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# Cost-Effectiveness of Bariatric Surgery for Type 2 Diabetes Mellitus

## *A Randomized Controlled Trial in China*

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**Abstract:** To compare the remission of type 2 diabetes mellitus (T2DM) through treatment with laparoscopic sleeve gastrectomy (LSG) or laparoscopic Roux-en-Y gastric bypass (LRYGB), and to analyze the cost-effectiveness of medical treatment, LSG, and LRYGB in T2DM patients (BMI  $\geq$  28).

A 2-group randomized controlled trial was conducted at Diabetes Surgery Centre, Beijing Shijitan Hospital in Beijing, China. Subjects were 80 patients ages 16 to 65 years with a body mass index of 28 kg/m<sup>2</sup> or more and duration of T2DM no more than 15 years. Subjects were randomly assigned (1:1) to undergo either LSG (n=40) or LRYGB (n=40) between February 3, 2011 and October 31, 2013. Of those patients, 72 (90%) were available at follow-up at 2 years. These patients included 34 (85%) who underwent LSG and 38 (95%) who underwent LRYGB. This study presents the follow-up data at 2 years, which compared LSG and LRYGB in T2DM patients. Partial remission and complete remission were determined, and weight loss, BMI, changes in abdominal circumference, cholesterol, and triglycerides were measured. The cost-effectiveness of each type of bariatric surgery was analyzed with a Markov simulation model that yielded quality-adjusted life-years (QALYs) and costs.

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WT designed the research; ZS and GX collected materials and data; QT performed statistical analysis and produced the initial draft; NZ, PS, and LX revised the manuscript; All authors were involved in the interpretation of the analyses and writing of the paper and approved the final version of the paper and take responsibility for its content.

Ethics, consent, and permissions: The ethics committee of Beijing Shijitan Hospital approved the study protocol (No: 8861). Patient records were anonymized and de-identified prior to analysis. All of the patients signed a consent form before surgery. All of the participants consented to publication of the study's results.

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From our analysis results, LSG and LRYGB are both have taken a great effect on the reduction of fasting plasma glucose (FPG), hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>), and bodyweight in patients with T2DM. The cost-effectiveness ratios of medical treatment, LSG, and LRYGB respectively are 1589.02, 1028.97, and 1197.44 dollars per QALY.

Our analysis indicates that LSG appear to provide a cost-effective method of T2DM treatment for the patients.

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**Abbreviations:** ADA = American Diabetes Association, BMI = body mass index, FPG = fasting plasma glucose, HbA<sub>1c</sub> = hemoglobin A<sub>1c</sub>, LRYGB = laparoscopic Roux-en-Y gastric bypass, LSG = laparoscopic sleeve gastrectomy, QALY = quality-adjusted life-years, T2DM = type 2 diabetes mellitus.

## INTRODUCTION

As society develops and lifestyles change, diabetes mellitus has become prevalent, threatening to reduce life expectancy for humans around the global.<sup>1-3</sup> Globally, there were a total of 415 million patients aged 20 to 79 with diabetes in 2015, and 90% of those patients had type 2 diabetes mellitus (T2DM).<sup>4</sup> As well as, recent studies have found that there were 109.6 million persons with diabetes in China in 2015, which have topped the world, following by India (69.2 million), U.S. (29.3 million), Brazil (14.3 million), and Russian Federation (12.1 million).<sup>5-8</sup>

In addition, prevalence rate of diabetes was 8.8% around the world in 2015 (Table 1).<sup>8</sup> Diabetes appears to be increasing rapidly in China. The overall prevalence of diabetes was estimated to be 11.6% in the Chinese adult population in 2010, which is considerably higher than its prevalence of less than 1% in 1980.<sup>9</sup>

At this point in time, T2DM is mainly treated medically, including diet restrictions, strengthening exercises, oral hypoglycemic drugs, and insulin injections.<sup>10-13</sup> However, there is no way to completely control the disease and its complications, and lifelong use of medications and insulin injections result in poor compliance among patients.<sup>14-17</sup>

A follow-up study by Mingrone et al<sup>18</sup> in the *Lancet* found that surgery is more effective than medical treatment for the long-term control of T2DM in obese patients. Their study involved a randomized controlled trial that compared conventional medical treatment with laparoscopic Roux-en-Y gastric bypass (LRYGB) or biliopancreatic diversion with duodenal switch in terms of their outcomes at 5 years in 60 obese patients with T2DM. Their results indicated that bariatric surgery was a viable option since surgery achieved a partial remission in 19 (50%) of the 38 patients at 5 years while medical treatment failed to achieve a partial remission in any of the 15 patients who were treated medically. Mingrone et al noted that neither

**TABLE 1.** Different Regions Ranked by Age-Adjusted Prevalence (%) of Diabetes (20–79 years) 2015

Region	Population, million	Prevalence, %
North America and Caribbean	44.3	11.5% (9.5–13.0%)
Middle East and North Africa	35.4	10.7% (7.4–14.2%)
South and Central America	29.6	9.6% (8.2–11.5%)
Western Pacific	153.2	8.8% (7.7–10.8%)
South-East Asia	78.3	8.8% (7.3–10.8%)
Europe	59.8	7.3% (5.5–10.9%)
Africa	14.2	3.8% (2.6–7.9%)
Global	415	8.8% (7.2–11.4%)

treatment achieved a complete remission in either group at 5 years according to the American Diabetes Association (ADA) definition. Hyperglycemia recurred in 15 (44%) of the 34 patients who underwent surgery that achieved a remission at 2 years.

