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# BMJ Open

## Comparative long-term effectiveness and safety of primary bariatric surgeries in treating type 2 diabetes mellitus in adults: a protocol for systematic review and network meta-analysis of randomized controlled trials

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-028430
Article Type:	Protocol
Date Submitted by the Author:	07-Dec-2018
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Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, Adult surgery < SURGERY, Adverse events < THERAPEUTICS

SCHOLARONE™  
Manuscripts

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4 **Comparative long-term effectiveness and safety of primary bariatric**  
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6 **surgeries in treating type 2 diabetes mellitus in adults: a protocol for**  
7  
8 **systematic review and network meta-analysis of randomized**  
9  
10 **controlled trials**  
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45 **Word Count:** 3941 words, excluding title page, abstract, and references.  
46  
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49

50 **Abstract**  
51

52  
53 **Introduction** Bariatric surgeries are effective in treating obesity related comorbidities, including  
54  
55 type 2 diabetes mellitus. More robust evidence is needed to facilitate choice of procedure. In this  
56  
57 systemic review, we aim to investigate the comparative long-term effectiveness in inducing  
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3  
4 remission of type 2 diabetes, halting diabetic complications, reducing mortality, and the safety, of  
5  
6 conventional and emerging bariatric surgeries.  
7

8  
9 **Methods and analysis** Databases including Cochrane Central Register, EMBASE, MEDLINE,  
10  
11 and clinical trial registries will be searched for randomized controlled trials with at least 3 years of  
12  
13 follow-up, including direct and/or indirect evidence regarding primary bariatric surgeries in  
14  
15 overweight or obese adults with type 2 diabetes mellitus, from inception of each database to 2019,  
16  
17 with no language or publication type limits imposed. Dual selection of studies, data extraction,  
18  
19 and risk of bias assessments will be performed. Primary outcomes include full diabetes remission,  
20  
21 composite outcome of full or partial diabetes remission, and adverse events profiles. Secondary  
22  
23 outcomes include anthropometric measurements, cardiovascular risk factor burden, medication  
24  
25 burden, diabetic complications, and all-cause mortality. Given sufficient homogeneity, network  
26  
27 meta-analyses will be performed in a random-effect model based on the Bayesian framework,  
28  
29 while assessing for consistency between direct and indirect estimates. Heterogeneities of studies  
30  
31 will be explored through meta-regression analysis, and robustness of findings will be checked by  
32  
33 sensitivity analysis, and an alternative method under a frequentist framework. All statistical  
34  
35 analysis and graphical presentations will be conducted by R software (Version 3.3.3, The R  
36  
37 Project for Statistical Computing). The overall quality of the evidence will be assessed using the  
38  
39 Grading of Recommendations, Assessment, Development, and Evaluation criteria for each  
40  
41 outcome.  
42  
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52  
53 **Ethics and dissemination** Ethics approval is not required as individual patient data will not be  
54  
55 included. This review will be subject for publication in a peer-reviewed journal.  
56  
57

58 **Registration Details** PROSPERO registration number CRD42018110775.  
59  
60

### Strengths and limitations of this study

► This will be the first systemic review and network meta-analysis to assess long-term relative effectiveness and safety of conventional and emerging bariatric surgeries in overweight or obese adults with type 2 diabetes mellitus.

► This study will comprehensively evaluate clinical important outcomes, including full or partial diabetes remission, anthropometric measurements, cardiovascular risk factor burden, medication burden, diabetic complications, all-cause mortality, and major adverse events.

► This protocol proposes an innovative scoring system for integral assessment of safety of bariatric surgeries.

► This protocol defines detailed plan for data synthesis, additional analysis concerning consistency, goodness-of-fit of models, potential effect modifiers, and validation of findings by an alternative method.

► Common to any aggregate data meta-analysis, the risk for ecological fallacy and heterogeneity across studies exists.

### BACKGROUND

Bariatric surgeries have shown long-term benefits with respect to inducing disease remission, reducing mortality, and decreasing microvascular and macrovascular complications in overweight or obese patients with type 2 diabetes mellitus, comparing with non-surgical therapy.[1] The currently performed bariatric surgeries include Roux-en-Y gastric bypass, sleeve gastrectomy, adjustable gastric banding, biliopancreatic diversion with duodenal switch, greater curvature plication, one-anastomosis gastric bypass, and single anastomosis duodenal-ileal bypass with

1  
2  
3  
4 sleeve gastrectomy.[2-5] Previous studies indicated that bariatric surgeries differed in both  
5  
6 efficacy, durability, and mechanisms in inducing remission of type 2 diabetes and complication  
7  
8 profiles.[2, 6-9] Current evidence is insufficient to support recommendation regarding choice of  
9  
10 specific procedure clearly over others, and more robust evidence is needed to facilitate informed  
11  
12 decision making.[2] Since comparisons of only two or a few bariatric procedures can be achieved  
13  
14 in randomized controlled trials, network meta-analysis, capable of integrating both direct and  
15  
16 indirect evidence, is a reasonable approach in this scenario.  
17  
18  
19  
20  
21

22 A recent elegant network meta-analysis of studies involving eight bariatric surgeries with median  
23  
24 follow-up duration of 3 months to 5 years (median 1 year) indicated that biliopancreatic diversion  
25  
26 and one-anastomosis gastric bypass achieved higher diabetes remission rates than the other  
27  
28 procedures.[6] However, biliopancreatic diversion is rarely performed currently due to  
29  
30 unfavorable complication profiles, while one-anastomosis gastric bypass is a relatively new  
31  
32 procedure, the safety and durability of which warrant further investigation.[3, 10] Furthermore,  
33  
34 remission rates of comorbidities may change over time after bariatric procedures,[11, 12] thus  
35  
36 comparing relative efficacies with different follow-up duration post bariatric surgeries may  
37  
38 introduce bias.  
39  
40  
41  
42  
43  
44

45 Type 2 diabetes mellitus can lead to increased risk of cardiovascular events, renal failure,  
46  
47 blindness, amputation, and increased mortality. Most of the evidence regarding the effects of  
48  
49 bariatric surgeries upon diabetic complications and mortality is derived from observational studies  
50  
51 and pairwise comparisons.[2] Defining the relative effectiveness of bariatric surgeries in halting  
52  
53 diabetic complications and in decreasing mortality should be addressed with the most robust  
54  
55 evidence possible, or at least, gaps in current knowledge should be identified to guide emphasis of  
56  
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60

1  
2  
3  
4 future research.[13]  
5

6  
7 Complication profiles of bariatric surgeries differ among procedures and between patients with  
8  
9 and without type 2 diabetes mellitus.[14, 15] However, efforts in investigating comparative safety  
10  
11 and tolerability of bariatric surgeries have been met with great difficulty, due to heterogeneity of  
12  
13 adverse events encountered and in ways reported among studies. Efforts have been made for  
14  
15 standard reporting of adverse events in studies of bariatric procedures.[16] We would like to  
16  
17 revisit this question, by defining major adverse events profiles of bariatric surgeries in adults with  
18  
19 type 2 diabetes mellitus, a group of patients already predisposed to increased risks of surgical  
20  
21 complications, depression and hypoglycemia.[17-19]  
22  
23  
24  
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29

## 30 **OBJECTIVES**

31  
32 The objectives of the study is to determine the relative effectiveness and safety of existing  
33  
34 bariatric surgeries in treating overweight or obese adults with type 2 diabetes mellitus through  
35  
36 systemic review and network meta-analysis, to perform meta-regression analysis, subgroup  
37  
38 analysis, and sensitivity analysis, if feasible, to explore what clinical and methodological  
39  
40 characteristics explain the heterogeneity in results, and to identify gaps in current studies to  
41  
42 provide directions for future research.  
43  
44  
45  
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49

## 50 **METHODS**

51  
52 This protocol follows Preferred Reporting Items for Systematic Reviews and Meta-analyses  
53  
54 Protocols and the accompanied checklist, and the study will follow Preferred Reporting Items for  
55  
56 Systematic Reviews and Meta-Analyses for Network Meta-Analyses.[20, 21] This protocol is  
57  
58  
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1  
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3  
4 registered with the International Prospective Register of Systematic Reviews (registration number  
5  
6 CRD42018110775). In circumstances when changes to the protocol are necessary, details and  
7  
8 rationales of the changes in the reported systematic review will be reported.  
9  
10

## 11 **Patient and public involvement**

12  
13  
14 Patients or the public were not involved in the design of this systemic review protocol.  
15  
16

## 17 **Eligibility criteria**

### 18 **Participants**

19  
20  
21 We will include studies which include overweight or obese adults with type 2 diabetes mellitus.  
22  
23

24 We will not include studies of participants restricted to specific diseases other than type 2 diabetes  
25  
26 mellitus. In studies in which general overweight or obese participants are enrolled, or in which  
27  
28 children or adolescents under the age of 18 are enrolled along with adults, we will extract the data  
29  
30 for the adult population with type 2 diabetes exclusively.  
31  
32  
33

### 34 **Interventions**

35  
36 We will include interventions encompassing currently performed primary bariatric surgeries,  
37  
38 including Roux-en-Y gastric bypass, sleeve gastrectomy, adjustable gastric banding,  
39  
40 biliopancreatic diversion with duodenal switch, greater curvature plication, one-anastomosis  
41  
42 gastric bypass, and single anastomosis duodenal-ileal bypass with sleeve gastrectomy. We will not  
43  
44 include studies examining revisional surgeries or procedures no longer performed, including  
45  
46 biliopancreatic diversion without duodenal switch, jejunioileal bypass, horizontal or vertical  
47  
48 gastroplasty, and banding that is not adjustable.  
49  
50  
51  
52  
53  
54

### 55 **Comparators**

56  
57  
58 We will include studies comparing currently performed bariatric surgeries with non-surgical  
59  
60



1  
2  
3  
4 treatment, or comparing at least 2 of the surgical procedures.  
5

#### 6 7 *Study designs*

8  
9 We will include randomized controlled trials, with at least 3 years of follow-up. To minimize  
10  
11 potential bias introduced by different follow-up period among studies, when including studies  
12  
13 with over 3 years of follow-up, data of measurements at 3 years (+/- 6 months) or earliest reported  
14  
15 time point after 3 years will be included in analysis.  
16  
17

#### 18 19 *Setting*

20  
21  
22 There will be no restrictions by type of setting.  
23

#### 24 25 *Language*

26  
27 We will include studies reported in the English and Chinese languages, and studies reported in  
28  
29 other languages if adequate translation is feasible by Bing Translate. A list of possibly relevant  
30  
31 studies not included in the review will be provided.  
32  
33

#### 34 35 *Publication status*

36  
37 Eligibilities of unpublished studies will be evaluated.  
38

#### 39 40 *Outcomes measures and prioritization*

##### 41 42 *Primary outcomes*

43  
44  
45 1. The number of patients in full remission of type 2 diabetes mellitus defined as HbA1c levels of  
46  
47 6.0% at consecutive annual visits, and no use of anti-hyperglycemic medication at either visit,[22]  
48  
49 or as defined by the studies.  
50  
51

52  
53 2. Composite outcome of number of patients in full or partial remission of type 2 diabetes  
54  
55 mellitus. Partial remission of type 2 diabetes mellitus is defined as HbA1c levels of 6.5% at  
56  
57 consecutive annual visits, and no use of anti-hyperglycemic medication at either visit,[22] or as  
58  
59  
60

1  
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3  
4 defined by the studies.  
5

6  
7 3. Cumulative scores of grade IIIa or higher complications according to Clavien-Dindo

8  
9 classification for surgical complications,[23] and grade 3 or higher other adverse events according  
10  
11 to the Common Terminology Criteria for Adverse Events version 5.0,[24] based on translation of  
12  
13 each IIIa, grade IIIb, grade IVa, grade IVb and grade V complication into 6, 7, 8, 9, 10 points,  
14  
15 respectively, and grade 3, grade 4, and grade 5 adverse events other than surgical complications  
16  
17 into 6, 8, 10 points, respectively, in the analogue scale (0=minimum severity, 10=maximum  
18  
19 severity). Surgical complication is defined as any deviation from the normal postoperative  
20  
21 course,[23] whereas adverse event is defined as any unfavorable and unintended sign, symptom,  
22  
23 or disease temporally associated with the use of a medical treatment or procedure that may or may  
24  
25 not be considered related to the medical treatment or procedure.[24] A scored appraisal of adverse  
26  
27 events profiles serves in two ways. Firstly, it allows evaluation of severity of adverse event based  
28  
29 on its impact upon patient regardless of its definition which may vary considerably among studies.  
30  
31 Secondly, a cumulative score based approach allow integral assessment of safety among  
32  
33 procedures. The reason for inclusion of only major adverse event is twofold. Firstly, the intensity  
34  
35 of surveillance may tamper overtime during follow-up, so as to only serious adverse event may be  
36  
37 recognized and reported at later stages of follow-up, precluding the ideal comparison of all clinical  
38  
39 significant adverse events among procedures. Secondly, we anticipate varied reporting of mild or  
40  
41 moderate adverse event, for example, post-surgical pain, which may be considered normal and not  
42  
43 reported in some studies.  
44  
45  
46  
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56 *Secondary outcomes*  
57

