Association of Preference-Based Health-Related Quality of Life with Weight Loss in Obese Adults

Erica LW. Lester, MD, Raj Padwal, MD, MSc, FRCP{C}, Sumit R. Majumdar, MD, MPH, FRCP{C}, F Ye, MSc, Daniel W. Birch, MD, MSc, FRCSC, FACS{C}, Scott W. Klarenbach, MD, MSc, FRCP{C}.*

1Department of Surgery, University of Alberta, Edmonton, Alberta, Canada; 2Department of Medicine, University of Alberta, Edmonton, Alberta, Canada

ABSTRACT

Background: The obesity epidemic is linked to substantial health care resource use, reduction in workforce and home productivity, and poor health-related quality of life (HRQOL). Changes in body mass index (BMI) are associated with improvements in HRQOL; the nature of this relationship, however, has not been reliably described.

Objectives: To determine the independent association between changes in BMI and change in utility-based HRQOL.

Methods: Data were prospectively collected on 500 severely obese adult patients enrolled in a single-center obesity management clinic. Univariable and multivariable linear regressions were performed, adjusting for the effect of the intervention itself, obesity-related comorbidities, BMI at enrollment, age, and sex.

Results: A 1-unit reduction in BMI was associated with a 0.0075 (95% confidence interval 0.0041–0.0109) increase in the EuroQol five-dimensional questionnaire score. This relationship was unaltered in various analyses, and is likely applicable to any health-care-induced changes in BMI.

Conclusions: The quantification of this association advances the understanding of the clinical benefits of interventions that affect BMI, and can inform more robust cost-utility analyses.

Keywords: body mass index, obesity, quality of life.

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Introduction

Obesity, defined as having a body mass index (BMI) of more than 30 kg/m², affects 24% of Canadians [1] and 13% of the population worldwide, with prevalence doubling since 1980 [2]. It is a well-established risk factor for many disorders, including diabetes, sleep apnea, coronary heart disease, depression, and several types of cancer [3]. The epidemic of obesity is linked to substantial health care resource use, costing between $5 and $11 billion annually in Canada [3,4]. It is associated with reduced workforce and home productivity as well as poor health-related quality of life (HRQOL) [5,5]. The burden of disease increases as BMI increases: moderate obesity, or class II obesity, is associated with an increased rate of chronic disease, and severe obesity, or class III obesity (BMI > 40 kg/m²), is associated with increased rate of chronic disease and 6.5 to 13.7 years of life lost, relative to the normal-weight population [6,7]. In recent years, numerous strategies have been introduced to treat high-risk obesity directly, and to treat other medical conditions via therapies with weight-neutral or weight-reducing effects. Examples of the latter include sodium-glucose cotransporter 2 inhibitors in diabetes mellitus [8] or antipsychotic medications that have a less harmful impact on weight than do commonly used agents [9]. Novel drugs, however, are typically far more costly [10], and therefore a thorough understanding of their impact on all clinically important outcomes, including quality of life mediated through weight modification, is required to estimate the cost-effectiveness and inform rational use [11,12].

Although interventions that reduce BMI are associated with improvements in HRQOL, this relationship has yet to be reliably and precisely determined in the severely obese adult population in a manner suitable for economic evaluation [5,13]. Previous studies have studied highly selected cohorts (such as patients with diabetes), have been underpowered, or have not used preference-based quality-of-life measures (utility) required for cost-utility analyses [5,14–17]. The application of inappropriately derived HRQOL values for a given change in weight can have a significant impact on incremental cost-effectiveness ratios [18]. Organizations such as the National Institute of Health and the Canadian Agency for Drugs and Technology in Health (CADTH) have highlighted the need for high-quality studies that are applicable to a comprehensive population of obese patients, emphasizing the necessity for reliable cost outcomes [19–21].

We sought to determine the independent association between changes in BMI and change in utility (HRQOL), controlling for baseline comorbidities and the type of treatment (medications, ...
surgical, or waitlisted), in a prospective, population-based cohort of adults with class III obesity enrolled in an obesity management program followed over a 2-year period. Greater understanding of this relationship will allow the clinical benefits of interventions that modify BMI, in the population with the greatest burden of disease, to be more accurately estimated.

