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#### ORIGINAL RESEARCH

# Cost-Effectiveness of Bariatric Surgery in Tunisia

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**Purpose:** Obesity is a growing global issue with evidence linking it to an increase in loss of disease-free years, reduced quality of life, increased mortality, and additional economic burden. This study sought to establish the cost-effectiveness of gastric bypass and sleeve gastrectomy, compared to conventional therapy in patients with obesity, from a Tunisian healthcare payor perspective.

Patients and Methods: A Markov model compared lifetime costs and outcomes of bariatric surgery with conventional treatment among patients with body mass index (BMI)  $\geq$  40 kg/m<sup>2</sup>, BMI  $\geq$  35 kg/m<sup>2</sup> with obesity-related co-morbidities (Group 1), or BMI  $\geq$  35 kg/m<sup>2</sup> with type 2 diabetes mellitus (T2DM) (Group 2). Inputs were sourced from the Tunisian Health Examination Survey, local clinician data and literature sources. Health states were associated with different cost and utility decrements. Changes in body mass index, systolic blood pressure, lipid ratio and diabetes remission rates were modelled on a yearly basis. The incremental cost-effectiveness ratio (ICER), quality-adjusted life years (QALYs) and net monetary benefit (NMB) were key outcomes. Sensitivity and scenario analyses were performed to test the model's robustness.

**Results:** The model showed that the benefits of bariatric surgery were favorable compared to conventional treatment, with an ICER of 1844 TND/QALY in Group 1 patients and 2413 TND/QALY in Group 2 patients. Bariatric surgery resulted in a QALY gain of 3.26 per patient in Group 1 and a gain of 1.77 per patient in Group 2. At a willingness to pay threshold of 31,379 TND/QALY, the incremental NMB was 96,251 TND and 51,123 TND for Group 1 and Group 2, respectively.

**Conclusion:** From the Tunisian healthcare payor perspective, bariatric surgery is cost-effective for patients with obesity and those with T2DM and obesity-related comorbidities. These findings may have impact on future decision-making on funding and reimbursement of bariatric surgery in Tunisia.

**Keywords:** cost-effectiveness analysis, diabetes, gastric bypass, obesity, sleeve gastrectomy, bariatric surgery

#### Introduction

Obesity is defined as having a body mass index (BMI) ≥30 kg/m<sup>2</sup>. Obesity is a growing global issue that is considered to be reaching pandemic status and is one of the most significant ongoing health challenges. According to reports by the World Health Organization (WHO), in 2016 as much as 13% of the world's adult population challenged with obesity, and over 340 million children and adolescents aged 5–19 were classified as overweight or obese in 2016. Once seen as a problem specific to high-income countries, the prevalence of obesity is increasing in low- and middle-income countries and across Africa, as reported in a recent analysis conducted by the WHO. Tunisia is also impacted by obesity, with effects seen in all age groups. The prevalence of female obesity (≥18 years old) in Tunisia increased from 23.7% in 1997 to 34.3% in 2016. During the same period, Tunisian male obesity (≥18 years old) grew substantially from 9.6% to 19.1%. Overall, obesity is reported as having a prevalence of 27.1% and is a serious problem in Tunisia.

There is substantial evidence linking obesity to the global increase in loss of disease-free years, reduced quality of life, increased mortality and significant economic burden. <sup>9–11</sup> Complications of obesity are linked to other comorbid conditions, such as cardiovascular disease, particularly heart failure and coronary heart disease, <sup>12</sup> liver disease, <sup>13</sup> and cancer <sup>14,15</sup> resulting in increased morbidity and mortality. Obesity can lead to an increase in diabetes-related mortality, with approximately 50% of diagnosed diabetic patients being obese, <sup>10</sup> resulting in impaired quality of life, decreased life

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expectancy and increase healthcare costs. 16 In Tunisia, diabetes and its complications have a high hospitalization and associated cost burden, accounting for 7.2% and 2.7% of hospitalizations of males and females, respectively. 17

In addition to the health-related burden of obesity, there is an economic burden. 18 A study by McKinsey in 2014 estimated the global economic impact of obesity as \$2.0 trillion, which is 2.8% of the global GDP. 19 A study in eight countries found that despite regional and economic variation, the economic impact of being overweight and obese is substantial and is projected to increase.<sup>20</sup>