58 1. Number of patients achieving diabetic management goals with respect to blood glucose, blood  
59  
60

1  
2  
3  
4 pressure and LDL-cholesterol defined as simultaneous achievement of HbA1c of less than 7.0%,  
5  
6 LDL-C of less than 2.59mmol/L, and systolic BP of less than 140 mmHg,[25] or as defined by the  
7  
8  
9 studies

10  
11  
12 2. Weight loss is an important determinant of resolution of comorbidities including type 2 diabetes  
13  
14 mellitus after bariatric surgery.[26] We will investigate anthropometric measurements including  
15  
16 percentage excess weight loss, body mass index, and weight at follow-up.  
17

18  
19  
20 3. Decrease in cardiovascular risk scores have been shown to translate into favorable  
21  
22 cardiovascular outcome post bariatric surgeries.[27] We will investigate the cardiovascular risk  
23  
24 score of validated tools, and parameters reflecting risk factor burden, including glycated  
25  
26 hemoglobin, fasting blood glucose, total cholesterol, low-density lipoprotein cholesterol, high-  
27  
28 density lipoprotein cholesterol, triglyceride, systolic and diastolic blood pressures.  
29

30  
31  
32 4. While persistence and relapse of type 2 diabetes mellitus is not uncommon post bariatric  
33  
34 surgeries, improvements can be reflected by the need for less intensive treatment.[28] We will  
35  
36 collect outcome data concerning change of medication burden, including number of patients  
37  
38 requiring less anti-diabetic drugs at follow-up, and number of patients achieving discontinuation  
39  
40 of insulin.  
41  
42

43  
44  
45 5. Number of patients exhibiting progression of diabetic retinopathy, nephropathy and neuropathy,  
46  
47 and number of patients experiencing myocardial infarction, stroke, amputation of at least one  
48  
49 digit, ischemic limb disease, and heart failure, and urine albumin/creatinine ratio as surrogate  
50  
51 marker for end organ damage.  
52  
53

54  
55  
56 6. All-cause mortality

57  
58  
59 Studies will not be excluded based on whether or not certain outcomes are reported.  
60

### Search methods for identification of studies

Comprehensive search of databases listed below will be conducted using medical subject headings (MeSH) or Embase subject headings (Emtree), as applicable, and text words, for studies in human, from inception of each database to December 2019, without language, or publication type restrictions. The search strategies are adapted from a previous research,[10] revised with input from the project team, and refined by a methodologist with expertise in systematic review searching. The search will be updated toward the end of the review to ensure efficacy of retrieving eligible studies. Cross-referencing of relevant systemic reviews retrieved and included studies will be conducted. Preliminary search strategy for PubMed, which will be adapted for each other database as required, is shown in supplementary material 1. We will search the following databases:

1. PubMed (Ovid interface)
2. EMBASE
3. Ovid Cochrane Central Register of Controlled Trials (CENTRAL)
4. US National Institutes of Health Ongoing Trials Register (<https://www.clinicaltrials.gov/>).
5. WHO International Clinical Trials Registry Platform (<http://www.who.int/ictrp/en/>).
6. International Standard Randomized Controlled Trial Number Register (<http://www.isrctn.org/>)
7. Trials Central (<http://www.trialscentral.org/>).

### Study records

Selection of eligible studies and data abstraction will be performed by two independent reviewers, with Covidence, an Internet based software facilitating collaboration. Screening questions based on the inclusion and exclusion criteria, and data extraction form (See supplementary file 2 for

1  
2  
3  
4 preliminary screening questions and data extraction form) will be developed, tailored in  
5  
6 Covidence, tested and refined by the team through discussion and pilot calibration exercises  
7  
8  
9 before formal screening and data extraction, respectively. Discrepancies will be resolved first with  
10  
11 discussion, and, if necessary, by a third arbitrator. We will contact investigators of studies, by a  
12  
13 maximal of three email attempts, if additional information is warranted for evaluation of study  
14  
15 eligibility, data extraction and risk of bias assessment of included studies.  
16  
17  
18

### 19 **Selection of studies**

20  
21  
22 Literature search results will be imported to Covidence, which will identify and remove  
23  
24 duplicates. Titles and abstracts of all references will be screened, and references will be graded as  
25  
26 relevant, maybe relevant, and not relevant. Relevant or maybe relevant references will be subject  
27  
28 to full-text screening for final decision upon eligibility. Reasons for excluding studies will be  
29  
30 recorded. Reviewers will not be blinded to journal titles or study authors or affiliations in study  
31  
32 selection. Included studies will be checked for potential double counting by identifying multiple  
33  
34 reports of the same study, overlapping or companion studies. We will record the selection process  
35  
36 in detail. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram  
37  
38 and characteristics of excluded studies will be presented.  
39  
40  
41  
42  
43  
44

### 45 **Data extraction and management**

46  
47  
48 The following information will be extracted for subsequent risk of bias assessment, data synthesis,  
49  
50 and appraisal of possible effect modifiers:  
51

- 52  
53 1. Study characteristics: Methodology characteristics including study design, methods for  
54  
55 sequence generation, allocation concealment, blinding of patients, interveners and/or evaluators of  
56  
57 all or some outcomes, whether intentional analysis is adopted, setting, time span of enrollment,  
58  
59  
60

1  
2  
3  
4 duration of follow-up, number and location of centers, funding, potential conflicts of interest, key  
5  
6 conclusion of authors of studies, and whether the study is concluded early, will be documented.  
7  
8

9 2. Participants: Number of participants, diagnostic criteria of type 2 diabetes mellitus, inclusion  
10  
11 and exclusion criteria, and baseline characteristics of participants including age, body mass index,  
12  
13 ethnicity, gender, duration of type 2 diabetes, will be extracted.  
14  
15  
16

17 3. Interventions: number of participants allocated to, and number and reasons for attrition of each  
18  
19 comparator arm will be extracted along with description of interventions, co-interventions, if any,  
20  
21 and comparisons.  
22  
23

24 4. Outcomes: Planned and reported primary and secondary outcomes and time of observation will  
25  
26 be extracted and compared for discrepancies. Criteria for diagnosis or evaluation will be extracted.  
27  
28 For laboratory investigation, assay method, unit, and reference range will be extracted. Laboratory  
29  
30 data adopting different analysis method will be transformed if known linear correlation have been  
31  
32 reported. For cardiovascular risk score, name of tool used, score range, if higher or lower value is  
33  
34 favorable, will be extracted. Necessary transformation will be made when indicated to ensure  
35  
36 alignment of the scales. For adverse events, information regarding timing, severity, presentation,  
37  
38 diagnosis, and management of all reported adverse events will be extracted, and will be sent to  
39  
40 two independent reviewers, who are blind to information regarding from which study the data is  
41  
42 extracted, and what intervention preceded the onset of the adverse event, for score translation. A  
43  
44 third arbitrator, also blind to information regarding study and intervention, will resolve  
45  
46 inconsistencies despite discussion. The sequence in which adverse events are organized will be  
47  
48 randomized by an online List Randomizer (<https://www.random.org>) before score translation, to  
49  
50 further minimize the risk of bias. Corresponding score for each intervention in each study will be  
51  
52  
53  
54  
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56  
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60

1  
2  
3  
4 added for data synthesis.  
5

6 Means and measures of dispersion will be approximated from figures in the reports by measuring  
7  
8 tools of Adobe Acrobat Reader when necessary if original data cannot be obtained from the  
9  
10 authors. Whenever possible, we will use results from an intention to treat analysis. If number of  
11  
12 missing data doesn't concord with attrition, the reason will be specified.  
13  
14  
15

### 16 **Risk of bias (quality) assessment**

17  
18 Risk of bias at the individual study level will be assessed by two independent reviewers, using the  
19  
20 Cochrane risk of bias tool. Studies will be classified to be at high, low or unclear risk of bias based  
21  
22 on adequacy of sequence generation, allocation concealment, blinding of participants and  
23  
24 personnel, blinding of outcome assessment, method of addressing incomplete data, selective  
25  
26 reporting, and other biases. Blinding of outcome assessment will be subdivided into subjective and  
27  
28 objective assessments. Subjective assessments include evaluation of disease remission, adverse  
29  
30 events, achieving treatment goals, progression of diabetic complications, and medication.  
31  
32 Objective assessments include anthropometric measurements, cardiovascular risk score, laboratory  
33  
34 investigations, and all-cause mortality. Disagreements will be resolved first by discussion and then  
35  
36 by consulting a third arbitrator. Graphic representations of potential bias within and across studies  
37  
38 will be generated using RevMan 5.1 (Review Manager 5.1).  
39  
40  
41  
42  
43  
44  
45  
46  
47

### 48 **Data analysis**

#### 49 **Measures of treatment effect.**

50  
51  
52 Dichotomous outcomes will be pooled using risk ratio (RR) with 95% credible intervals (CrI) or  
53  
54 confidence intervals (CI), as applicable. Continuous outcomes will be pooled using weighted  
55  
56 mean differences (with 95% CrI or CI) if uniform measurement scales are used, or standardized  
57  
58  
59  
60

1  
2  
3  
4 mean differences (with 95% CrI or CI) if different measurement scales are adopted. Adverse event  
5  
6 profiles will be assessed with mean (with 95% CrI or CI) of weighted adverse events per patient of  
7  
8 each surgical procedure, determined by cumulative adverse event score divided by the number of  
9  
10 patients in the corresponding treatment arm in each study.  
11  
12

### 13 14 Dealing with missing data

15  
16 In case of missing data, such as the standard deviation or other important variability measures, we  
17  
18 will first try to calculate through algebraic manipulation of the available information such as  
19  
20 confidence intervals, p or t values.[29] When such attempts fail, an imputation method will be  
21  
22 used,[30] which will be tested in sensitivity analysis.  
23  
24  
25

### 26 27 Assessment of heterogeneity

28  
29 Heterogeneity among included studies will be appraised by evaluating the variability in  
30  
31 participants (including age, ethnicity, body mass index, and comorbidities), in trials (including  
32  
33 blinding, attrition, surgical techniques, and co-interventions). Statistical heterogeneity will be  
34  
35 assessed by the Cochran Q (Chi-squared) and Higgins I-squared statistics. If high levels of  
36  
37 heterogeneity among the trials exist ( $Q$  statistic  $\leq 0.10$  and/or  $I^2$  value  $> 50\%$ ), the study design and  
38  
39 characteristics in the included studies will be analyzed. Source of heterogeneity will be rigorously  
40  
41 investigated by subgroup analysis, sensitivity analysis, and meta-regression.  
42  
43  
44  
45  
46  
47

### 48 49 Data synthesis

50  
51 If studies are sufficiently homogeneous in terms of design and comparator, we will conduct  
52  
53 network meta-analyses in a random-effect model using generalized linear model under a Bayesian  
54  
55 framework, while assessing for consistency between direct and indirect estimates of comparative  
56  
57 effectiveness of each study arm.[31, 32] Geometry of the network will be depicted by a network  
58  
59  
60



1  
2  
3  
4 map, and the treatments that are directly compared against each other and the amount of evidence  
5  
6 available for each treatment and its comparator will be described qualitatively. The assumption of  
7  
8 transitivity will be appreciated and systematic tabulated information extracted regarding potential  
9  
10 effect modifiers, including patient and study characteristics, will be provided. Non-informative  
11  
12 priors for model parameters will be used. We will run Markov Chain Monte Carlo sampling for  
13  
14 four chains. Results will be based on 100000 iterations, after a 100000-iterations burn in.  
15  
16  
17  
18  
19 Convergence will be judged based on visual inspection of time-series plots and the Brooks-  
20  
21 Gelman-Rubin test. Goodness of fit of the model will be tested using the Deviance Information  
22  
23 Criterion. Local inconsistency will be evaluated by comparing the magnitude and direction of  
24  
25 effect estimates from direct and indirect comparisons. Global inconsistency will be evaluated with  
26  
27 the pairwise p-values for inconsistency via back-calculation. Findings will be summarized in  
28  
29 treatment-level forest plots, rank probability matrix and rank plot, with the latter two illustrating  
30  
31 empirical probabilities that each treatment is ranked from best through worst, along with  
32  
33 corresponding estimates and absolute difference of pairwise comparisons between interventions.  
34  
35  
36  
37  
38 To determine adverse event profiles, a linear regression analysis will be performed with type of  
39  
40 surgical procedure as covariates, the adverse event outcome as the dependent variable, and a  
41  
42 dummy variable for each of the studies to adjust for differences in risk profiles and study setup  
43  
44 between trials, as described by Kessler et al.[33]  
45  
46  
47  
48  
49  
50 An alternative method based on graph theory methodology under a frequentist framework will be  
51  
52 adopted to validate the findings with league tables and rankings of treatments.[34, 35]  
53  
54  
55  
56 All statistical analysis and graphical procedures will be conducted by R software (Version 3.3.3,  
57  
58 The R Project for Statistical Computing).  
59  
60

