method different from EQ-5D, the reference approach in the literature.

Two independent reviewers reviewed the titles and abstracts of all articles. If the article received 2 approvals, it was advanced to full-text review. Any disagreements were resolved by a third reviewer. The same reviewers evaluated the full text, and in case of discrepancies, a third reviewer was consulted.

Data Collection Process and Synthesis of Results

With the selection of the final studies, a report validated by clinical experts was used, in which the following data were included for extraction: author, year, country, study design, population, assessment instrument, number of patients, categorization of patients with gastric cancer, utility value, and, in case the study uses an EQ-5D instrument, the tariff of utility. These data extraction criteria were first tested in a sample of 2 studies as a pilot study and then used in the remaining studies.

Because of the high heterogeneity usually obtained when attempting to group utility data of patients with cancer at different disease stages and differences in the classifications used for staging of patients, the studies were organized to ensure comparability. To do this, they were first grouped by valuation instrument, analyzing pooled data from those using the same valuation method. A review of tariffs (in the cases of studies using EQ-5D) was also performed, grouping studies that used the same tariffs or that evidence showed that tariffs could be homogenized.

Consistent with the guidelines of publications[16] that suggest different considerations for conducting a meta-analysis for HSUVs, it was decided to perform it only on publications reporting cancer-stage-specific utilities, which was the clinical grouping measure most reported by the selected studies.

This consideration allowed us to identify and analyze more comparable HSUVs in the context of high heterogeneity, thus generating a more reliable and simple interpretation of the meta-analysis estimates. Regarding the utilities calculated using the EQ-5D, it is important to mention that there is a different country-specific tariff.[17] This is a potential limitation when making comparisons of the country-specific tariff or estimating a summary

measure across countries. Nevertheless, studies have shown that tariffs are comparable across countries.[18] Therefore, for the meta-analysis, we grouped the studies that presented the same tariffs or those reported as comparable by the literature.

Finally, the categories of gastric cancer staging were grouped based on the information provided by the studies on the characteristics of the population. The American Joint Committee on Cancer (AJCC tumor node metastasis [TNM])[19] was used as the staging framework has been used for gastric cancer.

In the meta-analysis, estimates using EQ-5D (considering the tariff) and direct methods were included in the analysis, similar to other studies for oncological conditions.[20]

For the meta-analysis, the restricted maximum likelihood estimator was used to measure the residual heterogeneity[21] and quantify it using the statistic I^2. The results are presented using a random-effects model. When there is concern that the fixed effects hypothesis is overly restrictive to be satisfied by the data, that is, it is unrealistic to assume that all studies estimate exactly the same population effect size, random-effects models are preferred. This is the case in our study. Utility estimation studies tend to vary in the population considered, timing of preference assessment, and application methodologies.[22] This was mainly to make a more realistic estimate of the uncertainty of the utility outcome in each study. All data analyses were performed using R software with the metafor package.[23]

Risk of Bias of Individual Studies

Regarding the risk of bias in the selected studies, there are currently no standardized consensus instruments that allow assessments to be made for this type of studies.[16] What has been suggested by the guidelines for the development of systematic utility reviews[24] and what has been observed in other publications, is to analyze the strengths and limitations of the selected studies.

A systematic review[25] of the quality of studies on the utility values of health states indicated that a fundamental element of quality control is the evaluation of the amount of information provided. A well-informed study provides confidence in the results. In addition, although there are several potential quality assessment tools, we applied an evaluation instrument proposed in a previous systematic review of health status utilities based on Magnus[26] (see Appendix Table 1 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2024.101063). Magnus took note of the studies of Papaionnou,[5] Arnold,[27] and Hao,[28] who recommended that the utility values should be adequately measured, up-to-date, and relevant for the long term to allow an adequate scope for decision analysis models. Thus, to evaluate the quality of the studies, it is expected that they provide the following information: (1) numerical details of the recruitment of the population, (2) statistical distribution of the utility values, (3) transparency on the treatment of missing utility values, (4) discussion on the limitations and generalizations of the estimated values, (5) details on the sources of financing, and (6) source of tariffs (in case of indirect methods). A score was assigned to each of the 6 criteria for the indirect method (criteria 1-6) and 5 for the direct method (criteria 1-5). A score of 1 was assigned if the attribute information was not satisfactorily completed; otherwise, it was not assigned. Therefore, a lower score indicates a lower number of errors in the primary study, with reported utility values of better quality.