Our study presents follow-up data at 2 years to compare 80 patients with T2DM who underwent laparoscopic sleeve gastrectomy (LSG) or LRYGB. Partial remission and complete remission were determined, weight loss, the body mass index (BMI), changes in abdominal circumference, cholesterol, and triglycerides were measured, and diabetes-related complications were assessed. On the basis of clinical observations, the cost-effectiveness of medical treatment, LSG, and LRYGB for patients with T2DM was estimated with a Markov simulation model.

## METHODS

### Study Design and Patients

A 2-group randomized controlled trial was conducted at Diabetes Surgery Centre, Beijing Shijitan Hospital in Beijing, China. Inclusion criteria were: the patients ages  $\leq 65$  years; BMI  $\geq 28$  kg/m<sup>2</sup>; duration of T2DM  $\leq 15$  years, in accordance with the ADA definition for T2DM: fasting plasma glucose (FPG) 7.0 mmol/L or greater, diagnosis, or use of a glucose-lowering drug;<sup>19</sup> and ability to understand and comply with the study protocol.

In addition, the cost-effectiveness of each type of treatment was analyzed with a Markov simulation model. The Markov model has been used in health fields since the 1980s to depict the development of chronic disease. The model divides a disease into a number of different Markov states depending on their relationship to health, and it then simulates the development of that disease governed by the probability of a transition between states at a certain time. The model uses loop computations to

estimate the outcomes and gains or losses of disease development. Details of the model and its validation can be found in the literature.<sup>20,21</sup> Markov states of T2DM in the current study were Well, T2DM, and Death.

The mortality rate (used in Well state), prevalence rate, case fatality rate (used in T2DM state), and relevant parameters of T2DM are collected in *China Health and Family Planning Statistical Year-Book*, 2013 to 2015, and the remission rates for the 2 surgeries are based on the aforementioned data from research results. The total costs include direct health expenditures (outpatient costs, hospitalization costs, surgical fees, and drug costs), direct nonhealth expenditures (hiring caregivers, commercial medical insurance, board expenses, transportation, and health care products), and indirect expenses with data based on theoretical values and prices at Beijing Shijitan Hospital (Table 2).<sup>22</sup>

### Randomization

Eighty patients were randomly assigned (1:1) to undergo either LSG (n = 40) or LRYGB (n = 40) between February 3, 2011 and October 31, 2013. Of those patients, 72 (90%) were available at follow-up at 2 years. These patients included 34 (85%) who underwent LSG and 38 (95%) who underwent LRYGB (Figure 1). Study investigators were aware of treatment allocation from the point of randomization. There were no statistically significant differences in baseline values of the LSG group and the LRYGB group (Table 3).

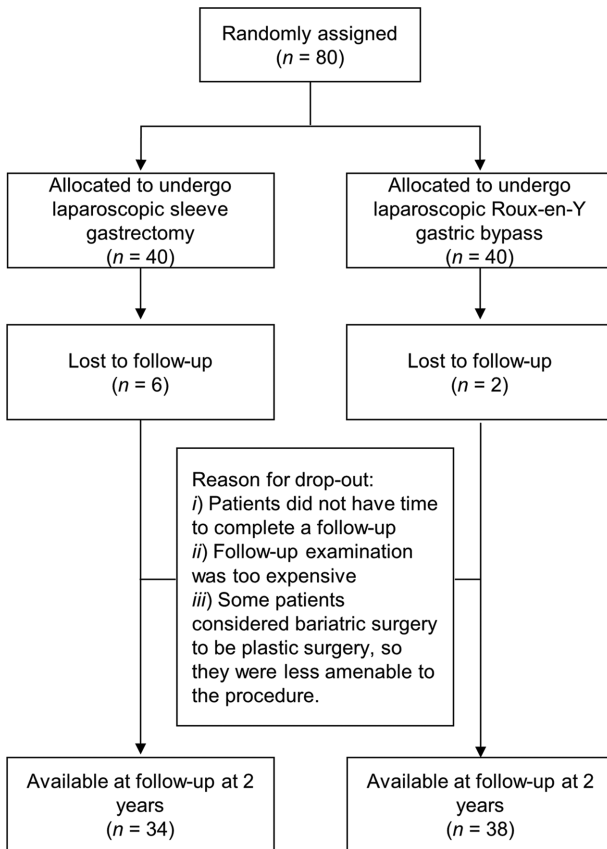
### Outcomes

The primary endpoint was the rate of partial remission and complete remission by T2DM at 2 years. According to the criteria recommended by the ADA: partial remission is defined as a FPG concentration of 6.9 mmol/L or less and a hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) concentration of 6.5% or less ( $\leq 47.5$  mmol/mol) without active pharmacological treatment for at least 1 year