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3  
4 If heterogeneity is substantial ( $I^2 > 90\%$ ), meta-analysis will not be performed; a narrative,  
5  
6 qualitative summary will be presented in text and tables to summarize the characteristics of the  
7  
8 included studies and findings both within and between the included studies, in accordance with the  
9  
10 guidance from the Centre for Reviews and Dissemination.  
11  
12

### 13 14 Investigation of heterogeneity and subgroup analysis

15  
16 Heterogeneity among included studies will be appraised, if possible, by evaluating the variability  
17  
18 in potential effect modifiers, including characteristics of participants (including age, gender-  
19  
20 distribution, baseline body mass index, duration of type 2 diabetes mellitus, and comorbidities), in  
21  
22 trials (including whether exclusively including patients with type 2 diabetes mellitus, whether  
23  
24 including patients with baseline BMI less than 30, less than 35, less than 40, over 50, or over  
25  
26 60kg/m<sup>2</sup>, whether including patients over 60 years old, whether adopting intensive life-style  
27  
28 intervention as control or during the follow-up period of bariatric surgeries in the same effective  
29  
30 arm, whether surgical procedures are laparoscopic, open, or both, whether an intention to treat  
31  
32 analysis was reported, publication year, publication status, and risk of bias items including  
33  
34 attrition, blinding, and missing data) through meta-regression analysis for primary outcomes.  
35  
36

37  
38 Subgroup analysis will be performed based on factors identified through meta-regression. The  
39  
40 likely impact of risk of bias, if studies of moderate or high risk of bias are included in the analysis,  
41  
42 upon the results will be discussed. Robustness of primary findings will be tested with sensitivity  
43  
44 analysis by excluding trials with high risk of bias, by performing leave-one-out analysis, and by  
45  
46 excluding studies requiring data imputation.  
47  
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### 54 55 56 Meta bias

57  
58 Reports will be checked against protocol to detect potential selective reporting and inconsistencies  
59  
60

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4 with respect to description of the design, number of patients analyzed, chosen significance level,  
5  
6 and outcomes, among all reports of the same study. Reporting bias will be further explored by the  
7  
8 Egger test. Visual inspection of funnel plots, along with trim-and-fill analysis for estimating and  
9  
10 adjusting for the number and outcomes of missing studies, will be performed if  $\geq 10$  studies are  
11  
12 available.  
13  
14  
15

### 16 17 Grading of quality of evidence

18  
19 The overall quality of the body of evidence of the meta-analysis findings, if feasible, will be  
20  
21 judged using the Grading of Recommendations, Assessment, Development and Evaluation  
22  
23 approach. We will assess the quality of the evidence across the domains of risk of bias,  
24  
25 consistency, directness, precision, publication bias, and additional domains where appropriate.  
26  
27  
28 The overall strength of evidence will be adjudicated as high, moderate, low or very low for each  
29  
30 outcome measure.  
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## 38 DISCUSSION

39  
40 Obesity is an important risk factor for type 2 diabetes mellitus, and bariatric surgery is effective in  
41  
42 inducing weight-loss and resolution of obesity-related comorbidities.[36] Bariatric surgeries are  
43  
44 growing worldwide, but are still underused.[37] Barriers preventing patients' access to bariatric  
45  
46 surgeries include concerns about postoperative complications, misperception regarding bariatric  
47  
48 surgery effectiveness, and professional society statement heterogeneity.[38] It is important to  
49  
50 appreciate the long-term benefit-risk ratio of bariatric surgeries in adults with type 2 diabetes  
51  
52 mellitus, to facilitate decision-making by patients, clinicians, and policy makers. This review will  
53  
54 summarize the current scientific findings, and will identify gaps for further research.  
55  
56  
57  
58  
59  
60

**ETHICS AND DISSEMINATION** Ethics approval is not required, because individual patient data will not be included in this review. This review will be published in a peer-reviewed journal.

**ACKNOWLEDGEMENTS** None.

**AUTHOR CONTRIBUTORS** ML is the guarantor. Research question and eligibility criteria were defined by ML, CJZ, LD, YXF, YLZ, HL, DWQ, SFT, JQC, and QH. LD, CJZ, and YXF contributed to the development of search strategy and data extraction form. CJZ provided methodological support for this review. The manuscript was first drafted by LD and YXF, and was revised and approved by all authors.

**COMPETING INTERESTS** None declared.

**FUNDING** This work was supported by the National Natural Science Foundation of China grant number 81570699, 81620108004, 81370895, and Tianjin Municipal Science and Technology Commission grant number 17ZXMFSY00150. The funders have no input on the protocol development, and will not have influence upon review conduct, data analysis, interpretation or publication of the study results.

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**LICENCE STATEMENT** Other than as permitted in any relevant BMJ Author's Self Archiving Policies, we confirm this Work has not been accepted for publication elsewhere, is not being

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6 authors consent to publication of this Work and authorize the granting of this licence.  
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## 10 11 REFERENCE

- 12  
13  
14 1. Sheng B, Truong K, Spitler H, et al. The Long-Term Effects of Bariatric Surgery on Type 2 Diabetes  
15  
16 Remission, Microvascular and Macrovascular Complications, and Mortality: a Systematic Review and  
17  
18 Meta-Analysis. *Obes Surg* 2017;27(10):2724-32 doi: 10.1007/s11695-017-2866-4 [published Online  
19  
20 First: 2017/08/13]  
21  
22  
23  
24 2. Pareek M, Schauer PR, Kaplan LM, et al. Metabolic Surgery: Weight Loss, Diabetes, and Beyond.  
25  
26 *Journal of the American College of Cardiology* 2018;71(6):670-87 doi: 10.1016/j.jacc.2017.12.014  
27  
28  
29 3. De Luca M, Tie T, Ooi G, et al. Mini Gastric Bypass-One Anastomosis Gastric Bypass (MGB-  
30  
31 OAGB)-IFSO Position Statement. *Obesity Surgery* 2018;28(5):1188-206 doi: 10.1007/s11695-018-  
32  
33 3182-3  
34  
35  
36 4. Brown WA, Ooi G, Higa K, et al. Single Anastomosis Duodenal-Ileal Bypass with Sleeve  
37  
38 Gastrectomy/One Anastomosis Duodenal Switch (SADI-S/OADS) IFSO Position Statement. *Obesity*  
39  
40 *Surgery* 2018;28(5):1207-16 doi: 10.1007/s11695-018-3201-4  
41  
42  
43  
44 5. ASMBS policy statement on gastric plication. *Surgery for obesity and related diseases : official*  
45  
46 *journal of the American Society for Bariatric Surgery* 2011;7(3):262 doi: 10.1016/j.soard.2011.03.004  
47  
48 [published Online First: 2011/05/31]  
49  
50  
51  
52 6. Kodama S, Fujihara K, Horikawa C, et al. Network meta-analysis of the relative efficacy of bariatric  
53  
54 surgeries for diabetes remission. *Obesity reviews : an official journal of the International Association*  
55  
56 *for the Study of Obesity* 2018;19(12):1621-29. doi: 10.1111/obr.12751 [published Online First:  
57  
58  
59  
60

1  
2  
3  
4 2018/10/03]

5  
6 7. Kang JH, Le QA. Effectiveness of bariatric surgical procedures: A systematic review and network  
7  
8 meta-analysis of randomized controlled trials. *Medicine (Baltimore)* 2017;96(46):e8632 doi:

9  
10 10.1097/md.00000000000008632 [published Online First: 2017/11/18]

11  
12  
13  
14 8. Buchwald H, Estok R, Fahrbach K, et al. Trends in mortality in bariatric surgery: a systematic  
15  
16 review and meta-analysis. *Surgery* 2007;142(4):621-32; discussion 32-5 doi:

17  
18 10.1016/j.surg.2007.07.018 [published Online First: 2007/10/24]

19  
20  
21  
22 9. Khan S, Rock K, Baskara A, et al. Trends in bariatric surgery from 2008 to 2012. *Am J Surg*  
23  
24 2016;211(6):1041-6 doi: 10.1016/j.amjsurg.2015.10.012 [published Online First: 2016/01/15]

25  
26  
27 10. Colquitt JL, Pickett K, Loveman E, et al. Surgery for weight loss in adults. *Cochrane Database of*  
28  
29 *Systematic Reviews* 2014;2014(8) doi: 10.1002/14651858.CD003641.pub4

30  
31  
32 11. Courcoulas AP, King WC, Belle SH, et al. Seven-year weight trajectories and health outcomes in  
33  
34 the Longitudinal Assessment of Bariatric Surgery (LABS) study. *JAMA surgery* 2018;153(5):427-34  
35  
36 doi: 10.1001/jamasurg.2017.5025

37  
38  
39 12. Ahmed B, King WC, Gourash W, et al. Long-term weight change and health outcomes for sleeve  
40  
41 gastrectomy (SG) and matched Roux-en-Y gastric bypass (RYGB) participants in the Longitudinal  
42  
43 Assessment of Bariatric Surgery (LABS) study. *Surgery* 2018;164(4):774-83. doi:

44  
45 10.1016/j.surg.2018.06.008 [published Online First: 2018/08/25]

46  
47  
48 13. Miras AD, le Roux CW. Metabolic surgery: Shifting the focus from glycaemia and weight to end-  
49  
50 organ health. *The Lancet Diabetes and Endocrinology* 2014;2(2):141-51 doi: 10.1016/S2213-

51  
52 8587(13)70158-X

53  
54  
55 14. Kabir A, Mousavi S, Pazouki A. The Complications of Bariatric Surgery Patients with Type 2  
56  
57  
58  
59  
60

- 1  
2  
3  
4 Diabetes in the World: A systematic Review and Meta-Analysis. *Current diabetes reviews* 2018 doi:  
5  
6 10.2174/1573399814666180403164529 [published Online First: 2018/04/07]  
7  
8  
9 15. Chang SH, Freeman NLB, Lee JA, et al. Early major complications after bariatric surgery in the  
10  
11 USA, 2003–2014: a systematic review and meta-analysis. *Obesity Reviews* 2018;19(4):529-37 doi:  
12  
13 10.1111/obr.12647  
14  
15  
16 16. Hopkins JC, Howes N, Chalmers K, et al. Outcome reporting in bariatric surgery: an in-depth  
17  
18 analysis to inform the development of a core outcome set, the BARIACT Study. *Obesity reviews*  
19  
20 2015;16(1):88-106 doi: 10.1111/obr.12240  
21  
22  
23 17. Frisch A, Chandra P, Smiley D, et al. Prevalence and clinical outcome of hyperglycemia in the  
24  
25 perioperative period in noncardiac surgery. *Diabetes Care* 2010;33(8):1783-8 doi: 10.2337/dc10-0304  
26  
27 [published Online First: 2010/05/04]  
28  
29  
30  
31 18. Black S, Kraemer K, Shah A, et al. Diabetes, Depression, and Cognition: a Recursive Cycle of  
32  
33 Cognitive Dysfunction and Glycemic Dysregulation. *Curr Diab Rep* 2018;18(11):118 doi:  
34  
35 10.1007/s11892-018-1079-0 [published Online First: 2018/09/30]  
36  
37  
38 19. Cryer PE. Severe hypoglycemia predicts mortality in diabetes. *Diabetes Care* 2012;35(9):1814-6  
39  
40 doi: 10.2337/dc12-0749 [published Online First: 2012/08/28]  
41  
42  
43 20. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-  
44  
45 analysis protocols (PRISMA-P) 2015 statement. *Systematic reviews* 2015;4(1):1 doi: 10.1186/2046-  
46  
47 4053-4-1  
48  
49  
50  
51 21. Hutton B, Salanti G, Caldwell DM, et al. The PRISMA extension statement for reporting of  
52  
53 systematic reviews incorporating network meta-analyses of health care interventions: checklist and  
54  
55 explanations. *Ann Intern Med* 2015;162(11):777-84 doi: 10.7326/m14-2385 [published Online First:  
56  
57  
58  
59  
60

1  
2  
3  
4 2015/06/02]

5  
6 22. Buse JB, Caprio S, Cefalu WT, et al. How Do We Define Cure of Diabetes? *Diabetes Care*

7  
8  
9 2009;32(11):2133.

10  
11 23. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with  
12 evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240(2):205-13.

13  
14  
15  
16 [published Online First: 2004/07/27]

17  
18 24. National Cancer Institute Common Terminology Criteria for Adverse Events v5.0 (CTCAE).