Results

The search returned 20 778 studies, which decreased to 3709 by eliminating duplicates. After selection by title and abstract, 16 full-text studies were analyzed, of which 12 met the inclusion criteria. Of the 4 studies eliminated, 2 studies were eliminated because of language retrictions[29,30] (1 in Japanese and 1 in Chinese). The remaining 2 studies were eliminated because they used data from other studies that were already included and were considered duplicated.[31,32]

A flowchart of the selection of studies using the Preferred Reporting Items for Systematic reviews and Meta-Analysis[33] model is shown in Figure 1. The main characteristics of the studies and their assessments of usefulness are reported in Tables 1[31,34,35] and 2,[36-44] respectively.

Six studies met all of the quality criteria,[34,35,39,41-43] 3 studies scored 3 points,[31,38,44] and 3 studies scored 1 point.[36,37,40] The absence of rate information was the most frequent error within the studies, and the rest was related to the recruitment process, treatment of missing values, and description of the nonnormal distribution of the utilities.

In contrast, all of the studies reported on the sources of financing and discussed the generalizability of the findings. The details of the evaluation can be found in Table 2.

Ten studies (84%) used indirect methods (EQ-5D), 1 study (8%) used a direct method (standard gamble), and 1 performed a mapping strategy from EORTC QLQ-C30 to EQ-5D (8%). Seven studies (58%) corresponded to randomized controlled trials, and 5 studies (42%) were cross-sectional. Three studies were from China (25%), 2 from Japan (17%), and 1 from multiple countries in Europe (8%). The rest of the studies were from South Korea, Portugal, Singapore, Greece, Canada, and the United States.

These studies used different health states to calculate the utility of gastric cancer by stage or clinical status, with the TNM[19] classification being the most commonly used. For example, the study by Lee[34] comprised the largest number of health states of gastric cancer, associated with stages of disease development with medical interventions, mainly surgical or palliative stages. In contrast, Curran et al[38] presented states linked to the treatment of different chemotherapy regimens for patients with advanced gastric cancer.

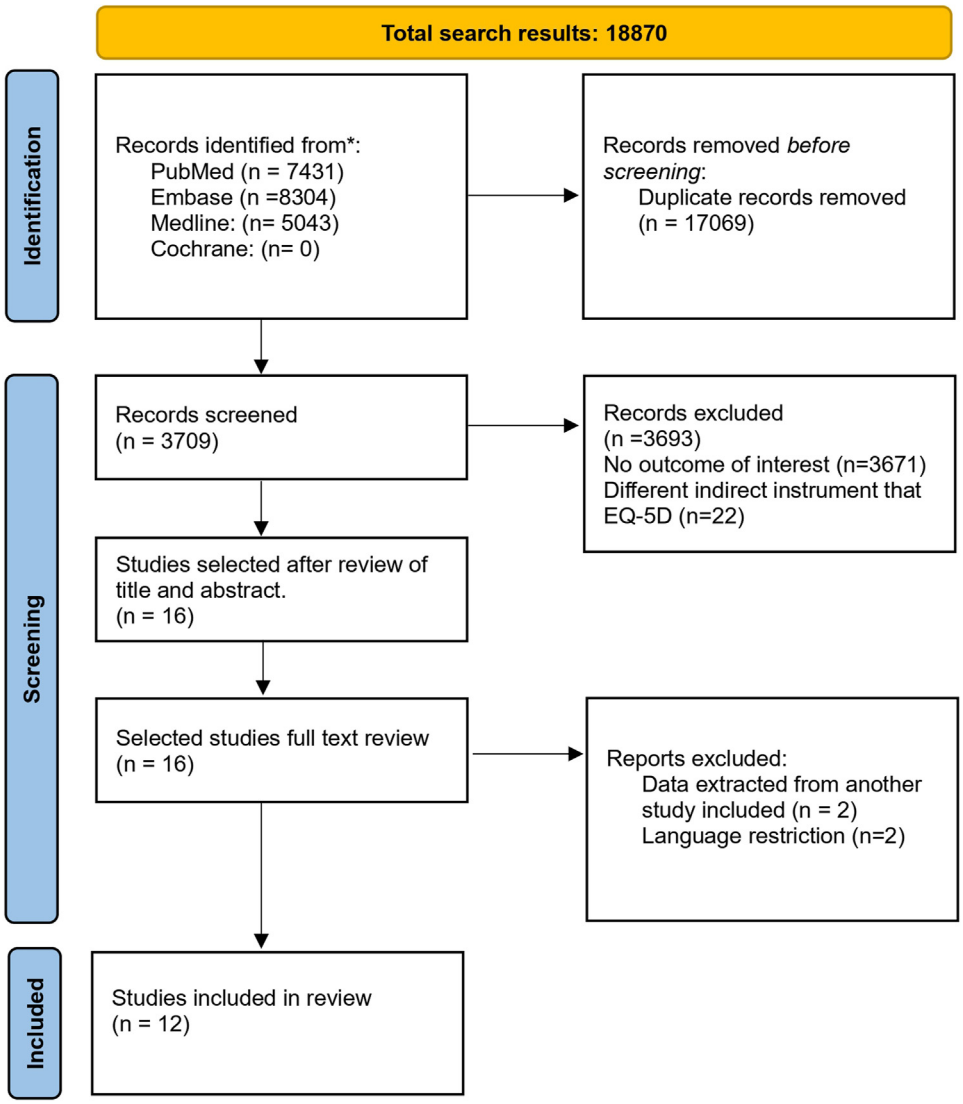
When observing the utility values reported by the studies, it stands out that most of them reported better health conditions in the first stages of gastric cancer, with stage IV being the worst evaluated, as expected. In the case of Zhang et al's[43] study, this trend was not observed where stage IV presented the best health status. The authors explained this situation by stating that all the selected patients were in treatment. Within the study, the patients in palliative care showed greater stabilization in their treatment, which is why they typically reported a better QOL.