**TABLE 2.** The Costs of Type 2 Diabetes Mellitus Used in the Markov Model in China (\$)

Cost	Medical Treatment	LSG	LRYGB
Direct health expenditures	1510.34	7968.20	9515.97
Direct nonhealth expenditures	75.53	164.30	174.44
Indirect expenses	351.95	377.77	393.70
Total	1937.83	8510.27	10084.11

LRYGB = laparoscopic Roux-en-Y gastric bypass, LSG = laparoscopic sleeve gastrectomy.



**FIGURE 1.** Trial profile. Eighty patients were randomly assigned (1:1) to undergo either LSG (n = 40) or LRYGB (n = 40) between February 3, 2011 and October 31, 2013. Of those patients, 72 (90%) were available for follow-up at 2 years. These patients included 34 (85%) who underwent LSG and 38 (95%) who underwent LRYGB. LRYGB = laparoscopic Roux-en-Y gastric bypass, LSG = laparoscopic sleeve gastrectomy.

while complete remission is defined as HbA<sub>1c</sub> < 6.0% and FPG < 5.6 mmol/L for at least 1 year without any medical or surgical treatment.<sup>23,24</sup> The following variables were assessed as secondary outcomes: FPG, HbA<sub>1c</sub>, changes in bodyweight, BMI, abdominal circumference, plasma total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides. Markov model outcomes included quality-adjusted life-years (QALYs) and costs.

**Statistical Analysis**

A  $\chi^2$  test was used to compare the remission of T2DM in the LSG group and the LRYGB group. All of the secondary outcomes, which were expressed in absolute values and in proportion to baseline values, were tested with a *t* test. All of the outcomes were analyzed with SPSS (version 16.0), and *P* < 0.05 was considered statistically significant for all tests. A Markov model was built and analyzed with Treeage Pro (version 2011) to compare the cost-effectiveness of treatments.

**RESULTS**

Eighty patients were randomly assigned (1:1) to undergo either LSG (n = 40) or LRYGB (n = 40) between February 3, 2011 and October 31, 2013. Of those patients, 72 (90%) were

available at follow-up at 2 years. These patients included 34 (85%) who underwent LSG and 38 (95%) who underwent LRYGB.

At 2 years, a partial remission was achieved in 26 (76.5%) in the LSG group and 22 (57.9%) in the LRYGB group. A total of 17 (50.0%) in the LSG group and 14 (36.8%) in the LRYGB group had met the standard of HbA<sub>1c</sub> < 6.0% and FPG < 5.6 mmol/L without glucose-lowering drugs, which indicates a complete remission. Similarly, 29 (85.3%) in the LSG group and 27 (71.1%) in the LRYGB group had HbA<sub>1c</sub> ≤ 6.5% with or without glucose-lowering drugs (Table 4). The 2 surgeries had a positive effect on the remission of T2DM. There were no significant differences in the results of the 2 groups (*P* > 0.05), which indicates that the 2 surgeries did not differ in terms of the remission of T2DM and glycemic control.

Secondary outcome measures included FPG, HbA<sub>1c</sub>, changes in bodyweight, BMI, abdominal circumference, plasma total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides. Data on these measures are presented as the absolute change and percent change at 2 years from the baseline (Table 5). Mean FPG and HbA<sub>1c</sub> concentrations at 2 years were slightly lower in the LSG group than in the LRYGB group. The 2 surgeries both caused weight loss and changes in BMI and abdominal circumference, and these measures did not differ significantly between the 2 groups. The absolute change and percent change in these secondary outcome measures at 2 years did not differ significantly between the 2 groups. The 2 surgeries both had a substantial effect on the reduction of FPG, HbA<sub>1c</sub>, and bodyweight in patients with T2DM. Moreover, outcomes of obesity comorbidities and diabetes complications for the LSG group and LRYGB group also be revealed (Table 6).

