Health State Utilities for Economic Evaluation of Bariatric Surgery: A Comprehensive Systematic Review and Meta-Analysis

Abstract

Health-state utilities (HSUs) are health economic metrics that capture and assess health-related quality of life (HRQoL). They are essential in health-economic evaluations when calculating quality-adjusted life years. We investigated published studies reporting bariatric surgery-related HSUs elicited through direct or indirect (multi-attribute utility instrument [MAUI]) patient-reported methods (PROSPERO registration number: CRD42019131725). Mean HSUs for different time points and HSU changes over time (where feasible) were meta-analysed using random-effects models. Of the 950 potentially relevant identified studies, n=28 (2004-2018) qualified for data extraction, with n=85 unique HSUs elicited mainly from the EQ-5D (88%). Most (75%) studies were published after 2013. The follow-up duration varied between studies and was often limited to 12 months. The pooled mean HSU was 0.72 (0.67–0.76) at baseline/pre-surgery (n=18) and 0.84 (0.79–0.89) one-year post-surgery (n=11), indicating a 0.11 (0.09-0.14) utility unit increment. EQ-5D showed the similar results. This positive difference can be partially explained by BMI and/or co-morbidities status improvement. This study provides a valuable summary of HSUs to future bariatric surgery-related cost-utility models. However, more well-designed higher-quality bariatric-related HSU studies are expected for future reviews to improve the available evidence. We suggest that researchers select a MAUI that is preferentially sensitive to the study population.

Abbreviations: 15D, 15-dimensional questionnaire; % EBMIL, percentage excess BMI loss; AGB, adjustable gastric banding; AQoL-8D, Assessment of Quality of Life 8-dimension; ASMBS, American Society for Metabolic and Bariatric Surgery; BMI, body mass index; CHEERS, Consolidated Health Economic Evaluation Reporting Standards; CI, confidence interval; CUA, cost-utility analysis; CVD, cardiovascular disease; EQ-5D, EuroQoL five-dimensions scale; MA-II, Moorehead-Ardelt II questionnaire; MAUI, multi-attribute utility instrument; HRQoL, health-related quality of life; HSUs, Health-state utilities; HUI, Health Utilities Index; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; QALY, quality-adjusted life year; QWB, Quality of Well-Being Scale; RYGB, Roux-en-Y gastric bypass; SD, standard deviation; SF-6D, Short Form-6-dimension; SG, sleeve gastrectomy; T2DM, type 2 diabetes mellitus; TTO, time trade-off; WMD, weighted mean difference.

1. INTRODUCTION

1.1 Obesity and bariatric surgery

Obesity (defined as body mass index [BMI] ≥30 kg/m^2) is epidemic worldwide.[1] Based on the World Health Organization's most recent data, 13% of adults worldwide were obese.[2] Moreover, the proportion of people with severe (BMI ≥35 kg/m^2) and morbid (BMI ≥40 kg/m^2) obesity is rising at a faster rate than obesity.[3-5] Obesity poses significant health risks (including physical and psychosocial co-morbidities and premature death) to the lives of affected patients, particularly for people who are morbidly obese.[6,7] Beyond health risks, obesity has also been consistently shown to negatively impact health-related quality of life (HRQoL).[8] Moreover, obesity imposes substantial economic burden from individual, health payer and societal perspectives for developed and developing countries due to, for example, direct healthcare costs and numerous indirect costs including productivity losses.[9,10]

Efficacious interventions to prevent or treat obesity are urgently needed to minimise the adverse HRQoL and direct and indirect cost consequences associated with this condition. An efficient healthcare system needs to offer cost-effective treatments for all diseases including obesity because of healthcare resource scarcity.[11] Based on the analysis of substantial primary data, we previously found that bariatric (weight loss, metabolic) surgery is a cost-saving treatment for patients with obesity over the lifetime.[12,13] Besides, bariatric surgery has been reported to be the only clinically effective and sustainable approach to severe and resistant obesity.[14,15] In addition to actual weight loss and the possible resolution of obesity-related co-morbidities following surgery, another widely recognised important outcome measure is the HRQoL improvement.