Methods
We used a prospective observational cohort study of 500 severely obese adults enrolled in an obesity management program in Northern Alberta (catchment population of 1.6 million) followed over 2 years. We previously reported that the minimal weight loss necessary to produce a clinically important change in the EuroQol five-dimensional questionnaire (EQ-5D) score was reached in more than 40% of this cohort [22]. Baseline characteristics and main study results have been described elsewhere [22–24]. Briefly, the cohort consisted of 150 waitlisted, 200 medically treated, and 150 surgically treated patients. All patients were deemed potentially eligible for bariatric surgery, on the basis of the region’s previously established surgical criteria, before enrollment. Patients could progress from the waitlist to medical treatment and through to bariatric surgery. Patients were censored if they transitioned to another treatment group, dropped out, died, became pregnant, or had a surgical procedure conducted outside of the region.

Waitlisted patients received no specific interventions but were advised to attend community-based education sessions. Medical management was tailored to individuals and specific causes of excess weight: patients underwent intensive lifestyle counseling and care by a multidisciplinary team in clinics every 4 to 8 weeks for a minimum of 24 weeks. Dietary strategies and antiobesity drug therapy were used, and obesity-related comorbidities (e.g., sleep apnea and mental health disorders) were assessed. Surgical patients underwent laparoscopic procedures, including adjustable gastric banding, sleeve gastrectomy, or Roux-en-Y gastric bypass, using previously described techniques [24].

Anthropometric, quality-of-life, demographic, and comorbidity measures were collected at each patient clinic visit every 6 months for 2 years; the mean number of visits was 5.1. Baseline measurements were recorded before the commencement of the respective treatment. Detailed case report forms have previously been published and are available elsewhere [23].

The primary exposure was the 2-year mean change in BMI (kg/m²), and the main outcome was the 2-year mean change in preference-based quality of life measured using the three-level EQ-5D. This self-completed, well-validated tool captures preferences for treatment group, age, sex, BMI at enrollment (baseline), and change in comorbidity status between first and final clinic visits for all comorbidities. Other models were created: a stepwise model with an addition criteria of P < 0.01 and a removal criteria of P > 0.05 (model 2) and a model examining change in BMI, baseline BMI, age, and sex only (model 3). In addition, models 1 and 2 were replicated using baseline obesity-related comorbidity status (not change in comorbidity over time).

Univariable analyses were conducted considering only those patients diagnosed with either diabetes, sleep apnea, hypertension, depression, or dyslipidemia, as well as by treatment group at baseline. The assumptions of the model were tested by plotting the residuals against the fitted values and calculating the variance inflation factor. There was no evidence that the assumptions of the model were violated. The analyses were conducted using Stata version 13 (StataCorp, College Station, TX).

Results
Mean age was 43.7 ± 9.6 years, mean BMI was 47.9 ± 8.1 kg/m², and 11.8% were men. There was no statistically significant difference between the baseline parameters among the three treatment groups, with the exceptions of mean BMI (lower in the surgical group; P = 0.003), health state utility score (higher in the surgical group; P = 0.0001), and presence of sleep apnea (more common in the surgical group; P = 0.01) (Table 1). At enrollment, 53 patients (10.6%) had no comorbidities, 132 (26.4%) had only one, and 315 (63.0%) had two or more. Among surgically treated patients, 51 patients (34%) had a sleeve gastrectomy, 48 (32%) had gastric banding, and 51 (34%) underwent Roux-en-Y gastric bypass.

The mean change in BMI for all subjects (Table 1) was −3.4 ± 5.2 kg/m². The surgical group experienced the largest mean change in BMI at −7.4 ± 5.6 kg/m². The mean change in the EQ-5D was 0.047 ± 0.137, and the greatest change was observed in the medical treatment group, with a 0.073 mean change in utility from baseline. The response variable, change in the EQ-5D score, ranged from −0.350 to 0.417.

In the univariable analysis, a 1-unit reduction in BMI was associated with an increase of 0.005 in mean change in the EQ-5D score (P < 0.001). Age and sex were not associated with change in the EQ-5D score when assessed independently. In the primary multivariable analysis, a 1-unit reduction in BMI was associated with a 0.0075 (95% CI 0.0041–0.0109) increase in the EQ-5D score (Table 2); this relationship was similar among alternate models, ranging from 0.0051 to 0.0068. The relationship was similar when subgroups of patients, by comorbidity and treatment groups, were considered (Table 3), although the medical treatment subgroup did not achieve statistical significance.

The assumptions of the linear model were tested, and there was no evidence of violation.