Given the similar outcomes of the surgeries, the question is then which is more cost-effective. The cost-effectiveness ratio was measured for the 3 different treatments. Costs and QALYs were discounted at an annual rate of 5% in accordance with China’s consumer price index. A tree diagram is depicted in Figure 2. There were 3 Markov states of T2DM: Well, T2DM, and Death. Each state has different parameters and a probability of a transition between the states for the 3 treatments. The total costs per capita for patients with T2DM include direct health expenditures, direct nonhealth expenditures, and indirect expenses, and the total cost of medical treatment was 1937.83 dollars per year, that of LSG was 8510.27 dollars, and that of LRYGB was 10,084.11 dollars. Clearly, the lowest cost treatment is medical treatment since surgical fees are a one-time fee option, and surgery is more expensive than basic medicines such as acarbose tablets, gliquidone tablets, and Novolin. Therefore, patients undergoing medical treatment pay the least in the short term. The relative cost of medical treatment was 37,183 dollars, that of LSG was 42,795 dollars, and that of LRYGB was 49,646 dollars. The QALYs were 23.4 years for medical treatment, 41.59 years for LSG, and 41.46 years for LRYGB. Medical treatment had the lowest relative cost and the shortest QALYs. The cost-effectiveness ratio was 1589.02 dollars per QALY for medical treatment, 1028.97 dollars per QALY for LSG, and 1197.44 dollars per QALY for LRYGB (Table 7). Accordingly, LSG yielded the greatest benefit at the lowest cost for patients with T2DM (Figure 3).

Sensitivity analysis was performed and tornado diagrams were constructed to determine the robustness of the current model and to identify key factors affecting the cost-effectiveness ratio. The 95% confidence interval of the remission rate was

**TABLE 3.** Baseline Values for Patients in the LSG Group and the LRYGB Group

Variable	LSG Group (n = 34)	LRYGB Group (n = 38)	Missing Value	P Value
Age, year	36.6 (8.0)	40.4 (12.3)	0	0.12
Male	12 (35.3%)	20 (52.6%)	0	0.16
Disease time, year	5.1 (4.1)	6.5 (4.1)	9	0.16
Obesity comorbidities*	26 (76.5%)	23 (60.5%)	0	0.12
Diabetes complications†	0 (0%)	5 (13.2%)	0	0.06
Weight, kg	108.8 (32.4)	106.5 (20.0)	0	0.72
Height, m	1.69 (0.1)	1.69 (0.1)	0	0.72
BMI, kg/m <sup>2</sup>	38.4 (8.6)	37.8 (5.6)	0	0.74
Abdominal circumference, cm	116.7 (19.2)	113.3 (14.5)	0	0.39
Hip circumference, cm	116.2 (18.4)	113.5 (14.2)	16	0.54
Fasting glucose, mmol/L	8.3 (2.2)	9.0 (3.4)	0	0.33
HbA <sub>1c</sub> , %	7.4 (1.8)	7.4 (1.8)	0	0.84
Insulin resistance index	10.3 (8.0)	7.5 (5.1)	2	0.08
Vital capacity, L	2.2 (1.2)	2.6 (1.3)	14	0.28
Total cholesterol, mmol/L	5.0 (0.8)	5.2 (2.0)	0	0.71
Triglycerides, mmol/L	2.3 (2.0)	2.5 (2.1)	0	0.80

BMI = body mass index, HbA<sub>1c</sub> = hemoglobin A<sub>1c</sub>, LRYGB = laparoscopic Roux-en-Y gastric bypass, LSG = laparoscopic sleeve gastrectomy.

\*Obesity comorbidities include hypertension, cataract, hyperlipemia, hyperuricemia, fatty liver, polycystic ovarian syndrome, and osteoarthritis.

†For the difficult early diagnosis and younger patients, we did not collect the samples for neuropathy and stroke of diabetes complications. Therefore, diabetes complications in this table include diabetic retinopathy, nephropathy, and coronary heart disease.

used to determine lower and upper values to enter into the model, and the cost values were halved or doubled since confidence intervals were unavailable.<sup>25</sup> Figure 4 shows the effect of varying each parameter on the cost-effectiveness ratio in tornado analyses. Cost was found to be a key factor. Doubling the cost leads to a lower cost-effectiveness ratio, and halving the cost leads to a higher cost-effectiveness ratio. Moreover, LSG remained the predominant strategy regardless of changes in variables.

## DISCUSSION

At the current time, there were few studies about the therapeutic effect and cost-effectiveness of bariatric surgery in Asia. Bariatric surgeries were performed in China but only in clinical trials until 2012, when the country began to recognize the appropriateness and validity of bariatric surgery. The Chinese Society for Metabolic & Bariatric Surgery was established in 2012. Japan has a similar society, the Japanese Society for the Surgery of Obesity and Metabolic Disorders, but bariatric

surgeries were still seldom performed in Japan.<sup>26</sup> As well, the economic aspects of conventional treatment and surgery have seldom been investigated in China. Western studies have found that surgery leads to greater gains in QALYs and is less costly than medical treatment for patients with T2DM over the long term.<sup>25,27,28</sup> However, these studies mostly focused on LRYGB and biliopancreatic diversion with duodenal switch and did not include a comparison to LSG. Moreover, the homeostasis model assessment of insulin resistance differs in populations in different countries.<sup>29–34</sup> Given China's diabetic population and the particularities of the Asian physique, this study will facilitate and guide cost-effective bariatric surgery for China specifically but for the rest of Asia as well.