1.2 Health-state utilities (HSUs) and associated measures

Cost-utility analysis (CUA), a type of cost-effectiveness analysis, has become increasingly popular in assisting the decision-making process in several countries, particularly for government reimbursement decisions.[16-18] In CUA, the cost effectiveness (or even cost savings) of an intervention is expressed in terms of the incremental cost per quality-adjusted life year (QALY), where the QALY combines increased life expectancy (quantity of life) and improvements in health status (quality of life).[19] QALY is a potentially useful measure of outcome for decision-making processes and enable direct comparisons to be made between treatment alternatives across various conditions. In order to generate QALYs, preference-based HRQoL weights (also known as HSUs) are combined with the length of time spent in the health states of interest.[20]

HSUs are scored between ‘0’ representing death and ‘1’ representing perfect health, and negative values represent health states deemed to be worse than death.[21] Methods for measuring HSUs for economic evaluation included direct and indirect scaling methods.[22] Direct measurement asks the person to value directly their own health under conditions of uncertainty by using a valuation technique such as time trade-off (TTO) or standard gamble methods.[23] Indirect measurement involves the use of multi-attribute utility instruments (MAUIs) such as the European EuroQoL five-dimensions scale (EQ-5D; http://www.euroqol.org), the Canadian Health Utilities Index (HUI; http://www.healthutilities.com), the UK Short Form-6-dimension (SF-6D; http://www.shef.ac.uk/scharr/sections/heds/mvh/sf-6d), the Finnish 15-dimensional questionnaire (15D; http://www.15d-instrument.net/15d), the US Quality of Well-Being Scale (QWB; https://eprovide.mapi-trust.org/instruments/quality-of-well-being-scale) and the Australian Assessment of Quality of Life 8-dimension (AQoL-8D; http://www.aqol.com.au), where patients complete the instrument's array of questions on their current health state and these responses are scored using a value set obtained from the general population.[24,25] With a burgeoning literature of HSUs, which values should be used as inputs in a model is becoming a challenging task. As these MAUIs are far from identical in terms of their descriptive system and covered health states, the choice of MAUI may affect the estimated HSUs, and in turn the CUA outcomes.[26] Supplement 1 provides a detailed comparison of the characteristics of these instruments. QWB is the first reported MAUI which was released in 1976 in the US, and the AQoL-8D is the most recently developed MAUI targeting both physical and psychosocial health dimensions. The EQ-5D dominates the economic evaluation literature (up to 63% of all MAUIs), as expected from the recommendations of the National Institute for Health and Care Excellence (NICE) guidelines to use the EQ-5D as the preferred measure of HRQoL in adults.[27]

1.3 Bariatric surgery-related HRQoL and research gaps

A number of structured or systematic reviews have shown that the HRQoL of patients suffering from obesity improved after surgery.[28-33] However, these studies are mainly comprised of disease-specific (e.g., Moorehead-Ardelt II questionnaire [MA-II]) or non-preference-based (e.g., Short Form [SF]-36) data that are unsuitable for cost-utility comparisons because they do not generate a utility value. An emerging literature has shown that HSUs have been used as a metric for quantifying HRQoL improvements regarding bariatric surgery,[34-61] nevertheless, meta-analyses of bariatric surgery-related HSUs have not been conducted to date. This is surprising, especially given the large number of routinely conducted economic evaluations of bariatric surgeries.[62-68] Consequently, these modelling studies have not been able to benefit from the meta-analytical HSU estimates, and most rely on the same source of HSUs, with variation in HSU assumptions across models.[65,69-71] HSUs from single study may not always be a reliable indicator of underlying HRQoL, particularly, where HSUs is not the main focus of the research. Meta-analyses, on the other hand, have the advantage of combining all published HSUs for a given population to maximize the generalizability and representativeness of the estimates used in any economic model, as well as providing insight into the factors that influence HRQoL.[21]

1.4 Objectives of our systematic review

We acknowledge the current debate regarding HSUs generated by differing MAUIs predominantly because of their descriptive systems, nevertheless, no previous studies have comprehensively investigated and meta-analysed HSU evidence regarding bariatric surgery. Therefore, to address this important research gap, this comprehensive systematic review and meta-analysis aims to generate a database of HSUs that could be used to populate future model-based cost-utility analyses of bariatric surgery procedures. The study as such has two main aims:

1) to undertake a systematic overview of published studies reporting HSU-based HRQoL in patients who underwent bariatric surgery procedures; and

2) to obtain bariatric surgery-related pooled HSUs (from baseline [pre-surgery] to various post-surgery time points) and HSU changes over time (where feasible) that can be used to adjust life expectancy in future CUA.

2. METHODS

The protocol of this systematic review was registered on 17 May 2019 at PROSPERO (registration number: CRD42019131725; https://www.crd.york.ac.uk/Prospero/). The search strategy, data screening, extracting and synthesising were followed by the protocol.