19  
20 Available:

21  
22  
23  
24  
25 [https://ctep.cancer.gov/protocoldevelopment/electronic\\_applications/docs/CTCAE\\_v5\\_Quick\\_Referen](https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf)  
26  
27  
28 [ce\\_8.5x11.pdf](https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf)

29  
30 25. American Diabetes Association. Standards of medical care in diabetes—2016. *Diabetes Care*

31  
32 2016;39(suppl 1):S1-S106.

33  
34 26. Polovina S. Management of obesity related conditions through weight. *Obesity Facts* 2018;11:20

35  
36  
37 doi: 10.1159/000489691

38  
39 27. Vest AR, Heneghan HM, Agarwal S, et al. Bariatric surgery and cardiovascular outcomes: A

40  
41  
42 systematic review. *Heart* 2012;98(24):1763-77 doi: 10.1136/heartjnl-2012-301778

43  
44 28. Rubino F, Nathan DM, Eckel RH, et al. Metabolic Surgery in the Treatment Algorithm for Type 2

45  
46  
47  
48 Diabetes: a Joint Statement by International Diabetes Organizations. *Surgery for obesity and related*  
49  
50  
51 *diseases* 2016;12(6):1144-62 doi: 10.1016/j.soard.2016.05.018

52  
53 29. Deeks JJ, Higgins JPT, Altman DG (editors) on behalf of the Cochrane Statistical Methods Group.

54  
55 Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Churchill R, Chandler J,

56  
57  
58 Cumpston MS (editors), *Cochrane Handbook for Systematic Reviews of Interventions* version 5.2.0



1  
2  
3  
4 (updated June 2017), Cochrane, 2017  
5

6 30. Furukawa TA, Barbui C, Cipriani A, et al. Imputing missing standard deviations in meta-analyses  
7  
8 can provide accurate results. *J Clin Epidemiol* 2006;59(1):7-10 doi: 10.1016/j.jclinepi.2005.06.006  
9

10 [published Online First: 2005/12/20]  
11

12  
13  
14 31. van Valkenhoef G, Lu G, de Brock B, et al. Automating network meta-analysis. *Research synthesis*  
15  
16 *methods* 2012;3(4):285-99 doi: 10.1002/jrsm.1054 [published Online First: 2012/12/01]  
17

18  
19 32. van Valkenhoef G, Dias S, Ades AE, et al. Automated generation of node-splitting models for  
20  
21 assessment of inconsistency in network meta-analysis. *Research synthesis methods* 2016;7(1):80-93  
22

23 doi: 10.1002/jrsm.1167 [published Online First: 2015/10/16]  
24

25  
26  
27 33. Kessler TM, Bachmann LM, Minder C, et al. Adverse event assessment of antimuscarinics for  
28  
29 treating overactive bladder: a network meta-analytic approach. *PLoS One* 2011;6(2):e16718. doi:  
30

31 10.1371/journal.pone.0016718 [published Online First: 2011/03/05]  
32  
33

34  
35 34. Konig J, Krahn U, Binder H. Visualizing the flow of evidence in network meta-analysis and  
36  
37 characterizing mixed treatment comparisons. *Statistics in medicine* 2013;32(30):5414-29 doi:  
38

39 10.1002/sim.6001 [published Online First: 2013/10/15]  
40  
41

42  
43 35. Krahn U, Binder H, Konig J. A graphical tool for locating inconsistency in network meta-analyses.  
44

45 *BMC medical research methodology* 2013;13:35 doi: 10.1186/1471-2288-13-35 [published Online  
46

47 First: 2013/03/19]  
48

49  
50 36. Singh GM, Danaei G, Farzadfar F, et al. The age-specific quantitative effects of metabolic risk  
51

52 factors on cardiovascular diseases and diabetes: a pooled analysis. *PLoS One* 2013;8(7):e65174 doi:  
53

54 10.1371/journal.pone.0065174 [published Online First: 2013/08/13]  
55  
56

57  
58 37. Ponce J, Nguyen NT, Hutter M, et al. American Society for Metabolic and Bariatric Surgery  
59  
60

1  
2  
3  
4 estimation of bariatric surgery procedures in the United States, 2011-2014. *Surgery for obesity and*  
5  
6  
7 *related diseases : official journal of the American Society for Bariatric Surgery* 2015;11(6):1199-200  
8  
9 doi: 10.1016/j.soard.2015.08.496 [published Online First: 2015/10/20]  
10

11  
12 38. Imbus JR, Voils CI, Funk LM. Bariatric surgery barriers: a review using Andersen's Model of  
13  
14 Health Services Use. *Surgery for obesity and related diseases : official journal of the American Society*  
15  
16  
17 *for Bariatric Surgery* 2018;14(3):404-12 doi: 10.1016/j.soard.2017.11.012 [published Online First:  
18  
19 2017/12/19]  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
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## Supplementary material 1

### **Preliminary Search Strategy in Medline (Ovid interface) for Comparative long-term effectiveness and safety of primary bariatric surgeries in treating type 2 diabetes mellitus in adults: a protocol for systematic review and network meta-analysis of randomized controlled trials**

#1 exp obesity/

#2 exp type 2 diabetes mellitus/

#3 exp weight loss/

#4 obes\*.ti,ab.

#5 over?weight.ti,ab.

#6 diabetes.ti,ab.

#7 T2D\*.ti,ab.

#8 NIDDM.ti,ab.

#9 or/1-8

#10 obesity/su

#11 exp Obesity, Morbid/su

#12 exp bariatric surgery/

#13 (surg\* adj5 bariatric).ti,ab.

#14 anti?obesity adj5 surg\*.ti,ab.

#15 malabsorptive adj5 procedure\*.ti,ab.

#16 (obes\* adj5 surg\*).ti,ab.

#17 (metaboli\* adj5 surg\*).ti,ab.

#18 exp gastric bypass/

#19 (gastroplast\* or gastrogastrostom\* or gastro?gastrostom\* or gastroenterostom\* or (gastric bypass) or (gastric surger\*) or (restrictive surger\*)).ti,ab.

#20 ((one Anastomosis) or (one-Anastomosis) or mini or (single Anastomosis)) adj5 (bypass or switch).ti,ab.

#21 ((greater curvature) or (gastric\*)) adj5 plicat\*.ti,ab.

1  
2  
3  
4 #22 gastrectom\*.ti,ab.

5 #23 LSG.ti,ab.

6  
7 #24 VSG.ti,ab.

8  
9 #25 gastrointestinal adj5 surg\*.ti,ab.

10  
11 #26 gastrointestinal diversion\*.ti,ab.

12  
13 #27 exp biliopancreatic diversion/  
14

15 #28 biliopancreatic diversion.ti,ab.

16  
17 #29 biliopancreatic bypass.ti,ab.

18  
19 #30 gastric adj5 stapl\*.ti,ab.

20  
21 #31 duodenal adj5 switch\*.ti,ab.

22  
23 #32 gastric band\*.ti,ab.

24  
25 #33 silicon band\*.ti,ab.

26  
27 #34 exp gastroenterostomy/  
28

29 #35 gastroplasty/  
30

31 #36 LAGB.ti,ab.

32  
33 #37 stomach adj5 stapl\*.ti,ab.

34  
35 #38 laparoscop\* adj5 band\*.ti,ab.

36  
37 #39 lap?band\*.ti,ab.

38  
39 #40 malabsorptive adj5 surg\*.ti,ab.

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41 #41 mason\* adj5 procedure.ti,ab.

42  
43 #42 Roux-en-Y.ti,ab.

44  
45 #43 anastomosis, Roux-en-Y/  
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47 #44 or/12-43

48 #45 9 and 44

49  
50 #46 10 or 11 or 45

51  
52 #47 limit 46 to yr=2004 - 2018

53  
54 #48 limit 47 to (clinical trial, phase iii or clinical trial, phase iv or clinical trial  
55 or comparative study or controlled clinical trial or evaluation studies or  
56 guideline or meta analysis or multicenter study or practice guideline or  
57 randomized controlled trial or scientific integrity review or technical report or  
58  
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4 twin study or validation studies or systemic review)

5 **#49** randomized controlled trial.pt

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7 **#50** controlled clinical trial.pt

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9 **#51** randomized.ab

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11 **#52** placebo.ab

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13 **#53** clinical trials as topic.sh.

14  
15 **#54** randomly.ab

16  
17 **#55** trial.ti

18  
19 **#56** groups.ti,ab

20  
21 **#57** or/49-56

22  
23 **#58** exp animals/ not humans.sh.

24  
25 **#59** 57 NOT 58

26  
27 **#60** 47 and 59

28  
29 **#61** 48 or 60

30 ab=abstract; adj = adjacent; exp =exploded; pt=publication type; sh = MeSH  
31 (Medical subject heading); su=surgery; ti=title; the asterisk mark (\*) substitutes  
32 one or no characters; the question mark (?) substitutes one character.  
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**Supplementary material 2**

**Preliminary Screening questions and Data Extraction Form for Comparative long-term effectiveness and safety of primary bariatric surgeries in treating type 2 diabetes mellitus in adults: a protocol for systematic review and network meta-analysis of randomized controlled trials**

Reference code \_\_\_\_\_

<b>Basic information</b>			
Code of Original study		Code of Report	
Code of Valuator		Date of Evaluation	
Contact info of Author			
Quotation format(author, study title, journal, Year of publication, volume)			
<b>Inclusion and exclusion criteria</b>			
Inclusion criteria	<p><b>Participants</b></p> <p>① Include overweight or obese adults with type 2 diabetes mellitus <span style="float:right">yes <input type="checkbox"/> no <input type="checkbox"/></span></p> <p><b>Interventions and control</b></p> <p>② Procedures and/or controls involved</p> <p><i>Roux-en-Y gastric bypass</i> <input type="checkbox"/> <i>sleeve gastrectomy</i> <input type="checkbox"/></p> <p><i>adjustable gastric banding</i> <input type="checkbox"/></p> <p><i>biliopancreatic diversion with duodenal switch</i> <input type="checkbox"/></p> <p><i>greater curvature plication</i> <input type="checkbox"/> <i>one-anastomosis gastric bypass</i> <input type="checkbox"/></p> <p><i>single anastomosis duodenal-ileal bypass with sleeve gastrectomy</i> <input type="checkbox"/></p> <p><i>Other surgical procedure(s) except procedures no longer performed, (including biliopancreatic diversion without duodenal switch, jejunoileal bypass, horizontal or vertical gastropasty, and banding that is not adjustable)</i> _____ <input type="checkbox"/></p> <p><i>non-surgical treatments</i> <input type="checkbox"/></p> <p><b>Comparisons</b></p> <p>③ Includes comparisons of at least two of the items above <span style="float:right">yes <input type="checkbox"/> no <input type="checkbox"/></span></p> <p><b>Study designs</b></p> <p>④ Randomized controlled trial <span style="float:right">yes <input type="checkbox"/> no <input type="checkbox"/></span></p> <p>⑤ Duration of follow-up <math>\geq 3</math> years <span style="float:right">yes <input type="checkbox"/> no <input type="checkbox"/></span></p>		
Exclusion criteria	<p><b>Participants</b></p> <p>① Restrict participatns to specific diseases other than type 2 diabetes mellitus <span style="float:right">yes <input type="checkbox"/> no <input type="checkbox"/></span></p> <p>② Do not include adults <span style="float:right">yes <input type="checkbox"/> no <input type="checkbox"/></span></p> <p>③ Do not include participants with type 2 diabetes mellitus</p> <p><b>Interventions and comparison</b></p>		

	<p>④ Revisional procedures <span style="float: right;">yes <input type="checkbox"/> no <input type="checkbox"/></span>          Comparisons between/among surgical procedure(s) no longer performed (biliopancreatic diversion without duodenal switch, jejunoileal bypass, horizontal or vertical gastroplasty, not adjustable banding, other _____) or between such procedures and non-surgical treatment <span style="float: right;">yes <input type="checkbox"/> no <input type="checkbox"/></span>          Comparisons between different techniques of the same procedure <span style="float: right;">yes <input type="checkbox"/> no <input type="checkbox"/></span></p> <p><b>Study designs</b></p> <p>⑤ Non-RCT, comparative studies <span style="float: right;">yes <input type="checkbox"/> no <input type="checkbox"/></span>          ⑥ Duration of follow-up &lt; 3 year <span style="float: right;">yes <input type="checkbox"/> no <input type="checkbox"/></span>          ⑦ Animal studies. <span style="float: right;">yes <input type="checkbox"/> no <input type="checkbox"/></span></p>
Conclusion of inclusion or exclusion	<input type="checkbox"/> inclusion <input type="checkbox"/> exclusion <input type="checkbox"/> undetermined Support for judgement: _____ _____