This allows us to observe, as pointed out in Zhang et al's[43] study, that in addition to the clinical staging of cancer, it is relevant to consider the type of treatment and the length of time it has been applied to adequately analyze health utility values reported in the literature.

For the meta-analysis, the utilities reported by the different studies were grouped according to the categorization of gastric cancer and the tariff used (in EQ-5D). Grouping by treatment type was not possible because the studies provided insufficient information in this regard. In contrast, no exclusions of primary studies were made for the meta-analysis for quality assessment because the scale considers different elements in which only one component is related to the generalization of the data, which is fulfilled by all the studies included in the review.

Regarding the utilities calculating with EQ-5D of country-specific tariff, we found tariffs from the United Kingdom and Spain, which in previously published[18] studies have been mentioned as not presenting large differences; therefore, we did not exclude studies from the meta-analysis for this reason.

Figure 1. PRISMA flowchart. PRISMA indicates Preferred Reporting Items for Systematic reviews and Meta-Analysis.



Regarding China's tariff, researchers point out that, although it is not interchangeable in all contexts, it is the closest to being homologous with that of the United Kingdom.[45]

Seven studies reported the clinical stages of gastric cancer of the included patients according to the TNM. Four studies reported the general classifications of tumor staging and information on the type of treatment. Based on the opinion of a committee of experts in oncology and information from the publications, a harmonization of the classification provided by the studies with AJCC clinical stages was performed. For example, in cases that were indicated as advanced stage or with metastasis in palliative treatment, the classification was homogenized to stage IV. The tariffs in Spain, Great Britain, and China were homogenized.