Bariatric surgery has been used to address weight control in people with obesity who are unable to lose weight by non-surgical methods (exercise, diet control). <sup>21,22</sup> The 2020 clinical practice guidelines from the European Association of Endoscopic Surgery (EAES) which are endorsed by International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO-EC), the European Association for the Study of Obesity (EASO) and the European Society for the Perioperative Care of the Obese Patient (ESPCOP) advocate that bariatric surgery should be considered for patients with a BMI≥ 40 kg/m<sup>2</sup> and for patients with BMI≥ 35–40 kg/m<sup>2</sup> with associated comorbidities that are expected to improve with weight loss.<sup>23</sup> The Cochrane review of 22 studies (1798 participants) in bariatric surgery concluded that bariatric surgery results in greater improvement in weight loss outcomes and weight-related comorbidities compared with nonsurgical interventions, regardless of the type of procedures used.<sup>24</sup> Beyond the long term clinical effects, it is also considered to provide improved health-related well-being, physical and psychological benefits to the patient. 25,26

The cost-effectiveness of bariatric surgery has been studied in several countries.<sup>27</sup> all of which suggest that bariatric surgery is cost-effective. Studies in Sweden and in the UK showed cost-saving<sup>28,29</sup> when compared to conservative management and other meta-analysis performed in many countries had the same findings.<sup>30</sup> In the USA, a study concluded that laparoscopic sleeve gastrectomy was more cost-effective in patients that were in the BMI group range of 35 kg/m<sup>2</sup> to 39.9 kg/m<sup>2</sup>, compared to laparoscopic Roux-en-Y gastric bypass, and laparoscopic adjustable gastric banding.<sup>27</sup>

To date, no studies nor health technology assessments of bariatric surgery have been performed in Tunisia. This study estimated the cost-effectiveness of 2 most common types of bariatric surgery, gastric bypass (GBP) and sleeve gastrectomy (SG)<sup>31</sup> from a healthcare payor perspective in Tunisia. It compared bariatric surgery to conventional therapy in patients with a BMI  $\ge$ 40 kg/m<sup>2</sup>, or BMI  $\ge$ 35 kg/m<sup>2</sup> with obesity-related comorbidities and patients with a BMI  $\ge$ 35 kg/m<sup>2</sup> m<sup>2</sup> with type 2 diabetes mellitus (T2DM). The objective was to quantify the economic benefits of the bariatric surgery in Tunisia to inform resource allocation decisions.

#### **Materials and Methods**

#### Model Structure

A cohort Markov was developed to explore the cost-effectiveness of bariatric surgery in Tunisia from the healthcare perspective based on a previously published study in the UK.<sup>29</sup> This UK model structure was used as it was deemed clinically relevant to the Tunisian clinical practice and it uses a Markov structure that can capture the complex nature of obesity and its associated comorbidities into the long-term, with varying risks over time. Similar Markov models have been used in other studies. 32,33 A systematic review of economic evaluations used to assess the value of bariatric surgery found that most used Markov models that reported benefits in terms of quality-adjusted life years (QALY) and the cost per QALY.<sup>34</sup>

The cost-effectiveness model depicts a cohort of patients with obesity and related comorbidities who transition between health states over time (Figure 1). The long-term outcomes and costs for patients who receive one of the 2 most common bariatric surgery options (gastric bypass, sleeve gastrectomy) according to surgery option distribution in Tunisia, were modelled in comparison to conventional treatment, defined as those managed with diet and exercise programs. The model operated as a health state transition model with all model inputs sourced from the literature, national databases and reimbursement institutions. Baseline characteristics were sourced from the Tunisian Health Examination Survey considered to be representative of the Tunisian population.<sup>35</sup> The number of patients transitioning between health states was determined at each yearly cycle, as a function of input parameters and transition probabilities sourced from the literature. In each cycle, a patient could remain in the same health state or progress to another health. Each state was associated with specific costs and utilities (based on health-related quality of life). Cost-effectiveness was evaluated over a lifetime horizon. Additional details of the study are provided in the Supplementary Material.