Discussion
In a large cohort of patients seeking treatment for severe obesity, we described the association between reduction in BMI and changes in utility-based quality of life. A 1-unit decrease in BMI was associated with an increase in health state utility score by 0.0051 to 0.0075, an association that was unaltered when using various analytic approaches and considering alternate subgroups within a cohort of obese patients seeking treatment for weight loss. This finding provides additional data to inform the clinical benefits of weight loss that may occur across various interventions, fills a knowledge gap, and is consistent with the utility data
There is, however, considerable variation in the way that individuals obtain the same utility values as a population average, particularly given the long-term complications of the disease. The change in utility over 6 months of follow-up was used to update the association between BMI and utility derived from a Visual Analogue Score. Updating the association between BMI and utility leads to weight loss in the treatment of type 2 diabetes, which has been demonstrated in the NICE report on this condition [28–31]. Other studies have used rating scales, such as the Visual Analogue Scale, converting these into utility values, a practice that often overestimates utility and is met with methodological dispute [30–33]. Conversion between metrics is inexact and results in error and subsequently in inaccurate estimations of utility [28–31]. This was demonstrated in the NICE report on liraglutide, a glucagon-like peptide (GLP)-1 receptor agonist that leads to weight loss in the treatment of type 2 diabetes, which initially used an association between BMI and utility derived from a Visual Analogue Score. Updating the association between BMI and utility, as calculated by Bagust and Beale specifically for patients with diabetes, increased the incremental cost-effectiveness ratios considerably [17,18].

Other authors have responded to the lack of utility data by assuming that after a weight loss/diabetes resolution intervention, patients acquire the same utility values as a population sample of the same age and weight [34,35]. There is, however, evidence that more than 10 years after weight loss, improvement in quality of life is not accurately estimated by population norms [36]. The misrepresentation of an intervention’s effectiveness can have a significant impact on cost-utility estimates, and may lead to suboptimal resource allocation, representing an opportunity cost and a loss of allocative efficiency. Using robust, preference-based quality-of-life data in cost-utility analysis can mitigate this risk.

The relationship determined in this study is similar to that published by Rothenberg et al. [37] in 2014. These authors calculated this coefficient using a smaller sample size of medically treated obese patients in the United States, unadjusted for age and sex, with 6 months of follow-up. The patients in their sample had different rates of comorbidity, with a higher prevalence of hypertension and dyslipidemia and a lower prevalence of depression, a lower average BMI at baseline, and a different demographic composition relative to the sample used in our study. The coefficient was 0.00730, similar to that in our primary analysis. Bagust and Beale [17] used a cohort of nearly 5000 patients with type 2 diabetes in five European countries to determine the change in the EQ-5D score attributable to the long-term complications of the disease. The change in utility for every additional 1 kg/m² increase in BMI (≥25) was −0.0061, which is similar to the coefficient determined in the diabetic subgroup in our study. The fact that the association is consistent in both these studies indicates that the relationship is reproducible, independent of era and sex, and suggests that it may be similar among varying severities of obesity, although a

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (n = 500)</th>
<th>Waitlisted (n = 150)</th>
<th>Medical (n = 200)</th>
<th>Surgical (n = 150)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: male (%)</td>
<td>11.8</td>
<td>9.3</td>
<td>13.0</td>
<td>12.7</td>
</tr>
<tr>
<td>Age (y), mean ± SD</td>
<td>43.7 ± 9.6</td>
<td>43.6 ± 9.2</td>
<td>43.9 ± 10.0</td>
<td>43.5 ± 9.5</td>
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<tr>
<td>BMI (kg/m²), mean ± SD</td>
<td>47.9 ± 8.1</td>
<td>49.4 ± 8.2</td>
<td>48 ± 8.2</td>
<td>46.2 ± 7.4</td>
</tr>
<tr>
<td>Comorbid disease (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>44.4</td>
<td>50.0</td>
<td>40.0</td>
<td>44.7</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>16.4</td>
<td>17.3</td>
<td>14.0</td>
<td>18.7</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>60.4</td>
<td>59.3</td>
<td>61.5</td>
<td>60.0</td>
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<td>Coronary heart disease</td>
<td>4.4</td>
<td>4.0</td>
<td>3.5</td>
<td>6.0</td>
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<tr>
<td>Sleep apnea</td>
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<td>44.0</td>
<td>58.0</td>
<td>65.0</td>
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<tr>
<td>Hypertension</td>
<td>65.0</td>
<td>66.0</td>
<td>67.0</td>
<td>61.3</td>
</tr>
<tr>
<td>Depression</td>
<td>63.8</td>
<td>65.3</td>
<td>66.5</td>
<td>58.7</td>
</tr>
<tr>
<td>Mean starting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>47.9 ± 8.1</td>
<td>49.4 ± 8.3</td>
<td>48 ± 8.2</td>
<td>46.2 ± 7.4</td>
</tr>
<tr>
<td>EQ-SD score</td>
<td>0.731 ± 0.191</td>
<td>0.691 ± 0.207</td>
<td>0.716 ± 0.196</td>
<td>0.792 ± 0.149</td>
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<tr>
<td>Mean change</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>−3.4 ± 5.2</td>
<td>−0.6 ± 2.2</td>
<td>−2.5 ± 4.5</td>
<td>−7.4 ± 5.6</td>
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<tr>
<td>EQ-SD score</td>
<td>0.047 ± 0.140</td>
<td>0.005 ± 0.131</td>
<td>0.073 ± 0.135</td>
<td>0.054 ± 0.146</td>
</tr>
</tbody>
</table>