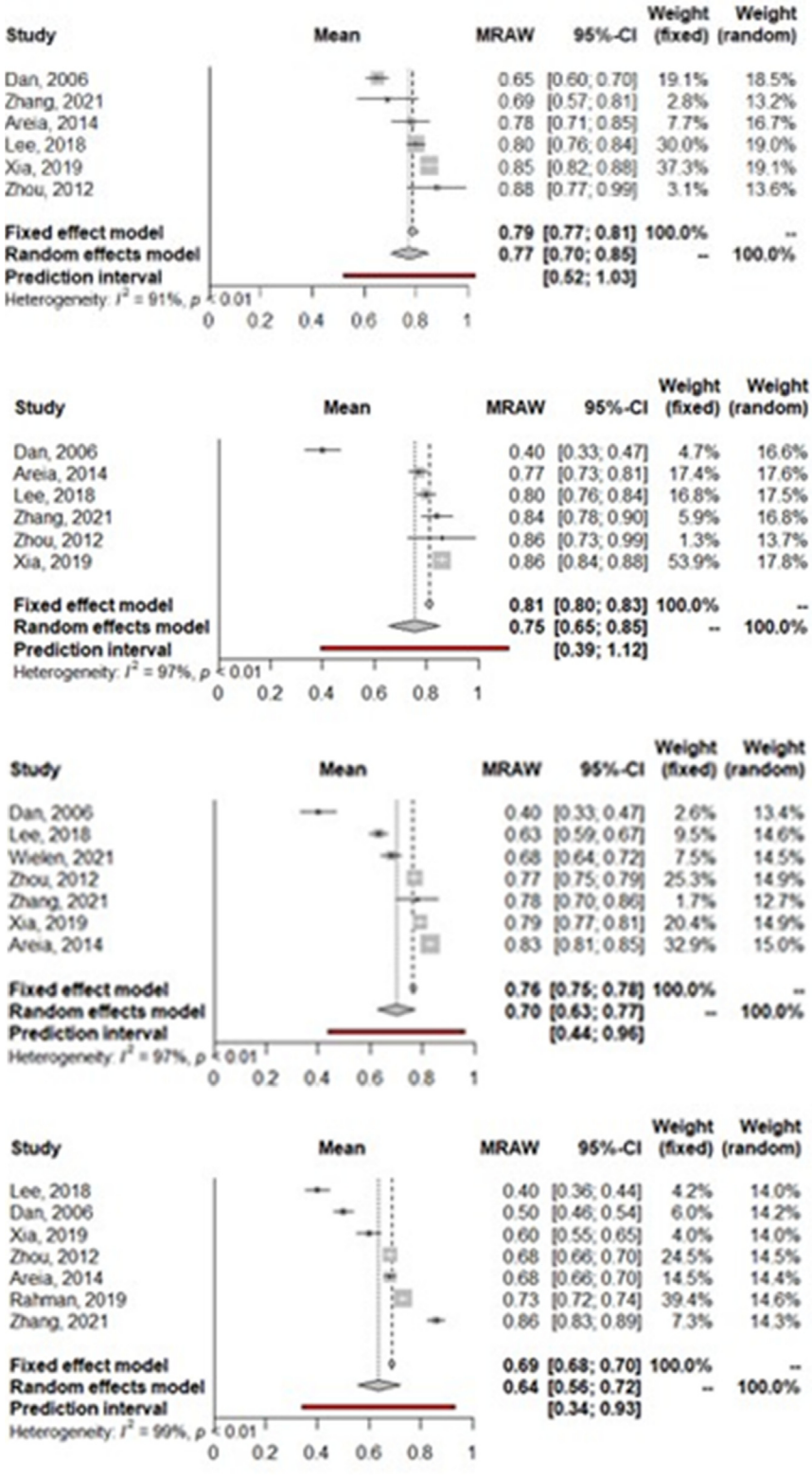
Finally, 4 meta-analyses were performed, one for each stage: stage 1,[31,34-36,39,43] stage 2,[31,34-36,39,43] stage 3[31,34-36,39,43] (see also van der Wielen,[44] 2021), and stage 4[27-30,33-35] (see also van der Wielen,[44] 2021).

The results of the meta-analysis for stage 1, in a total of 467 patients, showed a utility of 0.77 (95% CI 0.7–0.85; I^2 = 91%). For stage 2 with 690 patients, the utility was 0.75 (95% CI 0.65–0.85; I^2 = 97%). In stage III, the utility for 837 patients was 0.70 (95% CI 0.63–0.77, I^2 = 97%). Finally, stage 4 included 1184 patients with a utility value of 0.64 (95% CI 0.56–0.72; I^2 = 99%; Figure 2).

Discussion

This systematic review presents the best up-to-date evidence on HSUV of gastric cancer at the clinical stage. We included 12 studies from 9 countries, incorporating 4585 patients in total. Our meta-analyses estimated a utility of 0.77 on patients diagnosed with stage I, 0.75 in stage II, 0.7 in stage III, and 0.64 in stage IV. Utilities were obtained mainly from studies that used the EQ-5D as a valuation tool. The most updated previous systematic review[13] on gastric cancer utilities was conducted in 2015, in which 8 studies (7 publications and one poster presentation at a congress) reported utilities for gastric, esophageal, and gastro-esophageal junction cancers. The review identified a limited amount of data and patients, which mainly existed for advanced gastric and esophageal cancers, mixing cases with different

Figure 2. Meta-analysis of utility values according to clinical stage (American Joint Committee on Cancer-TNM).