2.1 Validated guidelines

This systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[72] and the Campbell and Cochrane Economics Methods Group guidelines.[73]

2.2 Literature search

Based on previous recommendations[74-76] and systematic reviews[77,78] in the field, the literature search was conducted from inception until September 2019 in three biomedical databases (PubMed, EMBASE via OVID and Scopus) and three economic databases (American Economic Association [EconLit], the Cost-Effectiveness Analysis [CEA] Registry, and the Centre for Reviews and Dissemination [CRD], which includes the Database of Abstracts of Reviews of Effects [DARE], Health Technology Assessment Database [HTA] and National Health Service Economic Evaluation Database [NHS EED]).

To ensure literature search saturation, a keyword search of Google Scholar, hand searches and citation tracking of all selected articles and relevant reviews were performed.

The search strategies were developed in consultation with a research librarian at the University of Tasmania. Since Medical Subject Headings (MeSH) terms provide little coverage of HSUs, we identified relevant free-text terms by referring to the published recommendations[74,76,79] and recent analogous systematic reviews[77,80]. The search strategy combined terms for direct and indirect methods of HSUs elicitations with terms for bariatric surgery. We initially kept the scope and identification of the evidence for HSUs broad. Supplement 2 outlines the initial search strategy for EMBASE via OVID database, which was also adapted for both biomedical and economic databases. Economic filters were considered when searching for evidence on generalist databases, such as PubMed. A simplified search was undertaken without using economic filters for evidence on economics databases such as EconLit.

Search results were exported to the Covidence online program (Veritas Health Innovation, Melbourne, Australia; https://www.covidence.org), and duplicate articles were removed before screening. Screening of eligible studies was conducted in three steps: first, titles and abstracts were screened by two co-authors (QX and JC) for evidence relevant to HSUs related to bariatric surgery; second, the two co-authors independently assessed the full-text of the remaining studies based on the inclusion criteria of qualitative analysis; third, shortlisted articles with requisite HSU data were further considered for data extraction/synthesis for the meta-analysis. Two additional co-authors (AP and HA) were consulted for a final decision in case of any discrepancies. The number of records identified, retrieved, screened, assessed, included, and excluded in the review, and reasons for exclusions, is summarized in a PRISMA flow diagram (Figure 1). Referencing was managed in EndNote X8.2 (Thomson Reuters).

2.3 Study eligibility

Studies were considered eligible if: 1) included participants (BMI ≥30 kg/m^2) undergoing any type of bariatric surgery with assessment of HSUs as primary or secondary patient-reported outcome measures; 2) based on direct (e.g., TTO, standard gamble) or indirect (MAUI based)

HSUs elicitation methods; and 3) published as full text (with no time restrictions) in English, German, Chinese, French and Italian languages.

Systematic reviews, meta-analyses, conference abstracts, editorials, letters as well as case reports were excluded. Studies that obtained HSU estimates from previously published literature other than patient-reported outcomes through research or those reporting simulation-based utilities were also excluded. If articles referred to the same study population and reported multiple HSUs estimates, the article with the most comprehensive data or the most relevant HSU measures were retained for data syntheses. Where the required HSU data for meta-analytical synthesis were missing, corresponding authors were contacted to improve the comprehensiveness of our study's meta-analyses. If the HSU data could not be provided, the study was excluded from the meta-analysis but still retained in the systematic review.

2.4 Data extraction

In order to foster the accuracy of data extraction, a preliminary data collection form was used to extract data from 10% of studies. Adjustments and improvements were made to the initial form. The first author (QX) used the improved data form to extract data independently, and then the co-author (JC) performed cross-checking. Discrepancies were resolved by consensus, and if agreement was not reached, two additional reviewers (AP and HA) were consulted to reach an agreement. Reviewers were not blinded to information about the authors, author affiliation, and journal name, because this has been shown to be unnecessary.[81] If HSUs had to be read from a graph, the figures were extracted using the plot digitizing tool -WebPlotDigitizer (Version 4.2).[82]

The data extraction was performed according to the requirements of the Cochrane Handbook for Systematic Review of Interventions (version 5.1.0)[73] and previous guidelines.[74,76]