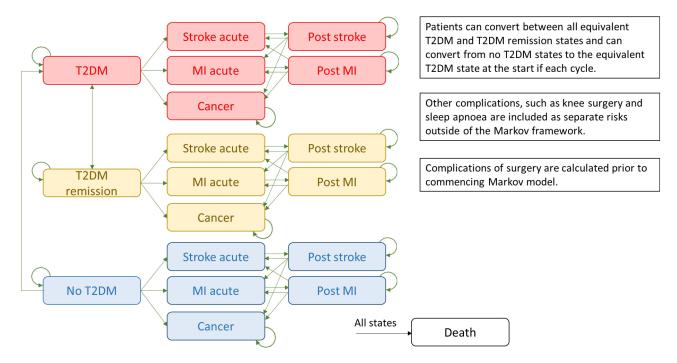


Figure I General Markov model structure.

Abbreviations: MI, myocardial infarction; T2DM, type 2 diabetes mellitus.

### **Target Populations**

In alignment with the 2nd Diabetes Surgery Summit (DSS-II) guidelines and NICE guidelines,  $^{36,37}$  two patient populations eligible for bariatric surgery were included in the model: (i) patients with a BMI  $\geq$ 40 kg/m<sup>2</sup>, or BMI  $\geq$ 35 kg/m<sup>2</sup> with obesity-related comorbidities (Group 1), and (ii) patients with a BMI  $\geq$ 35 kg/m<sup>2</sup> with T2DM (Group 2).

## Model Inputs

Comprehensive and targeted literature searches were conducted to obtain inputs to populate the model. Tunisia-specific data were used where available. When selecting clinical inputs, the validity and generalizability to Tunisian clinical practice was also considered. The literature review prioritized the hierarchy of evidence in scientific research, with metaanalyses and systematic reviews as the strongest type of evidence, randomized controlled trials next, and cohort and case-control studies last. The rationale for the selection of sources in the literature are shown in each of the Supplemental Tables. Model baseline characteristics used for the Tunisian population were obtained from local data and the literature (Supplementary Table 1). The probabilities of complication, reoperation and 30-day mortality due to surgery are shown in Supplementary Table 2. The clinical inputs of the probability of stroke at 1 year after myocardial infarction (MI) were obtained from the literature (Supplementary Table 3). The probability of MI and stroke were derived using the Framingham equations and adjusted to fit the 1-year model cycle (Supplementary Table 4). The mortality of acute stroke and MI, and post-stroke and post-MI health states were derived from the literature (Supplementary Table 5). Various parameters informed the dynamic transition probabilities used in the model. These included the change in BMI which was used to calculate BMI-associated changes in utility and diabetes incidence for Group 1 and Group 2 patients, Supplementary Tables 6 and 7, respectively, the changes in blood pressure as shown in Supplementary Tables 8 and 9 for Group 1 and Group 2, respectively. The changes in lipid from baseline for both patient groups are tabulated in Supplementary Table 10, diabetes remission in Supplementary Table 11. The risk of developing cancer and the cancer survival rate at 10 years are shown in Supplementary Tables 12 and 13, respectively. Additionally, the relative risk of mortality from causes other than stroke, MI and cancer was also included (Supplementary Table 14). Since knee pain (Supplementary Table 15) and obstructive sleep apnea (Supplementary Tables 16 and 17) are often prevalent in obesity, their inputs were also included.

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The cost inputs for the model were derived from a survey of Tunisian physicians and the literature (<u>Supplementary Table 18</u>). The utility inputs for health-related quality of life (HRQoL) ranged from 0 ("death") to 1 ("perfect health") and were dependent on the starting utility value that changed according to the impact of changes in BMI and the related comorbidities (MI, stroke, obstructive sleep apnea, knee pain, cancer) (Supplementary Table 19).

Based on the Tunisian guidelines for cost-effectiveness studies, a discount rate of 5% was applied to costs and clinical outcomes.<sup>38</sup> Where required, cost inputs were uplifted to the 2020 values using the appropriate inflation metric and methodology.<sup>39</sup>

## Comorbidity Inputs

Stroke and MI were modelled as mutually exclusive health states. Post-stroke and post-MI health states reflect decreased HRQoL and ongoing costs of rehabilitation following these events. Additionally, obesity-attributable cancers were modelled as a single health state because input parameters were based on meta-analyses of all cancer types, rather than a specific cancer type. A meta-analysis found that the sex-specific risk of cancer after bariatric surgery was reduced in women (RR 0.68 [0.60–0.77]), but not in men (RR 0.99 [0.74–1.32]), which was applied accordingly in the model. Incidence of stroke or MI for patients in the cancer state was not modelled due to the relatively short life-expectancy of cancer patients and the assumption that cancer in the model was incurable, and thus a terminal state.