On the baseline data of this study, the enrollment rate in the current trial was 100% because of the strict inclusion criteria. The follow-up rate was 90% and the reasons for drop-outs were: patients did not have time to complete a follow-up; follow-up examination was too expensive; and some patients viewed bariatric surgery as plastic surgery, so they were less amenable to the procedure.

**TABLE 4.** Type 2 Diabetes Mellitus Remission and Glycemic Control at the Follow-Up at 2 Years

Outcomes	LSG Group n = 34	LRYGB Group n = 38	P Value
Partial remission*	26 (76.5%)	22 (57.9%)	0.08
Complete remission†	17 (50.0%)	14 (36.8%)	0.19
HbA <sub>1c</sub> ≤ 6.5% with or without glucose-lowering drugs	29 (85.3%)	27 (71.1%)	0.12

FPG = fasting plasma glucose, HbA<sub>1c</sub> = hemoglobin A<sub>1c</sub>, LRYGB = laparoscopic Roux-en-Y gastric bypass, LSG = laparoscopic sleeve gastrectomy.

\*Partial remission means FPG ≤ 6.9 mmol/L and HbA<sub>1c</sub> < 6.5% for at least 1 year without treatment.

†Complete remission is defined as HbA<sub>1c</sub> < 6.0%; and fasting plasma glucose < 5.6 mmol/L for at least 1 year without any medical or surgical treatment.

**TABLE 5.** Secondary Outcome Measures for the LSG Group and the LRYGB Group

Measures	LSG Group (n = 34)	LRYGB Group (n = 38)	P Value*
Fasting glucose, mmol/L			
Baseline	8.3 (2.2)	9.0 (3.4)	0.33
At 2 years	5.6 (2.4)	6.8 (2.7)	0.04
Absolute change	-2.8 (2.8)	-2.1 (2.9)	0.37
Percent change, %	-0.3 (0.3)	-0.2 (0.3)	0.08
P value†	<0.001	<0.001	-
HbA <sub>1c</sub> , %			
Baseline	7.4 (1.8)	7.4 (1.8)	0.84
At 2 years	6.0 (0.6)	6.4 (1.6)	0.15
Absolute change	-1.4 (1.6)	-1.1 (1.8)	0.42
Percent change, %	-0.2 (0.1)	-0.1 (0.2)	0.32
P value†	<0.001	0.001	-
Weight, kg			
Baseline	108.8 (32.4)	106.5 (20.0)	0.72
At 2 years	90.2 (28.5)	87.8 (13.5)	0.65
Absolute change	-18.6 (13.6)	-18.8 (12.0)	0.96
Percent change, %	-0.2 (0.1)	-0.2 (0.1)	0.99
P value†	< 0.001	0.001	-
Abdominal circumference, cm			
Baseline	116.7 (19.2)	113.3 (14.5)	0.39
At 2 years	106.6 (17.6)	104.9 (9.3)	0.60
Absolute change	-10.1 (9.6)	-8.4 (14.4)	0.55
Percent change, %	-0.1 (0.1)	-0.1 (0.1)	0.39
P value†	<0.001	0.001	-
BMI, kg/m <sup>2</sup>			
Baseline	38.4 (8.6)	37.8 (5.6)	0.74
At 2 years	31.1 (9.6)	30.7 (5.5)	0.83
Absolute change	-7.3 (7.1)	-7.2 (5.4)	0.92
Percent change, %	-0.2 (0.2)	-0.2 (0.1)	0.92
P value†	<0.001	<0.001	-
Total cholesterol, mmol/L			
Baseline	5.0 (0.8)	5.2 (2.0)	0.71
At 2 years	4.7 (0.8)	4.2 (1.0)	0.03
Absolute change	-0.3 (0.7)	-1.0 (1.7)	0.42
Percent change, %	-0.1 (0.1)	-0.1 (0.2)	0.07
P value†	0.01	0.001	-
HDL cholesterol, mmol/L			
Baseline	1.0 (0.2)	1.0 (0.2)	0.60
At 2 years	1.0 (0.3)	1.1 (0.2)	0.34
Absolute change	0.1 (0.2)	0.1 (0.2)	0.59
Percent change, %	0.1 (0.2)	0.1 (0.2)	0.42
P value†	0.49	0.04	-
LDL cholesterol, mmol/L			
Baseline	3.3 (0.8)	2.8 (0.9)	0.03
At 2 years	3.1 (0.8)	2.4 (0.7)	0.02
Absolute change	-0.2 (0.8)	-0.4 (1.0)	0.30
Percent change, %	0.0 (0.4)	-0.1 (0.4)	0.56
P value†	0.26	0.03	-
Triglycerides, mmol/L			
Baseline	2.3 (2.0)	2.5 (2.1)	0.80
At 2 years	1.3 (0.6)	1.2 (0.7)	0.62
Absolute change	-1.0 (1.7)	-1.2 (1.8)	0.62
Percent change, %	-0.3 (0.3)	-0.4 (0.3)	0.39
P value†	0.001	<0.001	-
EWL	69.4 (39.9)	53.7 (30.1)	0.13

BMI = body mass index, EWL = excessive weight loss, HbA<sub>1c</sub> = hemoglobin A<sub>1c</sub>, HDL = high-density lipoprotein, LDL = low-density lipoprotein, LRYGB = laparoscopic Roux-en-Y gastric bypass, LSG = laparoscopic sleeve gastrectomy.