MRAW indicates raw or untransformed mean; TNM, tumor, node, metastasis.

conditions, and adding an additional source of heterogeneity to the results. These limitations precluded any firm conclusions on HSUVs for gastric cancer.

To contextualize the results of our meta-analysis, in one study, the estimated mean HSUV for a healthy population in China (from where the larger proportion of the patients included in our review

Table 1. Description and health utility statements for studies.

Reference (year)	Country	Study design	Total sample size (N)	Respondent type	Intervention	Valuation method	Tariff used	EQ5D mean utilities	
								Health state(intervention) [sample size]	Mean utility (SD)
Dan et al,[31] 2006	Japan	Randomized controlled trial	221	Patients diagnosed with gastric adenocarcinoma with a survival time of at least 4 weeks.	Palliative care (survival time at least 4 weeks)	Mapped from EORTC QLQ-C30 to EQ5D	Report the algorithm used for mapping	Stage 1 (surgery) [75]: Stage II and III (chemotherapy) [33] Stage IV (palliative care) [111]	0.650 (020) 0.400 (0.20) 0.500 (0.20)
Lee et al,[34] 2018	South Korea	Cross-sectional	326	General population (Over 19 years old, national sample of 15 Korean districts)	Patients under gastric cancer control	EQ5D standard gamble	Direct estimation	No gastric cancer with HP infection [188] Early gastric cancer (endoscopy) [184] CGD (subtotal gastrectomy) [164] CGD (total gastrectomy) [185] Advanced gastric cancer (subtotal gastrectomy and adjuvant chemotherapy) [175] Advanced gastric cancer (total gastrectomy and adjuvant chemotherapy) [175] Advanced gastric cancer (extended gastrectomy and adjuvant chemotherapy) [183] Gastric Metastatic Cancer (palliative chemotherapy) [166]: Recurrent gastric cancer (palliative chemotherapy) [194]	0.857 (0.218) 0.773 (0.274) 0.779 (0.254) 0.767 (0.263) 0.602 (0.270) 0.643 (0.264) 0.522 (0.265) 0.404 (0.292) 0.399 (0.295)
Areia et al,[35] 2014	Portugal	Cross-sectional	1434	Patients undergoing upper endoscopy	Endoscopy	EQ5D visual analog	Spain tariff	No gastric lesions (intervention if any, eg, endoscopy) [678] Gastric premalignant conditions: gastritis, atrophy, intestinal metaplasia (endoscopy) [391] Gastric adenocarcinoma (endoscopy) [148]	0.78 (80.2) 0.79 (0.2) 0.77 (0.4)
Zhou et al,[36] 2012	Singapore	Cross-sectional	75	Chinese patients with gastric cancer in the National University Hospital	Patients under gastric cancer control	EQ5D	NR	Curative [48] Palliative [19] Early stage: AJCC stages 0-3 [49] Late stage AJCC stage 4 [18]	0.860 (0.24) 0.650 (0.33) 0.840 (0.25) 0.680 (0.33)
Kontodimopoulos et al,[37] 2009	Greece	Randomized controlled trial	48	Gastric cancer patients undergoing chemotherapy without metastasis.	Chemotherapy	EQ5D	NR	Gastric cancer [48]	0.550 (0.218)
Curran et al,[38] 2009	USA	Randomized controlled trial	333	Patients with histologically confirmed adenocarcinoma and metastasis (Stage IV).	Chemotherapy	EQ5D time trade-off	NR	Advance gastric cancer, chemotherapy: folinic acid and 5-FU (IF arm) [170] Advance gastric cancer, chemotherapy: cisplatin with 5-FU (CF arm) [163]	0.76 (0.27) 0.66 (0.27)
Xia et al,[39] 2020	China	Randomized controlled trial	1038	Patients aged 40-69 years diagnosed with gastric cancer in China.	Patients under gastric cancer control	EQ5D time trade-off	China tariff	Stage I TNM AJCC [132] Stage II TNM AJCC [343] Stage III TNM AJCC [409] Stage IV TNM AJCC [154]	0.850 (0.19) 0.860 (0.19) 0.790 (0.25) 0.600 (0.29)
Abdel-Rahman,[40] 2019	Canada	Randomized controlled trial	654	Patients with advanced gastric cancer (stage IV) if treated with systemic therapy.	Chemotherapy	EQ5D time trade-off	NR	Patients with advanced gastric cancer (stage IV) if treated with systemic therapy [654]	0.730 (0.19)
Ding,[41] 2020	China	Randomized controlled trial	72	Patients with gastric cancer in different stages of treatment.	Patients under gastric cancer control	EQ5D time trade-off	China tariff	Stage I TNM AJCC [132] Stage II TNM AJCC [343] Stage III TNM AJCC [409] Stage IV TNM AJCC [154]	[0.870] (NR)
Ito et al,[42] 2020	Japan	Cross-sectional	45	Patients 21 years of age or older, with histologic diagnosis of gastric adenocarcinoma with evidence of intestinal obstruction by peritoneal dissemination. Utility measured at 3 months of palliative treatment with surgery.	Palliati-ve care	EQ5D time trade-off	UK tariff	AJCC (TNM) Stage IV	0.700 (0.20)