Patients transitioned between diabetes states in the same way that they would in a traditional Markov model, but due to this particular configuration, they were able to simultaneously occupy a T2DM-state and an additional comorbidity state. Based on the literature, patients in the model could transition between T2DM and diabetes remission on an ongoing basis as a function of the treatment group of bariatric surgery versus conventional treatment. This was achieved by assigning the diabetes status (either with T2DM, without T2DM, or in T2DM-remission) to each health state (stroke, MI, and cancer) as part of the traditional Markov structure. The incidence rate of diabetes was calculated as a function of BMI.<sup>33</sup>

Age-specific background mortality data were sourced from the 2020 Tunisia Public Health Institute.<sup>41</sup> The only T2DM-associated mortality rate identified also included mortality due to cardiovascular events, and as such, this was not applied to the model to avoid double counting. Obesity-related mortality was also not considered so as to avoid double counting with mortality associated with comorbidities.

## Additional Modeling

Additional parameters were modelled aside from the Markov model, which included the results of surgery versus conventional treatment and included changes in BMI, changes in blood pressure and lipid ratio, knee pain, and sleep apnoea, complications, re-operation and death. Blood pressure and lipid ratio were modelled and applied to the Framingham risk equation along with other risk factors including age, gender and diabetes status to evaluate the probability of experiencing acute stroke and MI in each cycle (Clinical model inputs are shown in Supplementary Material).

# **Model Outputs**

Model outputs included costs and QALYs which were used to calculate the cost-effectiveness of bariatric surgery (gastric bypass and sleeve gastrectomy) versus conventional treatment. The results, which are the weighted average of the two types of surgery, were represented as ICER. The net monetary benefit (NMB) was used as the metric of the value of each treatment in monetary terms. According to the WHO, the willingness to pay (WTP) threshold, corresponding to the maximum cost per health outcome (QALYs) should not exceed 3 times GDP per capita. The ICER threshold that the Tunisian health system is willing to pay was calculated as 31,379 TND/QALY.<sup>42,43</sup>

The robustness of the model results was tested using deterministic sensitivity analyses (assess the sensitivity of results to variations of individual parameters)<sup>44</sup> and probabilistic sensitivity analyses (account for parameter uncertainty in cost-effectiveness models).<sup>45</sup> Additional scenario analyses were conducted using (i) different time horizons (5, 10 and 20 years), (ii) different discount rates, namely 3.5%, 4% and 6% and (iii) Markov state costs and obesity complication costs which were estimated based on Purchasing Power Parity (PPP) and values from the UK (Supplementary Table 20).<sup>29</sup>

#### Results

The mean age of the patients with BMI  $\geq$ 40 kg/m<sup>2</sup> or  $\geq$ 35 kg/m<sup>2</sup> with obesity-related comorbidities was 49.5 years (standard deviation (SD) 14.5 years), of which 76.2% were female. The mean BMI was 39.8 kg/m<sup>2</sup> (SD 7.1). T2DM was prevalent in 33.4% of these patients. The mean age for the Tunisian population with BMI  $\geq$ 35 kg/m<sup>2</sup> with T2DM was 55.3 years (SD 14.0 years) with a BMI of 39.3 kg/m<sup>2</sup> (SD 7.6), and 50.8% of these patients were female.

The model base case results for costs and clinical outcomes over a lifetime horizon are shown in Table 1 for the combined surgical outcomes. For Group 1, the total costs of bariatric surgery per patient were 40,347TND and 34,339TND for conventional treatment. Bariatric surgery resulted in a QALY gain of 3.26, with an ICER of 1844 TND/QALY. Table 2 depicts the outcomes by different forms of surgery, which shows that for the Group 1 the ICER was 1925 TND/QALY for gastric bypass and 1841 TND/QALY for sleeve gastrectomy.

For the patients Group 2, the total costs were 41,178TND and 36,919TND for bariatric surgery and conventional treatments, respectively. The QALY difference was 1.77 in favor of bariatric surgery, yielding an ICER of 2413 TND/QALY. Similar results are shown for patients in Group 2 by surgical types, with a per-patient cost of 42,373TND and 36,919TND for gastric bypass and conventional treatment, respectively. The cost per patient in Group 2 was 40,960TND and 36,916TND for sleeve gastrectomy and conventional treatment, respectively. Bariatric surgery in Group 2 patients resulted in a QALY gain of 2.00 and 1.73 for gastric bypass and sleeve gastrectomy, respectively. The base case ICER for Group 2 patients was 2733 TND/QALY and 2343 TND/QALY for gastric bypass and sleeve gastrectomy, respectively.