\*P value means the differences between 2 groups.

†P value means the differences between before and after surgeries.

**TABLE 6.** Outcomes of Obesity Comorbidities\* and Diabetes Complications† for the LSG Group and LRYGB Group

Measures	LSG Group (n = 34)	LRYGB Group (n = 38)	P Value
Hypertension			
Baseline	12 (35.3%)	16 (42.1%)	0.36
At 2 years	7 (20.6%)	13 (34.2%)	0.15
P value	0.40	0.78	—
Cataract			
Baseline	0 (0%)	1 (2.6%)	0.53
At 2 years	0 (0%)	0 (0%)	—
P value	—	—	—
Hyperlipemia			
Baseline	11 (32.4%)	10 (26.3%)	0.38
At 2 years	2 (5.9%)	7 (18.4%)	0.11
P value	0.02	0.71	—
Hyperuricemia			
Baseline	2 (5.9%)	2 (5.3%)	0.65
At 2 years	1 (3.0%)	2 (5.3%)	0.54
P value	0.84	—	—
Fatty liver			
Baseline	15 (44.1%)	11 (28.9%)	0.14
At 2 years	10 (29.4%)	8 (21.1%)	0.30
P value	0.45	0.72	—
Polycystic ovarian syndrome			
Baseline	0 (0%)	0 (0%)	—
At 2 years	0 (0%)	0 (0%)	—
P value	—	—	—
Osteoarthropathy			
Baseline	0 (0%)	0 (0%)	—
At 2 years	0 (0%)	0 (0%)	—
P value	—	—	—
Diabetic retinopathy			
Baseline	0 (0%)	1 (2.6%)	0.53
At 2 years	0 (0%)	0 (0%)	—
P value	—	—	—
Nephropathy			
Baseline	0 (0%)	2 (5.3%)	0.28
At 2 years	0 (0%)	0 (0%)	—
P value	—	—	—
Coronary heart disease			
Baseline	0 (0%)	2 (5.3%)	0.28
At 2 years	0 (0%)	1 (2.6%)	0.53
P value	—	—	—

LRYGB = laparoscopic Roux-en-Y gastric bypass, LSG = laparoscopic sleeve gastrectomy.

\*Obesity comorbidities include hypertension, cataract, hyperlipemia, hyperuricemia, fatty liver, polycystic ovarian syndrome, and osteoarthropathy.

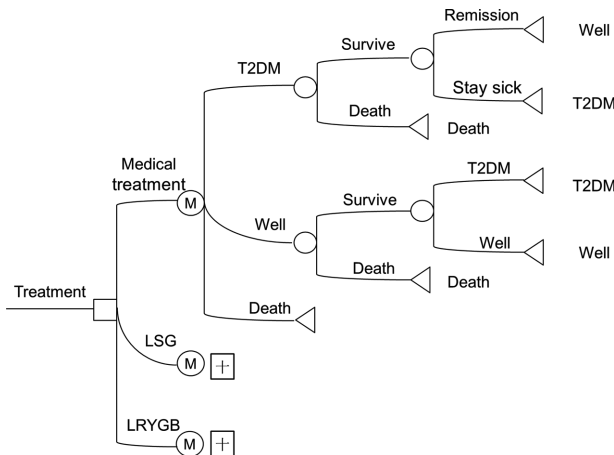
†For the difficult early diagnosis and younger patients, we do not collect the samples for neuropathy and stroke of diabetes complications. Therefore, diabetes complications in this table include diabetic retinopathy, nephropathy, and coronary heart disease.

In addition, the study population was relatively young and the age variation was minimal which was mainly from the small sample size. However, Annual Report (2014) and Diabetes Atlas (2015) of International Diabetes Federation both indicated that nearly half diabetes patients aged between 40 and 59 years in the world, with the Chinese patients being younger.<sup>8,35</sup> Besides, for duration of T2DM  $\leq 15$  years of the inclusion criteria in the study, the younger patients were more acceptable for the surgery, while elder patients tend to maintain the medical control, which was similar with several studies.<sup>36,37</sup>

Moreover, the standard deviations of BMIs were relatively low, which was also mainly due to the small sample size. However, based on the different inclusion criteria of BMI

between the guidelines of China and ADA, we can find diagnostic criteria of obesity also different in China, Europe, and America. The boundary of adult overweight is 24 of BMI, and adult obesity is 28 of BMI in China, so that the inclusion criteria were adjusted by changing a BMI  $\geq 35$  to a BMI  $\geq 28$ , which better accommodated the requirements of this study. And there are several studies that conduct the comparison between the LSG and LRYGB group with BMI measured by 40 or over and low standard deviations.<sup>38,39</sup>