The following information was extracted from primary studies: first author's name, year of publication, study location, study design of questionnaire assessment (retrospective or prospective), surgery type, comparison (e.g., before versus after, surgical versus non-surgical), target population, participants' sociodemographic characteristics (e.g., female proportion and mean age) at baseline, HSU elicitation method, modes of questionnaire administration (self- or interviewer-administered), types of value set used (local or foreign), sample size, reasons for participant dropout of the study, BMI and obesity-related co-morbidities in each observational time-point, number of follow-ups, follow-up durations (short-term follow-up was defined as from 1 year to 3 year according to the American Society for Metabolic and Bariatric Surgery [ASMBS] outcome reporting standards)[83], and HSUs in each observational time-point (mean and standard deviation [SD]). Where possible, the individual dimension scores or the proportions of individual dimension responses to each MAUI were extracted to identify the health aspects that were most impacted by bariatric surgery. In addition, the predictors for HSU changes (because of bariatric surgery) were also extracted from the primary studies.

Where HSU data were available only by respondent subgroups based on patient characteristics (e.g., sex), a weighted average of the change score and the score's precision estimate with weights proportional to the subgroup's size were obtained.[73] When this subgrouping was based on the alternative elicitation methods as described above (i.e., the type of direct-report) or the type of bariatric surgery, then each subgroup was considered independently.

2.5 Statistical methods for meta-analysis

We performed a meta-analysis to estimate a single HSU for each time point (i.e., baseline [pre-surgery] and follow-up [post-surgery] time points). Additionally, statistical meta-analyses to summarize the weighted mean difference (WMD) in HSU estimates before [baseline/pre-surgery] and after [one-year post-surgery] bariatric surgery were also performed in the form of forest plots.

All statistical analyses and graphing were carried out in STATA (STATA 15.1, StataCorp, College Station, Texas, USA). The command “metan” was used to conduct meta-analysis.[84] Random-effects models were used because of the variable nature of the source populations for each study to accommodate for likely between-study heterogeneity.[85]

Additional variability in meta-analysis estimates may stem from inter-MAUI differences related to instrument scales, instrument descriptive/classification systems and the sophisticated algorithms that derive the HSUs. Therefore, to examine the nature of these potential sources of heterogeneity, subgroup analyses regarding different elicitation methods were performed. Subgroup analyses for WMD before and after bariatric surgery were only estimated for studies using the EQ-5D instrument, owing to the small number of included studies using other instruments. Additionally, potential heterogeneity based on different surgery types and gender groups was also examined.

Formal quality assessment of primary studies eliciting utility values was not undertaken, given a lack of standard systems or checklists for grading the quality of such studies.[74,76] Consequently, we examined potential publication and small study bias, visually, using funnel plots (where a symmetrical plot suggested no or little bias) and using Egger’s regression asymmetry test (where a *p*-value of <0.1 indicated a statistically significant difference). Sensitivity analyses were undertaken to evaluate the stability of the meta-analysis results. Individual studies were excluded from all meta-analyses sequentially to gauge the influence of individual studies on the overall results (by using STATA “metaninf” command).[86] When the remaining pooled rates were not substantially altered, the results of this meta-analysis were deemed stable.

3. RESULTS

3.1 Eligible studies

Figure 1 presents the process of study selection based on PRISMA methodology. The search strategy yielded 950 citations, with 889 (94%) citations from biomedical databases, 55 (6%) from economic databases and six (<1%) from other sources. After removing duplicates 676 potentially relevant publications remained for title and abstract screening, with 137 studies included for full-text review. Of these, n=28 studies were included in the qualitative synthesis. We subsequently excluded 12 more studies as they either fully or partially relied on the same data sample,[34,46,54,58,59,61] or did not report requisite HSU data.[36,40,48,49,51,56] Consequently, only 16 studies were eligible for the meta-analysis.[35,37-39,41-45,47,50,52,53,55,57,60]

3.2 Study characteristics of the qualitative synthesis (n=28)

Overall, the 28 included studies reported a total of 85 unique HSUs related to bariatric surgery. Supplement 3 provides summary characteristics of the included studies, while all reported HSUs were summarised in Supplement 4. The first study regarding HSUs of bariatric surgery was published in 2004,[34] and most articles (n=21; 75%) were published after 2013 (Figure 2) which is consistent with the increased popularity of health economic evaluations of bariatric surgery in recent years. Only a small fraction of these studies (n=5; 18%) was published in health economics journals,[37,41,54,55,59] and the vast majority (n=23; 82%) in general medical journals.