<b>Characteristics of Methodology</b>																										
Study design(multiple choice)	<input type="checkbox"/> RCT <input type="checkbox"/> quasi-RCT <input type="checkbox"/> non-RCT <input type="checkbox"/> cluster randomized trial <input type="checkbox"/> cross-over trial Support for judgement: _____																									
Duration of study	Study beginning time: _____ year _____ month Study ending time: _____ year _____ month Mean(±SD) or median[inter-quartile range] follow-up period: _____																									
Sequence generation	randomized <input type="checkbox"/> non-randomized <input type="checkbox"/> quasi-randomized <input type="checkbox"/> undetermined <input type="checkbox"/> Support for judgement: _____																									
allocation concealment	yes <input type="checkbox"/> no <input type="checkbox"/> undetermined <input type="checkbox"/> Support for judgement: _____																									
Blinding participants*	<input type="checkbox"/> patients <input type="checkbox"/> intervenor <input type="checkbox"/> evaluator of all outcomes <input type="checkbox"/> evaluator of some, but not all outcomes <input type="checkbox"/> Statistical analyst comments(if blinding differs among outcomes): _____ Support for judgement: _____																									
Other factors that may introduce bias?	yes <input type="checkbox"/> no <input type="checkbox"/> Support for judgement: _____																									
Intentional analysis	yes <input type="checkbox"/> no <input type="checkbox"/> Support for judgement: _____																									
Other information of study	1. study site: single center <input type="checkbox"/> multi-center <input type="checkbox"/> Location of center(s) _____ 2. early conclusion of study: yes <input type="checkbox"/> no <input type="checkbox"/> 3. funding of study: _____ 4. potential conflict of interest: _____																									
Baseline information	comparable <input type="checkbox"/> ; non-comparable <input type="checkbox"/> ; undetermined <input type="checkbox"/> Support for judgement:( Mean±SD for continuous variables) <table style="width: 100%; border-collapse: collapse;"> <tr> <td></td> <td style="text-align: center;">intervention 1</td> <td style="text-align: center;">intervention2</td> <td style="text-align: center;">intervention3</td> <td style="text-align: center;">intervention4</td> </tr> <tr> <td>sex(M/F)</td> <td style="text-align: center;">/</td> <td style="text-align: center;">/</td> <td style="text-align: center;">/</td> <td style="text-align: center;">/</td> </tr> <tr> <td>Age(year)</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> </tr> <tr> <td>Weight(kg)</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> </tr> <tr> <td>BMI(kg/m<sup>2</sup>)</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> </tr> </table>		intervention 1	intervention2	intervention3	intervention4	sex(M/F)	/	/	/	/	Age(year)	±	±	±	±	Weight(kg)	±	±	±	±	BMI(kg/m <sup>2</sup> )	±	±	±	±
	intervention 1	intervention2	intervention3	intervention4																						
sex(M/F)	/	/	/	/																						
Age(year)	±	±	±	±																						
Weight(kg)	±	±	±	±																						
BMI(kg/m <sup>2</sup> )	±	±	±	±																						
<b>Characteristics of participants</b>																										
Total participants	_____																									
Settings	<input type="checkbox"/> hospital <input type="checkbox"/> community <input type="checkbox"/> nursing home <input type="checkbox"/> outpatient <input type="checkbox"/> chronic care institution Others: _____																									
Type of population	Healthy population: yes <input type="checkbox"/> no <input type="checkbox"/> BMI: BMI _____ to _____ kg/m <sup>2</sup> Or without complication BMI _____ to _____ kg/m <sup>2</sup> with complication BMI _____ to _____ kg/m <sup>2</sup> Type 2 diabetes: _____ Duration of type 2 diabetes: <input type="checkbox"/> unlimited <input type="checkbox"/> more than _____ months																									
Age	_____ to _____ years old   mean _____ SD _____ median _____ interquartile range _____																									
Sex	<input type="checkbox"/> Unlimited <input type="checkbox"/> Male only <input type="checkbox"/> Female only																									
Country	_____																									
Ethnicity	_____																									



Attrition	Lost to follow-up: Number of participants lost to follow-up: Group 1 _____, reason _____ Group 2 _____, reason _____ Group 3 _____, reason _____ Group 4 _____, reason _____		
	Drop-out: Number of drop-out participants: Group 1 _____, reason _____ Group 2 _____, reason _____ Group 3 _____, reason _____ Group 4 _____, reason _____		
<b>Intervention</b>			
Group	Number of Participants	Intervention	Description of intervention(intensity, frequency and duration etc.)
Group 1			
Group 2			
Group 3			
Group 4			
Integrity of interventions			
<b>Outcome Data</b>			
Planned outcomes	Planned: _____ Difference between report and plan: _____		
Planned time of Observation	Plan: _____ Difference between report and plan: _____		
Outcome data	Definition Diagnosis or evaluation: criteria for diagnosis or evaluation; Laboratory examination; assay method, unit, reference range; Scale: name, score range, state if higher or lower value is favorable If the evaluation time doesn't concord with the follow-up time, the time point of evaluation should be specified If number of missing data doesn't concord with attrition, the reason should be specified		
Full diabetes remission	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____		
Partial diabetes remission	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____		
Major adverse event	Evaluation criteria: _____ Criteria of major adverse effect: _____ Evaluation time (if not consistent) early complication: post-op _____ day; late complication: post-op _____ day- _____ year Reason for extra missing data _____		
Diabetes management goal	Evaluation criteria: _____ Evaluation time (if not consistent) _____		

including HbA1c, BP and LDL-C	Reason for extra missing data _____
Percentage excess weight loss (% EWL)	Definition: _____ Unit: <input type="checkbox"/> % <input type="checkbox"/> Other _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Body mass index (BMI) at follow-up	Definition: _____ Unit: <input type="checkbox"/> kg/m <sup>2</sup> <input type="checkbox"/> Other _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Weight (Wt) at follow-up	Definition: _____ Unit: <input type="checkbox"/> kg <input type="checkbox"/> Other _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Cardiovascular risk score	Scale name: _____ Score range: _____ which value is favorable <input type="checkbox"/> high score <input type="checkbox"/> low score Evaluation time (if not consistent) _____ Reason for extra missing data _____
Glycated hemoglobin (HbA1C)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Fasting blood glucose (FBG)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
total cholesterol (TC)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
low-density lipoprotein cholesterol (LDL)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
high-density lipoprotein cholesterol (HDL)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
triglyceride (TG)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Systolic blood pressure	Method: _____ Model _____ Unit: _____ Reference: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Diastolic blood pressure	Method: _____ Model _____ Unit: _____ Reference: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Requirement of less anti-diabetic drugs at follow-up	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
discontinuation of insulin	Evaluation criteria: _____ Evaluation time (if not consistent) _____

	Reason for extra missing data _____
Progression of diabetic retinopathy	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Progression of diabetic nephropathy	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Progression of diabetic neuropathy	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Number of pts experiencing myocardial infarction	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Number of pts experiencing stroke	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Number of pts experiencing amputation of at least one digit	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Number of pts experiencing ischemic limb disease	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Number of pts experiencing heart failure	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
urine albumin/creatinine ratio (ACR)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
All-cause mortality	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
<b>Other information</b>	
Key conclusion of authors	
Correspondence required	Study author contacted: yes <input type="checkbox"/> no <input type="checkbox"/> Study author replied: yes <input type="checkbox"/> no <input type="checkbox"/> Information asked: _____ Information provided: _____

Outcome data-Continuous data-1													
	Group 1 (Intervention_____)				Group 2 (Intervention_____)								
	Total number of participants	Reported cases for each outcome	mean	SD	Total amount	Case number	mean	SD	p-value	Estimate of effect	95%CI Lower limit	95%CI Upper limit	Comments (e.g., if the results shown in median and quartile range)
percentage excess weight loss													
BMI at follow-up													
Weight at follow-up													
Cardiovascular risk score													
Glycated hemoglobin (HbA1C)													
Fasting blood glucose (FBG)													
total cholesterol (TC)													
low-density lipoprotein													

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cholesterol (LDL)														
high-density lipoprotein cholesterol (HDL)														
triglyceride (TG)														
Systolic blood pressure (SBP)														
Diastolic blood pressure (DBP)														
urine albumin/creatinine ratio														
<b>Outcome data-Continuous data-2 (when applicable, i.e. more than 2 comparative arms involved)</b>														
	Group 3 (Intervention_____)				Group 4 (Intervention_____)									
	Total number of participants	Reported cases for each outcome	mean	SD	Total amount	Case number	mean	SD	p-value	Estimate of effect	95% CI Lower limit	95% CI Upper limit	Comments (e.g., if the results shown in median and quartile range)	
percentage excess weight loss														
BMI at follow-up														
Weight at follow-														

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up													
Cardiovascular risk score													
Glycated hemoglobin (HbA1C)													
Fasting blood glucose (FBG)													
total cholesterol (TC)													
low-density lipoprotein cholesterol (LDL)													
high-density lipoprotein cholesterol (HDL)													
triglyceride (TG)													
Systolic blood pressure (SBP)													
Diastolic blood pressure (DBP)													
urine albumin/creatinine ratio													

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Outcome data-dichotomous data-1											
	Group 1 (Intervention_____)			Group 2 (Intervention_____)							
	Total number of participants	Reported participants for each outcome	Case number	Total number of participants	Reported participants for each outcome	Total number of participants	p-value	Estimate of effect	95% CI Lower limit	95% CI Upper limit	Comments
Full remission of type 2 diabetes mellitsu											
Full or partial remission of type 2 diabetes mellitsu											
Achieve treatment goals with regard to blood glucose, blood pressure and lipids											
Requirement of less anti-diabetic drugs at follow-up											
Discontinuation of insulin											
Progression of diabetic retinopathy											
Progression of diabetic											

nephropathy											
Progression of diabetic neuropathy											
Number of patients experiencing myocardial infarction											
Number of patients experiencing stroke											
Number of patients experiencing amputation of at least one digit											
Number of patients experiencing ischemic limb disease											
Number of patients experiencing heart failure											
All-cause mortality											
<b>Outcome data-dichotomous data-2 (when applicable, i.e. more than 2 comparative arms involved)</b>											
	Group 3 (Intervention_____)			Group 4 (Intervention_____)							
	Total number of participants	Reported participants for each	Case number	Total number of participants	Reported participants for each	Total number of participants	p-value	Estimate of effect	95% CI Lower limit	95% CI Upper limit	Comments



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		outcome			outcome						
Full remission of type 2 diabetes mellitsu											
Full or partial remission of type 2 diabetes mellitsu											
Achieve treatment goals with regard to blood glucose, blood pressure and lipids											
Requirement of less anti-diabetic drugs at follow-up											
Discontinuation of insulin											
Progression of diabetic retinopathy											
Progression of diabetic nephropathy											
Progression of diabetic neuropathy											
Number of patients experiencing											

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myocardial infarction											
Number of patients experiencing stroke											
Number of patients experiencing amputation of at least one digit											
Number of patients experiencing ischemic limb disease											
Number of patients experiencing heart failure											
All-cause mortality											

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# PRISMA-P Checklist for *Comparative long-term effectiveness and safety of primary bariatric surgeries in treating type 2 diabetes mellitus in adults: a protocol for systematic review and network meta-analysis of randomized controlled trials*

This checklist has been adapted for use from Table 3 in Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Systematic reviews. 2015;4:1.

Section/topic	#	Checklist item	Information reported		Page (P) and Line (L) Number(s)
			Yes	No	
<b>ADMINISTRATIVE INFORMATION</b>					
<b>Title</b>					
Identification	1a	Identify the report as a protocol of a systematic review	√		P1, L4-12
Update	1b	If the protocol is for an update of a previous systematic review, identify as such			N/A
<b>Registration</b>	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	√		P2, L58
<b>Authors</b>					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	√		P1, L14-41; P18, L43-54
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	√		P18, L14-25
<b>Amendments</b>	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments			N/A
<b>Support</b>					
Sources	5a	Indicate sources of financial or other support for the review	√		P18, L30-36
Sponsor	5b	Provide name for the review funder and/or sponsor			N/A
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	√		P18, L35-41
<b>INTRODUCTION</b>					
<b>Rationale</b>	6	Describe the rationale for the review in the context of what is already known	√		P3, L43 - P5, L25
<b>Objectives</b>	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	√		P5, L32-46
<b>METHODS</b>					

Section/topic	#	Checklist item	Information reported		Page (P) and Line (L) Number(s)
			Yes	No	
<b>Eligibility criteria</b>	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	√		P6, L17 – P9, L59
<b>Information sources</b>	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	√		P10, L4-49
<b>Search strategy</b>	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	√		Supplementary material 1
<b>STUDY RECORDS</b>					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	√		P10, L53 - P11, L10
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	√		P10, L53 - P11, L12; P11, L22-44
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	√		P10, L53 - P11, L18
<b>Data items</b>	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	√		P11, L45 - P13, L15
<b>Outcomes and prioritization</b>	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	√		P7, L40 – P9, L60; P3, L43 - P5, L25
<b>Risk of bias in individual studies</b>	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	√		P13, L17-46; P16, L14-54
<b>DATA</b>					
<b>Synthesis</b>	15a	Describe criteria under which study data will be quantitatively synthesized	√		P14, L50-60; P16, L4-13
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., $I^2$ , Kendall's tau)	√		P13, L50-P15, L60
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	√		P16, L14-54
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	√		P16, L4-13
<b>Meta-bias(es)</b>	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	√		P16, L56 – P17, L15

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Section/topic	#	Checklist item	Information reported		Page (P) and Line (L) Number(s)
			Yes	No	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	√		P17, L17-34

Abbreviations: N/A: not applicable.