continued on next page

Table 1. Continued

Reference (year)	Country	Study design	Total sample size (N)	Respondent type	Intervention	Valuation method	Tariff used	EQ5D mean utilities	
								Health state(intervention) [sample size]	Mean utility (SD)
Zhang et al,[43] 2021	China	Cross-sectional	243	Patients over 18 years of age with a diagnosis of gastric cancer under treatment.	Patients under gastric cancer control	EQ5D time trade-off	UK tariff	Stage I TNM AJCC [40]	0.690 (0.38)
								Stage II TNM AJCC [46]	0.840 (0.21)
								Stage III TNM AJCC [100]	0.780 (0.32)
								Stage IV TNM AJCC [57]	0.860 (0.13)
Wielen et al,[44] 2021	Europa	Randomized controlled trial	96	Patients over 18 years of age with resectable gastric adenocarcinoma requiring total gastrectomy who have completed neoadjuvant chemotherapy.	Chemotherapy	EQ5D time trade-off	NR	AJCC (TNM) Stage III	0.680 (0.20)

HP indicates *Helicobacter pylori*; CGD, cáncer gastrico difuso; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire Core 30; 5-FU, 5-fluorouracil; AJCC, American Joint Committee on Cancer; NR, not reported; TNM, tumor node metastasis; USA, United States of America.

were recruited) was 0.94.[46] This allows us to observe that the HSUV found in gastric cancer patients (0.77 in patients diagnosed with stage I, 0.75 in stage II) is consistently lower, even at early stages of the disease. To compare our utility values for gastric cancer with estimates of other types of cancer by stage, we can look at, for example, a systematic review[47] of utilities for colon cancer patients that estimated that after 1-year post-surgical treatment, the utility for the stage IV population was 0.19 less than that for stage I to III. There is concordance in the difference between the early and advanced stages. In our systematic review, a study[39] reported utility valuations of 0.79 (SD 0.25) and 0.60 (SD 0.29) for stages III and IV, respectively, according to the TNM classification. Another study,[36] which categorized the population into early stage (AJCC stages 0-III) and late stage (AJCC stages IV), estimated values of 0.84 (SD 0.25) and 0.68 (SD 0.33), respectively. In our meta-analysis, we estimated 0.70 (95% CI 0.63–0.96) for stage 3 and 0.64 (95% CI 0.56–0.32) for stage 4. Lastly, a systematic review[48] of HSUVs by cancer stages of different kinds showed that mean utility values decrease with increased cancer stages, with consistently lower values seen in stage IV. Because earlier-stage (stages I-II) cancers tend to be associated with reduced symptom impact and can often be treated with curative intent, whereas later-stage or metastatic (stage IV) cancers are usually associated with increased symptomatology due to tumor growth and spread to other organs.

This observation highlights the degree of consistency between our utility estimates and those reported for other types of cancers. It is worth noting that we included studies with results that contradicted this trend, such as the study by Zhang et al,[43] in which utilities for stage IV were higher than those for stage 3. This discrepancy can be attributed to the different treatments received by both groups. The lack of information on the time after

Table 2. Quality assessment of the studies.