Of the included studies, half (n=14, 50%) were conducted in Europe (Finland [n=2], Spain [n=2], Netherlands [n=2], UK [n=2], Sweden [n=3], France [n=1] and Multicentre within Europe [n=2]), 28% from North America (n=8: US [n=4] and Canada [n=4]), 11% (n=3) from Australia, and 11% from Asia (n=3: South Korea [n=2] and Israel [n=1]). This concurred with the distribution of health economic evaluations of bariatric surgery worldwide.[12,13] Notably, no study was conducted in developing countries.

Roux-en-Y gastric bypass (RYGB), adjustable gastric banding (AGB) and sleeve gastrectomy (SG) were the three most prevalent procedures, with RYGB and AGB predominantly reported in earlier years, and SG in later years, and also reflecting the technical change of bariatric surgery.[13,87,88]

Study designs included: retrospective studies (n=8, 29%) and prospective studies (n=20, 71%). Across the twenty-eight identified studies, the baseline sample sizes varied between 23 and 893 (Mean: 194). The dropout was only occurred and was subsequently reported in n=9 studies, with n=4 studies also providing the reasons for dropout (Supplement 3).

Whilst most HSU estimates were available for multiple follow-up times (between 2 and 60 months), the follow-up duration varied between studies and was often limited to up-to 12 months (short-term follow-up). Synthesis of HSUs in each observational time point was shown in Section 3.3.

The mean age in many (23 out of 28, 82%) included studies ranged between 40 and 50 years. As to sex distribution, all studies except one reported a largely female dominance (average female proportion: 76%). Of the 26 studies that provided clear evidence regarding the BMI categories of obesity and associated co-morbidities, n=17 (65%) focused on patients with morbid obesity. The mean BMI at baseline was 45.65 (44.13, 47.16) kg/m^2. On average, the BMI decreased by 13.81 kg/m^2 (95% *CI*: 11.02–16.59) one-year post-surgery. Similarly, most studies (n=17) reported the improvements in co-morbidities' status of patients with obesity as a result of surgery, with T2DM and cardiovascular disease (CVD, mainly hypertension in this study) being the main beneficiaries.

In 63% of cases, HSU estimates for bariatric surgery were based on self-administered surveys, whereas 30% were based on interview-administered surveys. All HSU estimates were obtained indirectly using MAUIs, and no directly estimated HSUs were identified (Supplement 4). Of the 85 recorded HSUs, n=75 (88%) were measured using the EQ-5D suite of instruments and the associated value set for the particular country (3L: n=66; 5L: n=6). The remaining HSUs were based on the 15D (n=4; 5%), AQoL-8D (n=4; 5%), and SF-6D (n=2; 2%). Most HSU estimates (n=64, 75%) were elicited using the local population norms. HSUs were elicited using a single MAUI in most studies: 21 studies used the EQ-5D and two studies the 15D MAUI. In addition, there were five studies that used multiple MAUIs: three used the EQ-5D and AQoL-8D; and two used EQ-5D and SF-6D.

3.3 Impact of bariatric surgery on HSUs (n=16)

Tables 1 and 2 present the overall as well as subgroup pooled mean HSU estimates at baseline and different follow-up durations. The pooled mean HSU estimate was 0.72 (0.67-0.76), 0.81 (0.77-0.85) and 0.84 (0.79-0.89) units at baseline, six-month and one-year post-surgery, respectively (Table 1, Figure 3 [A] and [B]). HSUs captured by SF-6D and AQoL-8D were significantly lower than those from the EQ-5D suite of instruments and 15D (Table 1). However, the SF-6D, AQoL-8D and 15D-based HSUs in this comparison were only supported by single studies (Table 1). HSUs were similar among different surgery types (Table 2). Pooled results based on gender difference were not estimated due to insufficient data (Supplement 4).

Overall, the HSU estimate increased a 0.11 [0.09, 0.14] utility unit one-year post-surgery (Figure 3 [C]). Similar results were identified for the EQ-5D suite of instruments. On average, the EQ-5D HSU increased by 0.13 (0.09, 0.17) utility units one-year after bariatric surgery (Figure 3 [C]).

As shown in two studies,[44,47] patients' HSU improved more for the surgical group than the non-surgical group (Supplement 4), however, the combined data could not be further pooled and then analysed due to varying follow-up durations.

3.4 Impact of bariatric surgery on individual health dimensions

Five studies reported the proportion of individual dimension responses to the EQ-5D suite of instruments. As shown in Table 3, patients presented at baseline with more HRQoL impacts for the health dimensions of mobility, usual activities and pain/discomfort, and not a large impact on self-care. Improvements in the distribution of responses were recorded one-year post-surgery in four out of the five EQ-5D dimensions (i.e., mobility, usual activities, pain/discomfort and anxiety/depression), especially for mobility and usual activities.