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# BMJ Open

## Comparative long-term effectiveness and safety of primary bariatric surgeries in treating type 2 diabetes mellitus in adults: a protocol for systematic review and network meta-analysis of randomized controlled trials

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-028430.R1
Article Type:	Protocol
Date Submitted by the Author:	19-Feb-2019
Complete List of Authors:	Ding, Li; Tianjin Medical University General Hospital, Department of Endocrinology and Metabolism Zhuo, Chuanjun; Tianjin Municipal Mental Health Center, Laboratory of Psychiatric Neuroimaging Fan, Yuxin; Tianjin Medical University General Hospital, Department of Endocrinology and Metabolism Zhang, Yalan; Tianjin Medical University General Hospital, Department of Endocrinology and Metabolism Li, Hui; Tianjin Medical University General Hospital, Department of Endocrinology and Metabolism Qi, Dongwang; Tianjin Medical University General Hospital, Department of Endocrinology and Metabolism Tang, Shaofang; Tianjin Medical University General Hospital, Department of Endocrinology and Metabolism Cui, Jingqiu; Tianjin Medical University General Hospital, Department of Endocrinology and Metabolism He, Qing; Tianjin Medical University General Hospital, Department of Endocrinology and Metabolism liu, ming; Tianjin Medical University General Hospital, Department of Endocrinology and Metabolism
<b>Primary Subject Heading</b>:	Diabetes and endocrinology
Secondary Subject Heading:	Evidence based practice
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, Adult surgery < SURGERY, Adverse events < THERAPEUTICS

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Manuscripts



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4 **Comparative long-term effectiveness and safety of primary bariatric**  
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6 **surgeries in treating type 2 diabetes mellitus in adults: a protocol for**  
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8 **systematic review and network meta-analysis of randomized**  
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10 **controlled trials**  
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14 Li Ding<sup>1†</sup>, Chuanjun Zhuo<sup>2†</sup>, Yuxin Fan<sup>1</sup>, Yalan Zhang<sup>1</sup>, Hui Li<sup>1</sup>, Dongwang Qi<sup>1</sup>, Shaofang Tang<sup>1</sup>,

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17 Jingqiu Cui<sup>1</sup>, Qing He<sup>1</sup>, Ming Liu<sup>1‡</sup>  
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39 60817182;  
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45 **Word Count:** 3941 words, excluding title page, abstract, and references.  
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50 **Abstract**  
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52  
53 **Introduction** Bariatric surgeries are effective in treating obesity related comorbidities, including  
54  
55 type 2 diabetes mellitus. More robust evidence is needed to facilitate choice of procedure. In this  
56  
57 systemic review, we aim to investigate the comparative long-term effectiveness in inducing  
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4 remission of type 2 diabetes, halting diabetic complications, reducing mortality, and the safety, of  
5  
6 conventional and emerging bariatric surgeries.  
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9 **Methods and analysis** Databases including Cochrane Central Register, EMBASE, MEDLINE,  
10  
11 and clinical trial registries will be searched for randomized controlled trials with at least 3 years of  
12  
13 follow-up, including direct and/or indirect evidence regarding primary bariatric surgeries in  
14  
15 overweight or obese adults with type 2 diabetes mellitus, from inception of each database to 2019,  
16  
17 with no language or publication type limits imposed. Dual selection of studies, data extraction,  
18  
19 and risk of bias assessments will be performed. Primary outcomes include full diabetes remission,  
20  
21 composite outcome of full or partial diabetes remission, and adverse events profiles. Secondary  
22  
23 outcomes include anthropometric measurements, cardiovascular risk factor burden, medication  
24  
25 burden, diabetic complications, and all-cause mortality. Given sufficient homogeneity, network  
26  
27 meta-analyses will be performed in a random-effect model based on the Bayesian framework,  
28  
29 while assessing for consistency between direct and indirect estimates. Heterogeneities of studies  
30  
31 will be explored through meta-regression analysis, and robustness of findings will be checked by  
32  
33 sensitivity analysis, and an alternative method under a frequentist framework. All statistical  
34  
35 analysis and graphical presentations will be conducted by R software (Version 3.3.3, The R  
36  
37 Project for Statistical Computing). The overall quality of the evidence will be assessed using the  
38  
39 Grading of Recommendations, Assessment, Development, and Evaluation criteria for each  
40  
41 outcome.  
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53 **Ethics and dissemination** Ethics approval is not required as individual patient data will not be  
54  
55 included. This review will be subject for publication in a peer-reviewed journal.  
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57

58 **Registration Details** PROSPERO registration number CRD42018110775.  
59  
60

### Strengths and limitations of this study

- ▶ This will be the first systemic review and network meta-analysis to assess long-term relative effectiveness and safety of conventional and emerging bariatric surgeries in overweight or obese adults with type 2 diabetes mellitus.
- ▶ This study will comprehensively evaluate clinically important outcomes, including full or partial diabetes remission, anthropometric measurements, cardiovascular risk factor burden, medication burden, diabetic complications, all-cause mortality, and major adverse events.
- ▶ This protocol proposes a cumulative score based approach for integral assessment of safety of bariatric surgeries.
- ▶ This protocol defines detailed plan for data synthesis, additional analysis, and validation of findings by an alternative method.
- ▶ Common to any aggregate data meta-analysis, the risk for heterogeneity across studies exists.

### BACKGROUND

Bariatric surgeries have shown long-term benefits with respect to inducing disease remission, reducing mortality, and decreasing microvascular and macrovascular complications in overweight or obese patients with type 2 diabetes mellitus, compared with non-surgical therapy.[1] The currently performed bariatric surgeries include Roux-en-Y gastric bypass, sleeve gastrectomy, adjustable gastric banding, biliopancreatic diversion with duodenal switch, greater curvature plication, one-anastomosis gastric bypass, and single anastomosis duodenal-ileal bypass with sleeve gastrectomy.[2-5] Previous studies indicated that bariatric surgeries differed in both efficacy, durability, and mechanisms in inducing remission of type 2 diabetes and complication

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4 profiles.[2, 6-9] Current evidence is insufficient to support recommendation regarding choice of  
5  
6 specific procedure clearly over others, and more robust evidence is needed to facilitate informed  
7  
8 decision making.[2] Since comparisons of only two or a few bariatric procedures can be achieved  
9  
10 in randomized controlled trials, network meta-analysis, capable of integrating both direct and  
11  
12 indirect evidence, is a reasonable approach in this scenario.  
13  
14

15  
16 A recent elegant network meta-analysis of studies involving eight bariatric surgeries with median  
17  
18 follow-up duration of 3 months to 5 years (median 1 year) indicated that biliopancreatic diversion  
19  
20 and one-anastomosis gastric bypass achieved higher diabetes remission rates than the other  
21  
22 procedures.[6] However, biliopancreatic diversion is rarely performed currently due to  
23  
24 unfavorable complication profiles, while one-anastomosis gastric bypass is a relatively new  
25  
26 procedure, the safety and durability of which warrant further investigation.[3, 10] Furthermore,  
27  
28 remission rates of comorbidities may change over time after bariatric procedures,[11, 12] thus  
29  
30 comparing relative efficacies with different follow-up duration post bariatric surgeries may  
31  
32 introduce bias.  
33  
34

35  
36 Type 2 diabetes mellitus can lead to increased risk of cardiovascular events, renal failure,  
37  
38 blindness, amputation, and increased mortality. Most of the evidence regarding the effects of  
39  
40 bariatric surgeries upon diabetic complications and mortality is derived from observational studies  
41  
42 and pairwise comparisons.[2] Defining the relative effectiveness of bariatric surgeries in halting  
43  
44 diabetic complications and in decreasing mortality should be addressed with the most robust  
45  
46 evidence possible, or at least, gaps in current knowledge should be identified to guide emphasis of  
47  
48 future research.[13]  
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58 Complication profiles of bariatric surgeries differ among procedures and between patients with  
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4 and without type 2 diabetes mellitus.[14, 15] However, efforts in investigating comparative safety  
5  
6 and tolerability of bariatric surgeries have been met with great difficulty, due to heterogeneity of  
7  
8 adverse events encountered and in ways reported among studies. Efforts have been made for  
9  
10 standard reporting of adverse events in studies of bariatric procedures.[16] We would like to  
11  
12 revisit this question, by defining major adverse events profiles of bariatric surgeries in adults with  
13  
14 type 2 diabetes mellitus, a group of patients already predisposed to increased risks of surgical  
15  
16 complications, depression and hypoglycemia.[17-19]  
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## 25 **OBJECTIVES**

26  
27 The objectives of the study is to determine the relative effectiveness and safety of existing  
28  
29 bariatric surgeries in treating overweight or obese adults with type 2 diabetes mellitus through  
30  
31 systemic review and network meta-analysis, to perform meta-regression analysis, subgroup  
32  
33 analysis, and sensitivity analysis, if feasible, to explore what clinical and methodological  
34  
35 characteristics explain the heterogeneity in results, and to identify gaps in current studies to  
36  
37 provide directions for future research.  
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## 45 **METHODS**

46  
47 This protocol follows Preferred Reporting Items for Systematic Reviews and Meta-analyses  
48  
49 Protocols and the accompanied checklist, and the study will follow Preferred Reporting Items for  
50  
51 Systematic Reviews and Meta-Analyses for Network Meta-Analyses.[20, 21] This protocol is  
52  
53 registered with the International Prospective Register of Systematic Reviews (registration number  
54  
55 CRD42018110775). In circumstances when changes to the protocol are necessary, details and  
56  
57  
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rationales of the changes in the reported systematic review will be reported.

### Patient and public involvement

Patients or the public were not involved in the design of this systemic review protocol.

### Eligibility criteria

#### Participants

We will include studies which include overweight or obese adults with type 2 diabetes mellitus.

We will not include studies of participants restricted to specific diseases other than type 2 diabetes mellitus. In studies in which general overweight or obese participants are enrolled, or in which children or adolescents under the age of 18 are enrolled along with adults, we will extract the data for the adult population with type 2 diabetes exclusively.

#### Interventions

We will include interventions encompassing currently performed primary bariatric surgeries, including Roux-en-Y gastric bypass, sleeve gastrectomy, adjustable gastric banding, biliopancreatic diversion with duodenal switch, greater curvature plication, one-anastomosis gastric bypass, and single anastomosis duodenal-ileal bypass with sleeve gastrectomy. We will not include studies examining revisional surgeries or procedures no longer performed, including biliopancreatic diversion without duodenal switch, jejunoileal bypass, horizontal or vertical gastroplasty, and banding that is not adjustable.

#### Comparators

We will include studies comparing currently performed bariatric surgeries with usual care with or without life-style interventions, or comparing at least 2 of the surgical procedures.