The current results indicated that LSG and LRYGB were both remarkably effective at long-term control of hyperglycaemia and improving the metabolic profile, allowing significant reductions in medication use and use of glucose-lowering drugs

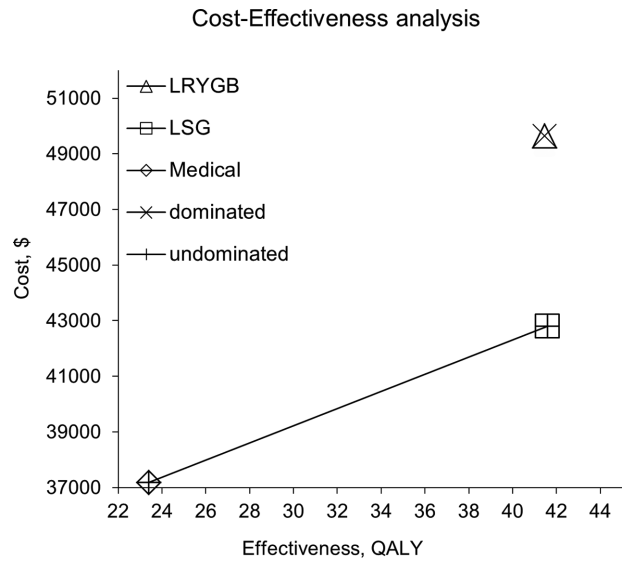


**FIGURE 2.** Tree diagram of a Markov model. Three Markov states are shown: Well, DM2, and Death. □ indicates a decision node, ○ indicates a chance node, Δ indicates a terminal node, and “M” indicates a Markov node.

shown in Table 4. This study used the standard defined by ADA, which is stricter than general standards, so the partial remission and complete remission that were achieved are relatively ideal. A point worth noting is that no deaths occurred after either surgery. The results of this study basically agree with those of other studies, that is to say the surgeries are reasonable approaches to treating diabetes.<sup>40</sup>

Although, as a trend to more diabetes remission in the LRYGB group, there was still no statistical difference between the 2 groups with the partial remission and complete remission, which was similar with western studies. This is because the baseline data in our study show the mean of BMI in LSG group is larger than the one in LRYGB group, which means that the prognosis effect of LSG is better because the curable effect of the patients were better for obese patients. Certainly, the results are mainly caused by the relatively small sample size.

Besides, LRYGB appears to have a better effect on LDL and total cholesterol while HDL and triglycerids are not different, which also mainly because of the mean of weight and BMI in LRYGB group are smaller than the one in LSG group, and obese patients are more suitable for LSG surgery. Several studies show that a few secondary outcomes, such as LDL cholesterol, HDL cholesterol, or triglycerids, have statistical differences between the 2 groups.<sup>18</sup> However, it is inadequate to prove the difference of clinical effect between the 2 groups only based on this individual or exceptional index, which may because of the small sample.



**FIGURE 3.** Cost-effectiveness analysis of Medical treatment, LSG, and LRYGB. The CEF is shown. × means the dominated strategy; + means the undominated strategy. LSG is the predominant strategy. CEF = cost-effective frontier, LRYGB = laparoscopic Roux-en-Y gastric bypass, LSG = laparoscopic sleeve gastrectomy.

Several studies commonly used the excessive weight loss to assess the clinical effect of surgery, which was calculated as the difference between the weight at the time of implantation and the ideal body weight corresponding to a BMI of 25 kg/m<sup>2</sup>, reaching the value of 50% means the effective results of weight loss at 1 year after surgery. The result of our study achieved the 61.1%, which is similar with other Asian research (Table 5).<sup>41,42</sup>

Furthermore, there were only 4 cases occurred the mild postoperative complication which were cured after conservative treatment, which manifested as mild nausea, pain, emesis, and bleeding. This result was also similar with other research results.<sup>41</sup>