Scores for the individual dimensions of the 15D (baseline vs. one-year) were available in one study.[39] At baseline, larger HRQoL impacts were reported in respiratory, sexuality and usual acts, and improvements were also recorded in these dimensions one-year after surgery (Supplement 5 [A]).

The AQoL-8D's individual dimensional scores were available in only one study for baseline versus one-year comparison.[55] At baseline, HRQoL impacts were larger in the psychosocial dimensions of health (e.g., mental health and happiness) compared to those in the physical dimensions of health (e.g., independent living and pain). The improvements were recorded in all dimensions especially for psychosocial dimensions (Supplement 5 [B]).

3.5 Predictors of HSU changes due to bariatric surgery

As shown in Supplement 6, eleven studies investigated the potential predictors of change in HSUs before and after bariatric surgery. The studies were informed by various statistical methods including correlations analysis and multiple regression models. All but one study investigated the relationship of weight/BMI reduction with change in HSUs due to bariatric surgery, with six recording a significant association. Baseline utility was reported as a significant predictor in one study only. No other significant predictors of HSUs change were identified in these studies.

3.6 Publication bias and sensitivity analysis

There was no evidence of publication bias based on Egger's test for HSU at one-year post-surgery (z= -1.36, P=0.18) and HSU changes before versus after one-year surgery (z= -0.37, P=0.71). Significant publication bias was found in baseline HSUs (z= -2.14, P=0.03). The trim-and-fill analysis was conducted, but no studies were imputed. After removing one study (the orange marker in Supplement 7 [A]) with extreme HSU data, publication bias was no longer evident (P=0.185) and the mean baseline HSU stabilized (0.727 [0.681, 0.773]). Funnel plots are shown in Supplement 7. Test of influence of an individual study on the overall meta-analysis estimate did not show significant outliers.

4. DISCUSSION

Our comprehensive study is the first to systematically summarise and meta-analyse HSUs regarding bariatric surgery treatment for obesity. Our research substantially overcomes the challenges associated with systematically selecting utility data for economic evaluations of bariatric surgery. The meta-analytical estimates that we have generated can be used as inputs to future bariatric surgery-related cost-utility models. We found that HSU estimates before and after bariatric surgery were largely elicited through the EQ-5D MAUIs. Limited studies used the SF-6D, AQoL-8D and 15D MAUIs, and no study used direct methods. A significant increase in mean HSUs was observed after bariatric surgery, particularly within the first postoperative year. We also found that the reporting of HSUs for bariatric surgery reflected the surgical technical change of bariatric surgery globally,[13] whilst more reporting is called for in proportion to the large number of bariatric surgery-related models.

All studies included in our comprehensive systematic review supported bariatric surgery as an effective option in improving HRQoL for people with obesity. We found a mean HSU difference of +0.11 units between the baseline and one-year after bariatric surgery (+0.13 units for EQ-5D), and this difference exceeds the minimal clinically important difference for all the MAUIs reported in previous studies (from +0.04 units [EQ-5D] to +0.08 units [AQoL-8D]).[54,55,89-91] In conjunction with this positive HSU difference (from baseline to one-year after bariatric surgery), our study also observed a substantial decrease in the mean BMI. Six out of ten studies reported an inverse relationship between weight/BMI and HSU post-surgery. The findings are in line with a systematic review of reviews that found a significant negative association between obesity and HRQoL, and that the relationship between weight loss and improved HRQoL was consistently demonstrated after bariatric surgery.[92] Besides, metabolic co-morbidities are reported to be associated with impaired HRQoL among patients who suffered from obesity, and the improvement of these conditions could improve patients' physical and psychosocial quality of life.[93] Accompanied with the reported weight loss, our study also observed an improvement of co-morbidities' status (e.g., T2DM and CVD) in most of the primary studies.[34,38,42,43,46] However, most studies did not independently consider the impact of co-morbidities on HSUs. Future studies should examine the impact of changes in co-morbidities status as a result of bariatric surgery on the HSU/HRQoL for patients with obesity.[94]