Studies/quality criteria	Patient recruitment information	Non-normality of utility distribution	Treatment of missing values	Generalizability	Funding source	Source of tariff	Dropouts quantification	Ptj
Dan et al,[31] 2006	1	1	1			..		3
Lee et al,[34] 2018								0
Areia et al,[35] 2014								0
Zhou et al,[36] 2012						1		1
Kontodimopoulos et al,[37] 2009						1		1
Curran et al,[38] 2009		1	1			1		3
Xia et al,[39] 2020								0
Abdel-Rahman,[40] 2019						1		1
Ding,[41] 2020								0
Ito et al,[42] 2020								0
Zhang et al,[43] 2021								0
Wielen et al,[44] 2021		1	1			1		3

Note. A score of 1 was assigned if the attribute information was not satisfactorily completed; otherwise, it was not assigned.

treatment or surgery of the patients included in the primary studies of our review does not allow a more precise analysis of the impact of the clinical stage and treatment provided on HSUV. For example, a study[1] about breast cancer showed that utility value in patients' treatment with chemotherapy was slightly lower than any other cancer treatment and even irrespective of stage. Therefore, stage differentiation of therapy is likely a relevant factor in understanding the higher utility value in stage IV. Eventually, it is also essential to consider that most patients included in the study were diagnosed at stage 4. We believe it relevant for clinicians to evaluate utility values in the context of treatment and not just stage.

This review had several strengths. First, we performed a thorough search, which allowed us to obtain studies from different countries. The most complete information regarding the population and their health status assessments was presented and used for the meta-analysis. Second, we adhered to a committee of experts in oncology and international recommendations to group the values reported by the studies, which allowed us to perform a meta-analysis that allowed us to obtain reference values for the health status of the population.

Among the main limitations encountered, we found high levels of heterogeneity, which is partly because most of the studies reported clinical stages that were not comparable or had missing information to achieve a correct grouping. As mentioned above, the impact of surgical interventions on the assessment of QOL could not be evaluated, nor could other patient characteristics have been included in the primary studies. Another limitation of the meta-analysis was the difficulty in finding utility results calculated using the same instruments. We combined the EQ-5D and standard gambling (SG) utility values. This is because an insufficient number of primary studies use the same method for utility estimation, which limits the ability to draw stronger conclusions. This limitation is often found in other systematic reviews of cancer utilities. For example, a systematic review of cancer and neck utility values showed high heterogeneity in the assessment instruments, with higher values in the estimates with EQ-5D than with time trade-off and SG.[49] In addition, another systematic review of colorectal cancer estimated that the utilities measured with EQ-5D were 0.2 points higher than those measured with time trade-off and SG.[47] Finally, a review[50] of utility values for hematologic cancer showed high variability in the definition of stage groups.

However, these variations cannot be generalized to all health states. Although there is no general rule regarding the use of only direct or indirect estimates,[27] performing a meta-analysis of utilities using a single instrument would probably improve the certainty of the results.

In contrast, the method of collecting information from patients is also reported to be an important factor to consider in shaping the meta-analysis.[51] In the case of EQ-5D, participants could autocomplete via postal surveys, clinics, and face-to-face interviews. This was also not possible to be analyzed because of limited data in the primary studies.

In summary, we could not find sufficiently homogeneous data to perform a more reliable meta-analysis. For authors performing an economic model, we recommend that subgroups of patients be generated depending on the decision problem. Such a decision should be based on the requirements of the economic model for the input data. For example, a possible solution to the heterogeneity of the meta-analysis is to perform it based on individual patient data. Hatswell et al[52] performed this approach for a meta-analysis of multiple myeloma utilities.

These findings have implications for researchers and decision-makers. Considering the preferences of people in different health states remains an important factor for policy decisions based on an explicit value framework in cancer care. This is particularly relevant for diseases such as gastric cancer, which result in significant morbidity, reduced QOL, and mortality across different populations.

Further research is needed to generate more and better data on QoL and utility information for gastric cancer populations in different settings using high-quality methods.

Conclusions

This systematic review and meta-analysis of 12 studies encompassing 4585 gastric cancer (GC) patients provides crucial updated utility values across disease stages. Our findings reveal a significant decrease in mean utility scores from stage I to stage IV, highlighting the substantial impact of disease progression on patients' quality of life. The considerable heterogeneity observed across studies underscores the influence of factors beyond disease stage, such as treatment type and duration, on reported utility values. This emphasizes the need for future research to consider these nuances for a more comprehensive understanding of patient preferences. These data are essential for informing healthcare resource allocation and clinical decision-making, ensuring that policies and treatment plans reflect the preferences and values of GC patients. The integration of patient-reported utility values into health economic evaluations could lead to more equitable and effective healthcare strategies for GC.

Author Disclosures

Author disclosure forms can be accessed below in the Supplemental Material section.

Supplemental Material

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