The results reflecting the cost and benefit changes over different time horizons from a Tunisian healthcare payor perspective are shown in Table 3. At the 5-year horizon, the ICER for the two types of bariatric surgery (gastric bypass and sleeve gastrectomy) studied was 4484 TND/QALY for the patients in Group 1 and 7021 TND/QALY for the cohort in Group 2, both compared to conventional treatment. At a 20-year horizon, the ICER for the two forms of bariatric surgery are 1921 TND/QALY for the patients in Group 1 and 2240 TND/QALY for patients in Group 2 compared to conventional treatment. These results demonstrate the long-term benefits of bariatric surgery compared to conventional treatment, resulting in higher QALYs. The incremental NMB at a WTP threshold of 31,379 TND/QALY at 20 years was 88,553TND and 47,293TND for Group 1 and Group 2, respectively. As seen in Table 3, the survival benefits at 20 years' horizon In Group 1 were 12.54 years and 12.48 years for bariatric surgery and conventional treatment, respectively, while those for Group 2 were 12.08 years and 11.97 years for bariatric surgery and conventional treatment, respectively.

Table I Base Case Results (Discounted) for Both Types of Surgery from the Tunisian Healthcare Payor Perspective

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	Group I			Group 2			
	Surgery	Conventional Treatment	Difference	Surgery	Conventional Treatment	Difference	
Total cost per patient (TND)	40,347	34,339	6008	41,178	36,919	4259	
Cost of treatment (surgery and obesity care) for the cohort (TND)	19,539,830	8,610,819	10,929,011	18,246,462	7,863,939	10,382,523	
Total obesity-related comorbidity costs for the cohort (TND)	20,807,034	27,728,328	-4,921,294	22,931,616	29,055,305	-6,123,689	
Survival (years per patient)	15.92	15.74	0.18	14.31	14.08	0.23	
QALYs per patient	9.52	6.26	3.26	7.15	5.38	1.77	
Net monetary benefit at 31,379 TND/QALY (TND)	285,310	162,058	96,251	183,114	131,991	51,123	
ICER	1844 TND/QALY			2413 TND/QALY			

Notes: Group 1: BMI ≥40 kg/m², or BMI ≥35 kg/m² with obesity-related comorbidities; Group 2: BMI ≥35 kg/m² with T2DM.

Abbreviations: ICER, Incremental cost-effectiveness ratio; NMB, Net monetary benefit; QALY, Quality-adjusted life year; TND, Tunisian Dinar.

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Table 2 Results by Surgery Type, from the Tunisian Healthcare Payor Perspective

	Group I			Group 2			
	Surgery	Conventional Treatment	Difference	Surgery	Conventional Treatment	Difference	
Gastric bypass			<u> </u>			<u> </u>	
Total cost per patient (TND)	41,574	34,339	7235	42,373	36,919	5453	
QALYs per patient	10.02	6.26	3.76	7.38	5.38	2.00	
Survival years per patient	15.91	15.74	0.17	14.31	14.08	0.23	
NMB at 31,379 TND/QALY (TND)	272,742	162,058	110,684	189,143	131,990	57,153	
ICER			1925 TND / QALY			2733 TND / QALY	
Sleeve gastrectomy							
Total cost per patient	40,172	34,339	5833	40,960	36,916	4041	
QALYs per patient	9.43	6.26	3.17	7.11	5.38	1.73	
Survival years per patient	15.93	15.74	0.18	14.31	14.08	0.23	
NMB at 31,379 TND/QALY (TND)	255,651	162,058	93,593	182,079	131,991	50,088	
ICER			1841 TND / QALY			2343 TND / QALY	

Notes: Group 1: BMI  $\geq$ 40 kg/m<sup>2</sup>, or BMI  $\geq$ 35 kg/m<sup>2</sup> with obesity-related comorbidities; Group 2: BMI  $\geq$ 35 kg/m<sup>2</sup> with T2DM. Abbreviations: ICER, Incremental cost-effectiveness ratio; NMB, Net monetary benefit; QALY, Quality-adjusted life year; TND, Tunisian Dinar.