According to the newest population norms for the EQ-5D-3L for 20 countries, HSUs for the general populations (with healthy body weight) ranged from 0.74 to 0.95.[95] Whilst for patients with obesity these values ranged from 0.69 to 0.76 as reported in a double-blind RCT study using a TTO score.[96] In our present study, similar HSU result was identified for people with obesity before undergoing surgery (0.72 [0.67-0.76]); however, an extraordinary higher HSU of 0.84 was reported in a longitudinal survey for waitlist patients through 15D MAUI.[39,97] Considering the baseline characteristics of these patients (waitlisted, morbidly obese, 83% comorbidities affected)[39,97], we suggest that the key reason for the higher HSU could be due to the relatively young age group (42.1±10.6 years) considered in this study; otherwise, the use of the 15D MAUI for a waitlisted population's HSUs needs further investigation because HSUs from the other four included studies that investigated patients waiting for bariatric surgery ranged from 0.51 to 0.70 (three from EQ-5D and one from AQoL-8D).[42,47,54,55]

As confirmed by previous studies, heterogeneity among studies may stem from various sources including the differences between various MAUIs due to their different instrument scales, descriptive systems and utility formula.[26] The choice of the utility assessment method can have a considerable effect on the predicted HSUs and, hence, on the outcome of economic evaluation.[98,99] For instance, in the present meta-analysis, we found that HSUs captured by the SF-6D and AQoL-8D were significantly lower than those from the EQ-5D and 15D (in particular) (Table 1). Our results should however be interpreted with some caution as being derived from a subgroup meta-analysis based on a limited number of studies (i.e., n=2 for AQoL-8D,[54,55] n=1 for SF-6D[37] and n=2 for 15D[34,39]).

Whilst the EQ-5D was the most commonly used MAUI to estimate HSUs, there is a debate as to whether the EQ-5D's descriptive system can capture and assess all the relevant domains of health for people who are waiting for and subsequently undergo bariatric surgery. Our study's findings suggest that the AQoL-8D preferentially captured the psychosocial domains of health compared to the EQ-5D. Moreover, our pooled findings are important because a recent publication in the Journal of the American Medical Association emphasised the importance of measuring the mental health impact of bariatric surgery.[100] We suggest that this paper's emphasis on mental health directly translates to the notion of choosing a MAUI that is preferentially sensitive to the relevant domains of health for the particular study population. We note that the AQoL-8D MAUI was specifically developed to achieve an increased sensitivity for capturing and assessing the complex physical and psychosocial HRQoL health states that are relatively neglected in other MAUIs, particularly for people with complex and chronic disease states.[101,102] However, as identified by our present study, only two HSU studies using the AQoL-8D MAUI longitudinally have been published to date. We therefore hope that the use of AQoL-8D or other MAUIs that are sensitive to the relevant domains of health for people with bariatric surgery, may provide more credible HSUs.

In addition to the elicitation method, other potential sources of variation in reported HSU values may include patients' socio-demographic characteristics (e.g., age, sex or initial BMI), surgery type, follow-up durations, mode of administration and co-morbidities status. However, these may not have a large impact on our meta-analyses results as patient-level HSUs were only considered in our study, and patients' socio-demographic characteristics in our study (i.e., sex proportion, mean age and mean BMI) were generally comparable across included studies (Supplement 8). Through additional subgroup meta-analysis (Table 2), we further established that surgery type did not contribute to this variation. Meta-regression was not possible for all variables due to the insufficient number of included studies. Future studies are recommended to investigate the magnitude of effect and relative contribution of each of the pertinent impact factors on HSUs of people who receive bariatric surgery.

Our study has unique strengths. This is the first study to systematically assess and summarise HSUs related to bariatric surgery, which provides a standard set of HSUs that could be used in health economic assessments of bariatric surgery procedures. An advantage of undertaking a meta-analysis is that it provides both an average value as well as extreme values that could be used in a sensitivity analysis. Providing a range of values alongside the summary HSUs is particularly important as there is considerable heterogeneity in the HSUs between bariatric surgery studies. Likewise, a further strength of our study is the broad range of study populations conducted in, for example, different countries and ethnicities, maximising the generalizability and representativeness of the HSU estimates used in bariatric surgery-related economic models.

This systematic review and meta-analyses also has limitations. First, our meta-analytical HSU estimates predominantly relied on the EQ-5D MAUIs with limited coverage of psychosocial health aspects, and potential ceiling and floor effects. Second, HSU follow-up times were generally limited to short term (up to one year), hence, our study failed to capture longer-term changes in HSUs as a result of bariatric surgery. The long-term data from this study should be interpreted with some caution when using in the models. Third, HSU differences between surgical and non-surgical groups were not available in current meta-analysis due to the lack of relevant data. Fourth, we have used mean with SD in data syntheses. The distribution of the HSU values was not reported in most of the primary studies, sometimes these values can be negatively skewed which may bias the pooled HSU estimates downwards. Fifth, recall biases could not be neglected from few studies due to the observational nature. Finally, quality appraisal of the included studies was not undertaken in the current study, given a lack of standard systems or checklists for grading the quality of HSU studies; nevertheless, our study is the first gold-standard systematic review and meta-analysis that provides a baseline of studies to date.