BMI, body mass index; EQ-SD, EuroQol five-dimensional questionnaire.

Table 2 – Coefficient of change in the EQ-5D score with reduction in BMI (1 kg/m²) in ordinary least-squares models with 95% CI.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Primary analysis</th>
<th>Stepwise approach — change in comorbidity status</th>
<th>Age, sex, baseline BMI</th>
<th>Age, sex, baseline BMI, baseline comorbidity, treatment group</th>
<th>Stepwise approach — baseline presence comorbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in BMI (−1 kg/m²)</td>
<td>0.0075</td>
<td>0.0066</td>
<td>0.0052</td>
<td>0.0068</td>
<td>0.0051</td>
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</tbody>
</table>

BMI, body mass index; CI, confidence interval; EQ-SD, EuroQol five-dimensional questionnaire.

* Addition criteria P < 0.01; removal criteria P > 0.05.
study including subjects with a range of initial BMI would be required to confirm.

A meta-analysis of randomized trials published by Warkentin et al. in 2014 found that there was no significant association between BMI and HRQOL, with the authors noting that quality of life was generally a secondary outcome, with potentially selective and incomplete reporting [5]. Furthermore, the degree of heterogeneity in the data precluded metaregression of generic preference-based quality-of-life measures, inhibiting a potential numerical estimation of change in utility associated with change in BMI [5]. Our cohort study was designed to evaluate quality-of-life outcomes, and thus provides robust data from which to derive the association between the EQ-5D and change in BMI.

The applicability of this coefficient of change in utility to change in BMI (in adults with class III obesity), derived from various health care interventions, is supported by the subgroup analyses, which demonstrate no significant difference in the association of BMI and utility between the medical and surgical groups. The former does lose statistical significance; this is, however, likely due to lack of power, given how few patients had substantial weight loss without surgery. Furthermore, the association is not significantly altered within comorbidity subgroups, indicating that this measurement is likely applicable to a range of severely obese adult cohorts, whether they are homogeneous or heterogeneous in comorbidity composition.

Several limitations of our work need to be considered. First, this was a single-center study, but it captured patients from a large health region. Second, the naturalistic design of the study resulted in some missing data with respect to outcomes. Within the intent-to-treat framework, determined a priori, a last-observation-carried forward imputation was used to account for patients in the control and medical therapy groups that progressed to the next phase of treatment. This assumes that early changes observed from baseline were maintained over 2 years; this may overestimate or underestimate the effectiveness of the treatment. Third, there is potential for both reporting and social desirability bias, because patients were aware of the purposes of data collection, and the EQ-5D is a patient-completed survey. Other than completing these questionnaires, patients underwent therapies in the same way other nonenrolled patients would have, which we believe minimizes bias. Given the age range of the sample used, this relationship may not be generalizable to elderly or pediatric populations. Finally, the cohort comprised patients referred for treatment of class III obesity, with a high baseline BMI level, and the relationship of change in BMI and quality-of-life gain may differ in other populations, such as those classified as overweight or having class I obesity.

Conclusions

In a prospective cohort (n = 500) of patients with severe obesity receiving medical, surgical, or no treatment, we determined the relationship between changes in BMI and preference-based quality of life over a 2-year period. The nature of this relationship was unaltered when adjusting for multiple confounders and in subgroups of patients, which suggests independence and generalizability of the results. This relationship fills an existing knowledge gap, offering a more reliable and applicable estimate to be applied to future studies of patients with class III obesity. This will allow for improved evaluation of therapies that modify weight, both primarily and secondarily, calculation of cost utility, and guidance on technology adoption and resource allocation.

Acknowledgments

Source of financial support: The data used for the analysis were collected with the help of financial support from the Canadian Institute for Health Research. The first author, E. Lester, received salary support from Alberta Innovates Health Solutions.

References