#### Study designs

1  
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3  
4 We will include randomized controlled trials, with at least 3 years of follow-up. To minimize  
5  
6 potential bias introduced by different follow-up period among studies, when including studies  
7  
8 with over 3 years of follow-up, data of measurements at 3 years (+/- 6 months) or earliest reported  
9  
10 time point after 3 years, and at 5 years (+/- 6 months) or earliest reported time point after 5 years,  
11  
12 if applicable, will be included in analysis, respectively.  
13  
14  
15

### 16 17 *Setting*

18  
19 There will be no restrictions by type of setting.  
20  
21

### 22 23 *Language*

24  
25 We will include studies reported in the English and Chinese languages, and studies reported in  
26  
27 other languages if adequate translation is feasible by Bing Translate. A list of possibly relevant  
28  
29 studies not included in the review will be provided.  
30  
31

### 32 33 *Publication status*

34  
35 Eligibilities of unpublished studies will be evaluated.  
36  
37

### 38 39 *Outcomes measures and prioritization*

#### 40 41 *Primary outcomes*

42  
43 1. The number of patients in full remission of type 2 diabetes mellitus defined as HbA1c levels of  
44  
45 less than 6.0% at consecutive annual visits, and no use of anti-hyperglycemic medication at either  
46  
47 visit,[22] or as defined by the studies.  
48  
49

50  
51 2. Composite outcome of number of patients in full or partial remission of type 2 diabetes  
52  
53 mellitus. Partial remission of type 2 diabetes mellitus is defined as HbA1c levels of less than 6.5%  
54  
55 at consecutive annual visits, and no use of anti-hyperglycemic medication at either visit,[22] or as  
56  
57 defined by the studies.  
58  
59  
60

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3  
4 3. Cumulative scores of grade IIIa or higher complications according to Clavien-Dindo  
5  
6 classification for surgical complications,[23] and grade 3 or higher other adverse events according  
7  
8 to the Common Terminology Criteria for Adverse Events version 5.0,[24] based on translation of  
9  
10 each IIIa, grade IIIb, grade IVa, grade IVb and grade V complication into 6, 7, 8, 9, 10 points,  
11  
12 respectively, and grade 3, grade 4, and grade 5 adverse events other than surgical complications  
13  
14 into 6, 8, 10 points, respectively, in the analogue scale (0=minimum severity, 10=maximum  
15  
16 severity). Surgical complication is defined as any deviation from the normal postoperative  
17  
18 course,[23] whereas adverse event is defined as any unfavorable and unintended sign, symptom,  
19  
20 or disease temporally associated with the use of a medical treatment or procedure that may or may  
21  
22 not be considered related to the medical treatment or procedure.[24] A scored appraisal of adverse  
23  
24 events profiles serves in two ways. Firstly, it allows evaluation of severity of adverse event based  
25  
26 on its impact upon patient regardless of its definition which may vary considerably among studies.  
27  
28 Secondly, a cumulative score based approach allow integral assessment of safety among  
29  
30 procedures. The reason for inclusion of only major adverse event is twofold. Firstly, the intensity  
31  
32 of surveillance may tamper overtime during follow-up, so as to only serious adverse event may be  
33  
34 recognized and reported at later stages of follow-up, precluding the ideal comparison of all  
35  
36 clinically significant adverse events among procedures. Secondly, we anticipate varied reporting  
37  
38 of mild or moderate adverse event, for example, post-surgical pain, which may be considered  
39  
40 normal and not reported in some studies.  
41  
42  
43  
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### 52 *Secondary outcomes*

53  
54  
55  
56 1. Number of patients achieving diabetic management goals with respect to blood glucose, blood  
57  
58 pressure and LDL-cholesterol defined as simultaneous achievement of HbA1c of less than 7.0%,  
59  
60



1  
2  
3  
4 LDL-C of less than 2.59mmol/L, and systolic BP of less than 140 mmHg.[25] or as defined by the  
5  
6 studies

7  
8  
9 2. Weight loss is an important determinant of resolution of comorbidities including type 2 diabetes  
10  
11 mellitus after bariatric surgery.[26] We will investigate anthropometric measurements including  
12  
13 percentage total body weight loss, percentage excess weight loss, fat mass and fat free mass  
14  
15 derived from bio-electrical impedance analysis or dual-energy X-ray absorptiometry, as well as  
16  
17 body mass index and weight both at baseline and at follow-up.  
18  
19

20  
21  
22 3. Decrease in cardiovascular risk scores have been shown to translate into favorable  
23  
24 cardiovascular outcome post bariatric surgeries.[27] We will investigate the cardiovascular risk  
25  
26 score of validated tools, and parameters reflecting risk factor burden, including glycated  
27  
28 hemoglobin, fasting blood glucose, total cholesterol, low-density lipoprotein cholesterol, high-  
29  
30 density lipoprotein cholesterol, triglyceride, systolic and diastolic blood pressures.  
31  
32

33  
34  
35 4. While persistence and relapse of type 2 diabetes mellitus is not uncommon post bariatric  
36  
37 surgeries, improvements can be reflected by the need for less intensive treatment.[28] We will  
38  
39 collect outcome data concerning change of medication burden, including number of patients  
40  
41 requiring less anti-diabetic drugs at follow-up, and number of patients achieving discontinuation  
42  
43 of insulin.  
44  
45

46  
47  
48 5. Number of patients exhibiting progression of diabetic retinopathy, nephropathy and neuropathy,  
49  
50 and number of patients experiencing myocardial infarction, stroke, amputation of at least one  
51  
52 digit, ischemic limb disease, and heart failure, and urine albumin/creatinine ratio as surrogate  
53  
54 marker for end organ damage.  
55  
56

57  
58 6. All-cause mortality  
59  
60

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3  
4 Studies will not be excluded based on whether or not certain outcomes are reported.  
5

### 6 **Search methods for identification of studies**

7  
8  
9 Comprehensive search of databases listed below will be conducted using medical subject headings  
10  
11 (MeSH) or Embase subject headings (Emtree), as applicable, and text words, for studies in human,  
12  
13 from inception of each database to December 2019, without language, or publication type  
14  
15 restrictions. The search strategies are adapted from a previous research,[10] revised with input  
16  
17 from the project team, and refined by a methodologist with expertise in systematic review  
18  
19 searching. The search will be updated toward the end of the review to ensure efficacy of retrieving  
20  
21 eligible studies. Cross-referencing of relevant systemic reviews retrieved and included studies will  
22  
23 be conducted. Preliminary search strategy for PubMed, which will be adapted for each other  
24  
25 database as required, is shown in supplementary material 1. We will search the following  
26  
27 databases:  
28  
29

- 30 1. PubMed (Ovid interface)
- 31 2. EMBASE
- 32 3. Ovid Cochrane Central Register of Controlled Trials (CENTRAL)
- 33 4. US National Institutes of Health Ongoing Trials Register (<https://www.clinicaltrials.gov/>).
- 34 5. WHO International Clinical Trials Registry Platform (<http://www.who.int/ictrp/en/>).
- 35 6. International Standard Randomized Controlled Trial Number Register (<http://www.isrctn.org/>)
- 36 7. Trials Central (<http://www.trialscentral.org/>).

### 37 **Study records**

38  
39 Selection of eligible studies and data abstraction will be performed by two independent reviewers,  
40  
41 with Covidence, an Internet based software facilitating collaboration. Screening questions based  
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4 on the inclusion and exclusion criteria, and data extraction form (See supplementary file 2 for  
5  
6 preliminary screening questions and data extraction form) will be developed, tailored in  
7  
8  
9 Covidence, tested and refined by the team through discussion and pilot calibration exercises  
10  
11 before formal screening and data extraction, respectively. Discrepancies will be resolved first with  
12  
13 discussion, and, if necessary, by a third arbitrator. We will contact investigators of studies, by a  
14  
15 maximal of three email attempts, if additional information is warranted for evaluation of study  
16  
17 eligibility, data extraction and risk of bias assessment of included studies.  
18  
19  
20

### 21 22 **Selection of studies**

23  
24 Literature search results will be imported to Covidence, which will identify and remove  
25  
26 duplicates. Titles and abstracts of all references will be screened, and references will be graded as  
27  
28 relevant, maybe relevant, and not relevant. Relevant or maybe relevant references will be subject  
29  
30 to full-text screening for final decision upon eligibility. Reasons for excluding studies will be  
31  
32 recorded. Reviewers will not be blinded to journal titles or study authors or affiliations in study  
33  
34 selection. Included studies will be checked for potential double counting by identifying multiple  
35  
36 reports of the same study, overlapping or companion studies. We will record the selection process  
37  
38 in detail. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram  
39  
40 and characteristics of excluded studies will be presented.  
41  
42  
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### 48 **Data extraction and management**

49  
50 The following information will be extracted for subsequent risk of bias assessment, data synthesis,  
51  
52 and appraisal of possible effect modifiers, i.e. variables that affect the magnitude of the effects of  
53  
54 bariatric surgeries on outcomes:  
55  
56

- 57  
58 1. Study characteristics: Methodology characteristics including study design, methods for  
59  
60

1  
2  
3  
4 sequence generation, allocation concealment, blinding of patients, interveners and/or evaluators of  
5  
6 all or some outcomes, whether intentional analysis is adopted, setting, time span of enrollment,  
7  
8 duration of follow-up, number and location of centers, funding, potential conflicts of interest, key  
9  
10 conclusion of authors of studies, and whether the study is concluded early, will be documented.  
11  
12

13  
14 2. Participants: Number of participants, diagnostic criteria of type 2 diabetes mellitus, inclusion  
15  
16 and exclusion criteria, and baseline characteristics of participants including age, body mass index,  
17  
18 ethnicity, gender, duration of type 2 diabetes, will be extracted.  
19  
20

21  
22 3. Interventions: number of participants allocated to, and number and reasons for attrition of each  
23  
24 comparator arm will be extracted along with description of interventions, co-interventions, if any,  
25  
26 and comparisons.  
27  
28

29  
30 4. Outcomes: Planned and reported primary and secondary outcomes and time of observation will  
31  
32 be extracted and compared for discrepancies. Criteria for diagnosis or evaluation will be extracted.  
33  
34

35 For laboratory investigation, assay method, unit, and reference range will be extracted. Laboratory  
36  
37 data adopting different analysis method will be transformed if known linear correlation have been  
38  
39 reported. For cardiovascular risk score, name of tool used, score range, if higher or lower value is  
40  
41 favorable, will be extracted. Necessary transformation will be made when indicated to ensure  
42  
43 alignment of the scales. For adverse events, information regarding timing, severity, presentation,  
44  
45 diagnosis, and management of all reported adverse events will be extracted, and will be sent to  
46  
47 two independent reviewers, who are blind to information regarding from which study the data is  
48  
49 extracted, and what intervention preceded the onset of the adverse event, for score translation. A  
50  
51 third arbitrator, also blind to information regarding study and intervention, will resolve  
52  
53 inconsistencies despite discussion. The sequence in which adverse events are organized will be  
54  
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3  
4 randomized by an online List Randomizer (<https://www.random.org>) before score translation, to  
5  
6 further minimize the risk of bias. Corresponding score for each intervention in each study will be  
7  
8 added for data synthesis.  
9

10  
11 Means and measures of dispersion will be approximated from figures in the reports by measuring  
12  
13 tools of Adobe Acrobat Reader when necessary if original data cannot be obtained from the  
14  
15 authors. Whenever possible, we will use results from an intention to treat analysis. If number of  
16  
17 missing data doesn't concord with attrition, the reason will be specified.  
18  
19

### 20 21 22 **Risk of bias (quality) assessment**

23  
24 Risk of bias at the individual study level will be assessed by two independent reviewers, using the  
25  
26 Cochrane risk of bias tool. Studies will be classified to be at high, low or unclear risk of bias based  
27  
28 on adequacy of sequence generation, allocation concealment, blinding of participants and  
29  
30 personnel, blinding of outcome assessment, method of addressing incomplete data, selective  
31  
32 reporting, and other biases. Blinding of outcome assessment will be subdivided into subjective and  
33  
34 objective assessments. Subjective assessments include evaluation of disease remission, adverse  
35  
36 events, achieving treatment goals, progression of diabetic complications, and medication.  
37  
38 Objective assessments include anthropometric measurements, cardiovascular risk score, laboratory  
39  
40 investigations, and all-cause mortality. Disagreements will be resolved first by discussion and then  
41  
42 by consulting a third arbitrator. Graphic representations of potential bias within and across studies  
43  
44 will be generated using RevMan 5.1 (Review Manager 5.1).  
45  
46  
47  
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51

### 52 53 **Data analysis**

#### 54 55 **Measures of treatment effect.**

56  
57  
58 Dichotomous outcomes will be pooled using risk ratio (RR) with 95% credible intervals (CrI) or  
59  
60

1  
2  
3  
4 confidence intervals (CI), as applicable. Continuous outcomes will be pooled using weighted  
5  
6 mean differences (with 95% CrI or CI) if uniform measurement scales are used, or standardized  
7  
8 mean differences (with 95% CrI or CI) if different measurement scales are adopted. Adverse event  
9  
10 profiles will be assessed with mean (with 95% CrI or CI) of weighted adverse events per patient of  
11  
12 each surgical procedure, determined by cumulative adverse event score divided by the number of  
13  
14 patients in the corresponding treatment arm in each study.  
15  
16  
17

### 18 19 Dealing with missing data

20  
21  
22 In case of missing data, such as the standard deviation or other important variability measures, we  
23  
24 will first try to calculate through algebraic manipulation of the available information such as  
25  
26 confidence intervals, p or t values.[29] When such attempts fail, an imputation method will be  
27  
28 used,[30] which will be tested in sensitivity analysis.  
29  
30  
31

### 32 33 Assessment of heterogeneity

34  
35 Heterogeneity among included studies will be appraised by evaluating the variability in  
36  
37 participants (including age, ethnicity, body mass index, and comorbidities), in trials (including  
38  
39 blinding, attrition, surgical techniques, and co-interventions). Statistical heterogeneity will be  
40  
41 assessed by the Cochran Q (Chi-squared) and Higgins I-squared statistics. If high levels of  
42  
43 heterogeneity among the trials exist (Q statistic  $\leq 0.10$  and/or  $I^2$  value  $> 50\%$ ), the study design and  
44  
45 characteristics in the included studies will be analyzed. Source of heterogeneity will be rigorously  
46  
47 investigated by subgroup analysis, sensitivity analysis, and meta-regression.  
48  
49  
50