Summary of recommendations for future HSU analyses:

- A preferentially sensitive MAUI should be selected that appropriately captures and measures both the complex and interdependent physical and psychosocial health needs of the bariatric surgery study population;

- Before versus after comparisons, to some extent, underestimated the impairment of obesity on HRQoL due to the fact that this study design does not consider the effect of follow-up on patients with obesity who do not receive bariatric surgery. To avoid it, future studies should consider simultaneous control group to balance the time effect among patients with and without surgery;
- Studies with longer time horizons are needed to assess the long-term effects of bariatric surgery on utility based HRQoL;
- Future studies also need to test and report the distribution of HSU data to improve the reporting quality;
- Future studies that examine the HRQoL impact of changes in obesity-associated co-morbidities status (as well as other potential factors such as complications and revisional procedures) as a result of surgery are also needed;
- More HSU research from developing countries are needed. For example, obesity prevalence is increasing, and obesity surgery is also prevalent in China; however, relative to population health economic evaluation is less reported, and despite the inclusion criteria of various languages including Chinese this study did not capture any HSU estimates from China or other similar countries;
- Guidelines or structured recommendations are urgently needed to support authors and reviewers in assessing their study quality.

5. CONCLUSIONS

This study represents the first systematic review and meta-analysis of HSUs regarding bariatric surgery treatment for obesity, demonstrating the relative lack of published HSU-based HRQoL for bariatric surgery. We have seen the increasing trend of health economic evaluations of bariatric surgery since 2013. Meta-analysis results suggest that HSU-based quality of life increased at least within one-year after surgery, and this positive difference can be partially explained by BMI and/or co-morbidities status improvement. The meta-analytical estimates that we have generated can be used as more reliable inputs to future bariatric surgery-related cost-utility models. However, more well-designed higher-quality bariatric-related HSU studies are expected for future reviews to improve the available evidence, including longer follow-up times.[103]

AUTHORS' CONTRIBUTIONS

QX conceived the study, collaborated in the design and implementation of the study and wrote the paper. JC conceived the study, collaborated in the design and implementation of the study, and critically reviewed and edited the manuscript. HA collaborated in the design and implementation of the study, and critically reviewed and edited the manuscript. BdG collaborated in the design of the study and edited the paper. LS collaborated in the design of the study and edited the paper. AP conceived the study, collaborated in the design of the study, and critically reviewed and edited the paper. All authors read and approved the final paper.

CONFLICTS OF INTEREST

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LEGENDS:

Table 1: Meta-analysis (random effects) results in each observational time points, by elicitation method (n=16);

Table 2: Meta-analysis (random effects) results in each observational time points, by surgery type (n=16);

Table 3: Proportion of individual dimension response to EQ-5D instrument (pre-surgery versus post-surgery);

Figure 1: Flow of studies into the narrative systematic review and meta-analyses, informed by PRISMA guidelines;

Figure 2: Number of studies reporting HSUs of bariatric surgery: (A) from 2004 to 2018; (B) before and after the year of 2013;

Figure 3: Forest plots (random-effects) of HSUs regarding bariatric surgery, by elicitation method: (A) baseline HSUs; (B) HSUs at one-year post-surgery; and (C) HSU changes before versus one-year post-surgery;

Supplement 1: Comparisons of the dimensions and content of multi-attribute utility instruments;

Supplement 2: Search strategy for EMBASE via OVID;

Supplement 3: Characteristics of studies included in systematic review (n=28);

Supplement 4: Details of HSUs reported by included studies;

Supplement 5: Radar charts comparing individual dimensional score before and after bariatric surgery: (A) 15D and (B) AQoL-8D;

Supplement 6: Predictors for HSU changes before and after bariatric surgery;

Supplement 7: Funnel plots of HSUs regarding bariatric surgery: (A) baseline HSUs; (B) HSUs at one-year post-surgery; and (C) HSU changes before versus one-year post-surgery;

Supplement 8: Univariate meta-regression of patients' socio-demographic characteristics in reported HSUs.

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