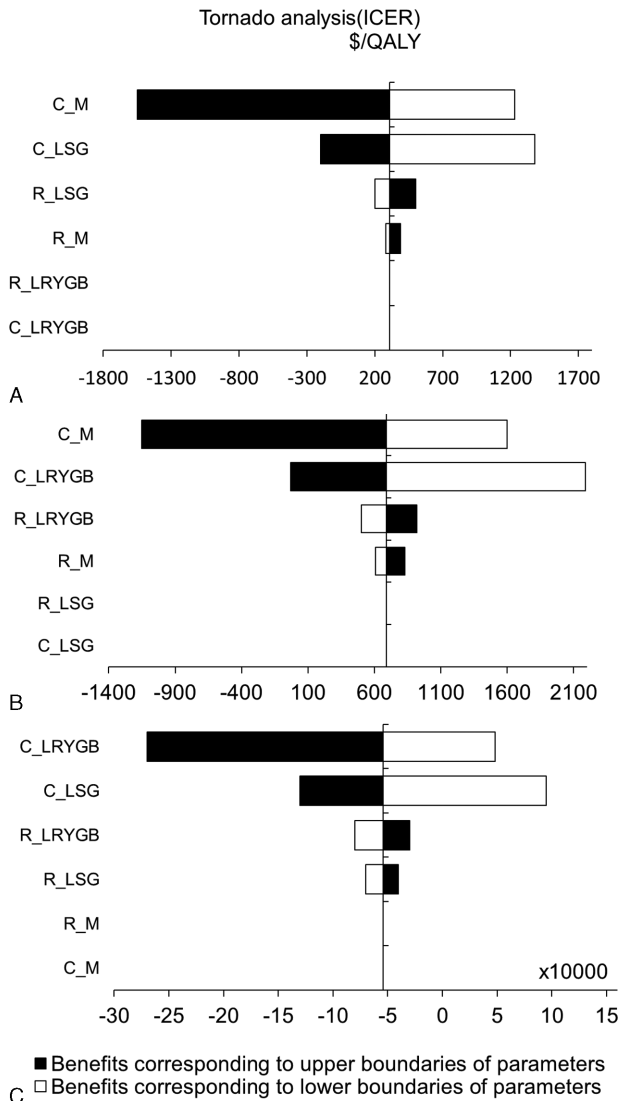
Determining which surgery is more cost-effective is another important issue in this study. First, what warrants special attention is whether different medications will affect the total costs for the medically treated group. Medications of T2DM patients in China according to the guideline are basically metformin, sulfonylurea, and insulin. This is the first one of the considered 4 conventional treatment strategies by Yuanhui Zhang et al,<sup>43</sup> which includes metformin, sulfonylurea, and insulin; metformin, a dipeptidyl peptidase-4 inhibitor, and insulin; metformin, a glucagon-like peptide-1 agonist, and insulin; and metformin and insulin, proving different ways

**TABLE 7.** Life-Years Gained and Cost-Effectiveness Ratios for Medical Treatment and Two Surgical Procedures

Treatment	Total Cost,* \$	Relative Cost, \$	QALYs,* years	Cost-Effectiveness Ratio, \$/QALY
Medical treatment	1937.83	37,183	23.40	1589.02
LSG	8510.27	42,795	41.59	1028.97
LRYGB	10,084.11	49,646	41.46	1197.44

LRYGB = laparoscopic Roux-en-Y gastric bypass, LSG = laparoscopic sleeve gastrectomy, QALYs = quality-adjusted life-years.

\*Costs and QALYs are discounted at an annual rate of 5%.



**FIGURE 4.** Tornado diagrams of each treatment: (A) medical treatment versus LSG; (B) medical treatment versus LRYGB; (C) LSG versus LRYGB. C\_M means the cost of medical treatment, C\_LSG means the cost of LSG, C\_LRYGB means the cost of LRYGB, R\_M means the remission rate for medical treatment, R\_LSG means the remission rate for LSG, and R\_LRYGB means the remission rate for LRYGB. When, as an example, C\_M in (A) is halved, an increased cost leads to a lower cost-effectiveness ratio. When C\_M in (A) is doubled, a reduced cost leads to a higher cost-effectiveness ratio. LRYGB = laparoscopic Roux-en-Y gastric bypass, LSG = laparoscopic sleeve gastrectomy.

of drug use little impact on the cost. Therefore, different medications have no effect on our cost-effectiveness analysis.

According to the model, LSG and LRYGB appear to be relatively cost-effective treatments for diabetics, with cost-effectiveness ratios ranging from \$1028.97 to \$1197.44/QALY, as compared to \$1589.02/QALY for medical treatment. Therefore, the one-off charge of surgeries is high, but they lead to greater gains in QALYs and are less costly than medical treatment for patients with T2DM over the long term. Relatively, LSG is as effective as LRYGB and is slightly more

cost-effective than LRYGB, so that LSG therapy appears to be the cost-effective option for managing patients with T2DM.

The current study has several limitations. The first stems mainly from its relatively small sample size. Second, the current authors are cognizant of the lack of data on medical treatment in contrast to data on surgery. However, the patients who included in this study were all under medication more than 2 years with no remission and the primary endpoint of our study was conducted as 2 years, so that they accepted surgical treatment and had drug withdrawal after surgery. Third, limited data on the long-term effects of bariatric surgery are available, which means the follow-up in this study was only 2 years, so a consistent remission as defined by the ADA was not evident.

In conclusion, bariatric surgery is not a cost-saving way to control T2DM since the one-time fee is prohibitive for some patients, but the increased costs of that surgery come with greater benefits. From an economic perspective, LSG is a cost-effective intervention for managing T2DM. The hope is that estimates of the cost-effectiveness of bariatric surgery will become more systematic, helping to facilitate and guide future policy decisions regarding the treatment of diabetes.

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