The deterministic sensitivity analysis (Supplementary Figure 1) depicts that the results for the patients in Group 1 were most sensitive to variations in surgical costs and inputs related to BMI, namely, disutility per unit increase in BMI and BMI changes over years. Similarly, in Group 2, the results were most sensitive to surgical costs, and also to diabetes-related costs and the discount rate (Supplementary Figure 2). Although the model used the Tunisian HTA discount rate of 5%, <sup>38</sup> further scenario analyses of the discount rate were performed. These demonstrate that the ICER varies from 1.676 TND/QALY to 1.960 TND/QALY at a discount rate of 3.5% and 6%, respectively, when comparing bariatric surgery with conventional treatment in Group 1 patients. In Group 2 patients, the ICER ranged from 2.237 TND/QALY to 2.552 TND/QALY at a discount rate of 3.5% and 6%, respectively, when comparing bariatric surgery with conventional treatment. Therefore, deterministic scenario analyses using different discount rates (3.5%, 4% and 6%) corroborate the base case findings that bariatric surgery is cost-effective when compared to conventional treatment (Supplementary Table 21).

The cost-effectiveness planes resulting from the probabilistic sensitivity analysis showed that bariatric surgery generates more health gains than conventional therapy, and bariatric surgery was cost-effective (additional QALYs and additional costs) in 100% of the simulation runs at a WTP threshold of 31,379 TND/QALY in both Group 1 (Supplementary Figure 3) and Group 2 patients (Supplementary Figure 4). It was also cost-effective in 100% of the simulation runs at a WTP threshold of 1 GDP per capita (10,460 TND/QALY) in both groups.

The scenario analyses, using the purchasing power parity, corroborated the sensitivity analyses results, showing bariatric surgery to be cost-saving with higher QALYs in both the patient groups compared to conventional treatment from the healthcare payor perspective (Supplementary Table 22).

#### Discussion

This study sought to establish the cost-effectiveness of two types of bariatric surgery, gastric bypass and sleeve gastrectomy, compared to conventional therapy in patients with obesity in Tunisia, from a healthcare perspective, and accounting for post-surgery complications and co-morbidities. The results of this study show that bariatric surgery is expected to reduce the overall economic burden to the healthcare system, with patients experiencing an improvement in

Table 3 Cost and Benefit Sensitivity Analysis Results for the Different Patient Groups, from the Tunisian Healthcare Perspective

Outcomes at Different Time Horizons		Group I		Group 2			
	Surgery	Conventional Treatment	Difference	Surgery	Conventional Treatment	Difference	
At 5 years							
Total costs per patient (TND)	13,948	8470	5477	14,542	10,345	4197	
QALYs per patient	3.09	1.87	1.22	2.36	1.76	0.60	
Survival years per patient	4,51	4,51	0.00	4,48	4,48	0.00	
NMB at 31,379 TND/QALY (TND)	82,895	50,042	32,852	59,559	44,999	14,560	
ICER	4484 TND / QALY			7021TND / QALY			
At 10 years			-				
Total costs per patient (TND)	20,501	14,916	5585	21,588	18,065	3523	
QALYs per patient	5.36	3.22	2.14	4.17	3.07	1.10	
Survival years per patient	7.97	7.97	0.00	7.85	7.83	0.02	
NMB at 31,379 TND/QALY (TND)	147,774	86,178	61,596	109,346	78,273	31,074	
ICER	2609 TND / QALY			3195 TND / QALY			
At 20 years			-				
Total costs per patient (TND)	30,765	24,991	5774	33,010	29,374	3636	
QALYs per patient	8.00	5.00	3.00	6.26	4.64	1.62	
Survival years per patient	12.54	12.48	0.05	12.08	11.97	0.11	
NMB at 31,379 TND/QALY (TND)	220,160	131,606	88,553	163,414	116,121	47,293	
ICER	1921 TND / QALY			2240 TND / QALY			

**Notes**: Group 1: BMI  $\geq$ 40, or BMI  $\geq$ 35 with obesity-related comorbidities; Group 2: BMI  $\geq$ 35 with T2DM.

Abbreviations: ICER, Incremental cost-effectiveness ratio; NMB, Net monetary benefit; QALY, Quality-adjusted life year; TND, Tunisian Dinar.

HRQoL, yielding a substantial NMB over a lifetime horizon, thereby corroborating with several other similar studies. <sup>28,30</sup> Overweight or obese people experience an increased risk of comorbidities such as diabetes, hypertension and cardio-vascular diseases that can lead to an increased risk of hospitalizations and mortality <sup>46,47</sup> resulting in increased costs to healthcare systems <sup>48,49</sup> thereby strengthening the case for avoiding delayed bariatric surgery in patients who do not respond to conventional treatment. Although the survival benefits shown here are modest, the meaningful improvement and gains in quality of life from reduced obesity are the core outcomes that influence the overall cost-effectiveness conclusions.

While the sensitivity analyses showed a slight waning effect of the ICERs over the 20-year horizon, the benefits of bariatric surgery were nevertheless superior to those of conventional treatment for all time horizons included in the model. Despite the small gain in survival benefit with bariatric surgery, of great importance is the significant weight reduction that bariatric surgery enables. With this weight loss, all-cause mortality risks from the related co-morbidities of diabetes, cardiac disease, high blood pressure, obstructive sleep apnea and cancer risk are significantly improved.<sup>22</sup> Similarly, although not included in this model, depression, anxiety and the social stigma related to obesity are reduced, <sup>50,51</sup> suggesting that the cost and health-related quality of life benefits presented are underestimated.

Cost-effectiveness studies relating to countries in the WHO Eastern Mediterranean region are scarce. To the best of our knowledge, this is the first study of its kind in the Tunisian healthcare system. The results in our study are

corroborated by several studies in other countries, which show that bariatric surgery is a cost-effective treatment option for healthcare providers<sup>28,33,52,53</sup> with benefits to health and well-being for people living with obesity and T2DM<sup>54,55</sup> and substantial resolution of preoperative diabetes. <sup>56</sup> Furthermore, since the prevalence and cost of obesity and its comorbidities (diabetes, cardiovascular disease, hypertension, cancer, etc.) are of growing concern in Tunisia, <sup>6,7,57,58</sup> this study, may influence decision-makers and encourage reimbursement of bariatric surgery. Evidence from studies in other countries suggests that bariatric surgery has a positive impact on the workforce, <sup>59,60</sup> and can reduce absenteeism (regularly staying away from work) and presenteeism (lost productivity when employees are not fully functioning in the workplace because of an illness). When people with obesity are unable to work, the patient's family might suffer economically, and the government may experience an additional cost burden due to disability payments. <sup>61</sup> By demonstrating that bariatric surgery is cost-effective in Tunisia, this study supports the Tunisian national plan for the prevention of disabilities, <sup>62</sup> and addresses the burden associated with obesity thereby potentially improving the labor force participation, not only due to reduction in obesity but also from the positive impact on obesity-related comorbidities. <sup>56,63</sup>

Modeling the complexity of obesity and its related comorbidities invariably results in some study limitations. Firstly, the use of model inputs from different sources in the literature and the Tunisian healthcare system can be considered to be a weakness in this study. Given the paucity of Tunisian data, the literature provided the next best context. However, even despite this limitation, the authors used a standard hierarchical literature search framework<sup>64,65</sup> with systematic reviews and meta-analyses being given priority and accounting for key parameters such as the size of the study population, nature of the study population, interventions studied, outcomes reported, measure of effects between interventions. Furthermore, the same approach was used for each of the patient groups which nonetheless allows for a clear comparison of the results, that are in favor of bariatric surgery compared to conventional treatment. A second limitation arises because of the lack of disease modeling for cancer with other comorbidities (MI and stroke), therefore, the current study adopted the assumption that cancer in the model was incurable, and thus a terminal state. This may have overestimated mortality and utility losses in those with cancer that may favor those treated with bariatric surgery. Additionally, the utility scores used represent a further limitation of the modeling. Due to a paucity of utility data for Tunisia, the utility values for the UK population were used as it provides different categories of BMI with, and without diabetes, and a large sample size. However, as we are interested in the incremental benefit of different interventions, the difference in QALY outcomes is what influences the overall analysis, hence we believe this does not undermine the credibility of the analysis. Another study limitation relates to the use of the Framingham Heart Study. The Framingham equations were derived from North American populations from the 1960s to the 1980s and have been found to overestimate the risk of cardiovascular events in contemporary European populations, whilst under-estimating the cardiovascular risk in people with diabetes and in people from the socially deprived population.<sup>66</sup> Similarly, this is likely to apply to the Tunisian population which could influence the findings reported here. Furthermore, not all relevant risk factors are included the Framingham equation, which limits the precision of the cardiovascular risk estimations. Additional risk factors of relevance include (amongst others): self-assigned ethnicity, family history of premature coronary heart disease, deprivation, blood pressure treatment, BMI, rheumatoid arthritis, chronic kidney disease and atrial fibrillation. These additional risk factors are considered by the QRISK2 algorithm, but this algorithm could not be applied to this model as the underlying equations to the QRISK2 algorithm are not publicly available.<sup>67</sup> However, the strength of the Framingham risk equation is that it allows for the calculation of the yearly risk of stroke and MI based on age, sex, blood pressure, the ratio of total cholesterol to HDL cholesterol and diabetes. These variables are reported in clinical trials as the efficacy parameters for bariatric surgery. This approach has been used by several previous cost-effectiveness models on bariatric surgery. 28,33 In this study, concerns were expressed by the authors that the cost data that were derived from a survey of 3 Tunisian surgeons were perhaps underestimated. To address uncertainty with the cost data collection in Tunisia, we conducted a scenario analysis using cost data from the UK, where a similar model had already been developed<sup>29</sup> and adjusting for purchasing power parity between the UK and Tunisia. The PPP scenario analysis highlighted that there was a likelihood for surgery to be cost-saving compared to conventional treatment. The cost per patient saving for patients with BMI ≥40 kg/m<sup>2</sup>, or BMI ≥35 kg/m<sup>2</sup> with obesity-related comorbidities, a savings of 2683 TND was observed, and for BMI ≥ 35 kg/m<sup>2</sup> the savings was estimated to be 10,793TND.

Despite the study limitations, the results of this simulation model draw on the best possible available data specific to Tunisia. Further comparative studies in the appropriate setting are likely to corroborate the positive outcomes of bariatric surgery, and to highlight the need to improve access to bariatric surgery in patients who do not respond to exercise and controlled diets and should evaluate population with other comorbidities than T2DM.

#### **Conclusion**

Within the Tunisian setting and from a healthcare payor perspective, bariatric surgery is cost-effective for patients with BMI  $\geq$ 40 kg/m<sup>2</sup>, patients with BMI  $\geq$ 35 kg/m<sup>2</sup> and obesity-related comorbidities, and for those with BMI  $\geq$ 35 kg/m<sup>2</sup> with T2DM. This study provides an economic analysis for bariatric surgery tailored specifically for the Tunisian healthcare system and possible other countries in the Eastern Mediterranean Region. This analysis hopes to influence decision-makers on funding and reimbursement of bariatric surgery in Tunisia.

#### **Abbreviations**

BMI, Body mass index; DNA, deoxyribonucleic acid; GBP, Gastric bypass; HRQoL, Health-related quality of life; ICER, Incremental cost-effectiveness ratio; kg/m², kilogram per squared-metre; MI, Myocardial infarction; NMB, Net monetary benefit; OECD, Organization for Economic Co-operation and Development; OR, Odds ratio; OSA, Obstructive sleep apnea; PPP, Purchasing power parity; QALY, Quality-adjusted life year; QRISK2, Cardiovascular disease risk calculator; RR, Relative risk; SD, Standard deviation; SG, Sleeve gastrectomy; T2DM, Type 2 diabetes mellitus; TND, Tunisian Dinar.

#### **Ethics Declaration**

The study is exempt from review by an Ethics Committee on the basis that this study is non-human subject research, and waived the need for informed consent.

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#### **Author Contributions**

Study conception and design: TG, MPB, NJ and NBM. Data collection: TG, MPB, NJ and NBM. Formal analysis and economic model development: TG. Interpretation of the results: TG, MPB, NJ and NBM. Writing – Original Draft: TG, MPB, NJ and NBM. All authors reviewed the results, gave final approval of the version to be published, have agreed on the journal to which the article has been submitted and agree to be accountable for all aspects of the work.

#### **Disclosure**

TG, MPB & NJ are employees of Johnson & Johnson. This study was sponsored by Johnson & Johnson. NBM did not receive any incentives (financial or other). The authors report no other conflicts of interest in this work.

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