### 51 52 Data synthesis

53  
54  
55 If studies are sufficiently homogeneous in terms of design and comparator, we will conduct  
56  
57 network meta-analyses in a random-effect model using generalized linear model under a Bayesian  
58  
59  
60

1  
2  
3  
4 framework, while assessing for consistency between direct and indirect estimates of comparative  
5  
6 effectiveness of each study arm.[31, 32] Geometry of the network will be depicted by a network  
7  
8 map, and the treatments that are directly compared against each other and the amount of evidence  
9  
10 available for each treatment and its comparator will be described qualitatively. The assumption of  
11  
12 transitivity will be appreciated and systematic tabulated information extracted regarding potential  
13  
14 effect modifiers, including patient and study characteristics, will be provided. Non-informative  
15  
16 priors for model parameters will be used. We will run Markov Chain Monte Carlo sampling for  
17  
18 four chains. Results will be based on 100000 iterations, after a 100000-iterations burn in.  
19  
20  
21  
22  
23  
24  
25 Convergence will be judged based on visual inspection of time-series plots and the Brooks-  
26  
27 Gelman-Rubin test. Goodness of fit of the model will be tested using the Deviance Information  
28  
29 Criterion. Local inconsistency will be evaluated by comparing the magnitude and direction of  
30  
31 effect estimates from direct and indirect comparisons. Global inconsistency will be evaluated with  
32  
33 the pairwise p-values for inconsistency via back-calculation. Findings will be summarized in  
34  
35 treatment-level forest plots, rank probability matrix and rank plot, with the latter two illustrating  
36  
37 empirical probabilities that each treatment is ranked from best through worst, along with  
38  
39 corresponding estimates and absolute difference of pairwise comparisons between interventions.  
40  
41  
42  
43  
44  
45 To determine adverse event profiles, a linear regression analysis will be performed with type of  
46  
47 surgical procedure as covariates, the adverse event outcome as the dependent variable, and a  
48  
49 dummy variable for each of the studies to adjust for differences in risk profiles and study setup  
50  
51 between trials, as described by Kessler et al.[33]  
52  
53  
54  
55  
56 An alternative method based on graph theory methodology under a frequentist framework will be  
57  
58 adopted to validate the findings with league tables and rankings of treatments.[34, 35]  
59  
60

1  
2  
3  
4 All statistical analysis and graphical procedures will be conducted by R software (Version 3.3.3,  
5  
6 The R Project for Statistical Computing).

7  
8  
9 If heterogeneity is substantial ( $I^2 > 90\%$ ), meta-analysis will not be performed; a narrative,  
10  
11 qualitative summary will be presented in text and tables to summarize the characteristics of the  
12  
13 included studies and findings both within and between the included studies, in accordance with the  
14  
15 guidance from the Centre for Reviews and Dissemination.  
16  
17

#### 18 19 Investigation of heterogeneity and subgroup analysis

20  
21  
22 Heterogeneity among included studies will be appraised, if possible, by evaluating the variability  
23  
24 in potential effect modifiers, including characteristics of participants (including age, gender-  
25  
26 distribution, baseline body mass index, duration of type 2 diabetes mellitus, and comorbidities), in  
27  
28 trials (including whether exclusively including patients with type 2 diabetes mellitus, whether  
29  
30 including patients with baseline BMI less than 30, less than 35, less than 40, over 50, or over  
31  
32 60kg/m<sup>2</sup>, whether including patients over 60 years old, whether adopting intensive life-style  
33  
34 intervention as control or during the follow-up period of bariatric surgeries in the same effective  
35  
36 arm, whether surgical procedures are laparoscopic, open, or both, whether an intention to treat  
37  
38 analysis was reported, publication year, publication status, and risk of bias items including  
39  
40 attrition, blinding, and missing data) through meta-regression analysis for primary outcomes.  
41  
42

43  
44  
45 Subgroup analysis will be performed based on factors identified through meta-regression. The  
46  
47 likely impact of risk of bias, if studies of moderate or high risk of bias are included in the analysis,  
48  
49 upon the results will be discussed. Robustness of primary findings will be tested with sensitivity  
50  
51 analysis by excluding trials with high risk of bias, by performing leave-one-out analysis, and by  
52  
53 excluding studies requiring data imputation.  
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### Meta bias

Reports will be checked against protocol to detect potential selective reporting and inconsistencies with respect to description of the design, number of patients analyzed, chosen significance level, and outcomes, among all reports of the same study. Reporting bias will be further explored by the Egger test. Visual inspection of funnel plots, along with trim-and-fill analysis for estimating and adjusting for the number and outcomes of missing studies, will be performed if  $\geq 10$  studies are available.

### Grading of quality of evidence

The overall quality of the body of evidence of the meta-analysis findings, if feasible, will be judged using the Grading of Recommendations, Assessment, Development and Evaluation approach. We will assess the quality of the evidence across the domains of risk of bias, consistency, directness, precision, publication bias, and additional domains where appropriate. The overall strength of evidence will be adjudicated as high, moderate, low or very low for each outcome measure.

## DISCUSSION

Obesity is an important risk factor for type 2 diabetes mellitus, and bariatric surgery is effective in inducing weight-loss and resolution of obesity-related comorbidities.[36] Bariatric surgeries are growing worldwide, but are still underused.[37] Barriers preventing patients' access to bariatric surgeries include availability of surgical resources, concerns about postoperative complications, misperception regarding bariatric surgery effectiveness, and professional society statement heterogeneity.[38] It is important to appreciate the long-term benefit-risk ratio of bariatric

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4 surgeries in adults with type 2 diabetes mellitus, to facilitate decision-making by patients,  
5  
6 clinicians, and policy makers. This review will summarize the current scientific findings, and will  
7  
8 identify gaps for further research.  
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14 **ETHICS AND DISSEMINATION** Ethics approval is not required, because individual patient  
15  
16 data will not be included in this review. This review will be published in a peer-reviewed journal.  
17  
18

19 **ACKNOWLEDGEMENTS** None.  
20

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22 **AUTHOR CONTRIBUTORS** ML is the guarantor. Research question and eligibility criteria  
23  
24 were defined by ML, CJZ, LD, YXF, YLZ, HL, DWQ, SFT, JQC, and QH. LD, CJZ, and YXF  
25  
26 contributed to the development of search strategy and data extraction form. CJZ provided  
27  
28 methodological support for this review. The manuscript was first drafted by LD and YXF, and  
29  
30 was revised and approved by all authors.  
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35 **COMPETING INTERESTS** None declared.  
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37  
38 **FUNDING** This work was supported by the National Natural Science Foundation of China grant  
39  
40 number 81570699, 81620108004, 81370895, and Tianjin Municipal Science and Technology  
41  
42 Commission grant number 17ZXMFSY00150. The funders have no input on the protocol  
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44 development, and will not have influence upon review conduct, data analysis, interpretation or  
45  
46 publication of the study results.  
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6 **LICENCE STATEMENT** Other than as permitted in any relevant BMJ Author's Self Archiving  
7

8 Policies, we confirm this Work has not been accepted for publication elsewhere, is not being  
9

10 considered for publication elsewhere and does not duplicate material already published. All  
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12 authors consent to publication of this Work and authorize the granting of this licence.  
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17  
18  
19 **REFERENCE**  
20

- 21  
22 1. Sheng B, Truong K, Spitler H, et al. The Long-Term Effects of Bariatric Surgery on Type 2 Diabetes  
23 Remission, Microvascular and Macrovascular Complications, and Mortality: a Systematic Review and  
24 Meta-Analysis. *Obes Surg* 2017;27(10):2724-32 doi: 10.1007/s11695-017-2866-4 [published Online  
25 First: 2017/08/13]  
26  
27  
28  
29  
30  
31  
32 2. Pareek M, Schauer PR, Kaplan LM, et al. Metabolic Surgery: Weight Loss, Diabetes, and Beyond.  
33 *Journal of the American College of Cardiology* 2018;71(6):670-87 doi: 10.1016/j.jacc.2017.12.014  
34  
35  
36  
37 3. De Luca M, Tie T, Ooi G, et al. Mini Gastric Bypass-One Anastomosis Gastric Bypass (MGB-  
38 OAGB)-IFSO Position Statement. *Obesity Surgery* 2018;28(5):1188-206 doi: 10.1007/s11695-018-  
39 3182-3  
40  
41  
42  
43  
44  
45 4. Brown WA, Ooi G, Higa K, et al. Single Anastomosis Duodenal-Ileal Bypass with Sleeve  
46 Gastrectomy/One Anastomosis Duodenal Switch (SADI-S/OADS) IFSO Position Statement. *Obesity*  
47 *Surgery* 2018;28(5):1207-16 doi: 10.1007/s11695-018-3201-4  
48  
49  
50  
51  
52  
53 5. ASMBS policy statement on gastric plication. *Surgery for obesity and related diseases : official*  
54 *journal of the American Society for Bariatric Surgery* 2011;7(3):262 doi: 10.1016/j.soard.2011.03.004  
55  
56  
57  
58 [published Online First: 2011/05/31]  
59  
60

- 1  
2  
3  
4 6. Kodama S, Fujihara K, Horikawa C, et al. Network meta-analysis of the relative efficacy of bariatric  
5  
6 surgeries for diabetes remission. *Obesity reviews : an official journal of the International Association*  
7  
8 for the Study of Obesity 2018;19(12):1621-29. doi: 10.1111/obr.12751 [published Online First:  
9  
10 2018/10/03]  
11  
12  
13  
14 7. Kang JH, Le QA. Effectiveness of bariatric surgical procedures: A systematic review and network  
15  
16 meta-analysis of randomized controlled trials. *Medicine (Baltimore)* 2017;96(46):e8632 doi:  
17  
18 10.1097/md.0000000000008632 [published Online First: 2017/11/18]  
19  
20  
21  
22 8. Buchwald H, Estok R, Fahrbach K, et al. Trends in mortality in bariatric surgery: a systematic  
23  
24 review and meta-analysis. *Surgery* 2007;142(4):621-32; discussion 32-5 doi:  
25  
26 10.1016/j.surg.2007.07.018 [published Online First: 2007/10/24]  
27  
28  
29  
30 9. Khan S, Rock K, Baskara A, et al. Trends in bariatric surgery from 2008 to 2012. *Am J Surg*  
31  
32 2016;211(6):1041-6 doi: 10.1016/j.amjsurg.2015.10.012 [published Online First: 2016/01/15]  
33  
34  
35 10. Colquitt JL, Pickett K, Loveman E, et al. Surgery for weight loss in adults. *Cochrane Database of*  
36  
37 *Systematic Reviews* 2014;2014(8) doi: 10.1002/14651858.CD003641.pub4  
38  
39  
40 11. Courcoulas AP, King WC, Belle SH, et al. Seven-year weight trajectories and health outcomes in  
41  
42 the Longitudinal Assessment of Bariatric Surgery (LABS) study. *JAMA surgery* 2018;153(5):427-34  
43  
44 doi: 10.1001/jamasurg.2017.5025  
45  
46  
47  
48 12. Ahmed B, King WC, Gourash W, et al. Long-term weight change and health outcomes for sleeve  
49  
50 gastrectomy (SG) and matched Roux-en-Y gastric bypass (RYGB) participants in the Longitudinal  
51  
52 Assessment of Bariatric Surgery (LABS) study. *Surgery* 2018;164(4):774-83. doi:  
53  
54 10.1016/j.surg.2018.06.008 [published Online First: 2018/08/25]  
55  
56  
57  
58 13. Miras AD, le Roux CW. Metabolic surgery: Shifting the focus from glycaemia and weight to end-  
59  
60

- 1  
2  
3  
4 organ health. *The Lancet Diabetes and Endocrinology* 2014;2(2):141-51 doi: 10.1016/S2213-  
5  
6 8587(13)70158-X  
7  
8  
9 14. Kabir A, Mousavi S, Pazouki A. The Complications of Bariatric Surgery Patients with Type 2  
10  
11 Diabetes in the World: A systematic Review and Meta-Analysis. *Current diabetes reviews* 2018 doi:  
12  
13 10.2174/1573399814666180403164529 [published Online First: 2018/04/07]  
14  
15  
16 15. Chang SH, Freeman NLB, Lee JA, et al. Early major complications after bariatric surgery in the  
17  
18 USA, 2003–2014: a systematic review and meta-analysis. *Obesity Reviews* 2018;19(4):529-37 doi:  
19  
20 10.1111/obr.12647  
21  
22  
23 16. Hopkins JC, Howes N, Chalmers K, et al. Outcome reporting in bariatric surgery: an in-depth  
24  
25 analysis to inform the development of a core outcome set, the BARIACT Study. *Obesity reviews*  
26  
27 2015;16(1):88-106 doi: 10.1111/obr.12240  
28  
29  
30  
31 17. Frisch A, Chandra P, Smiley D, et al. Prevalence and clinical outcome of hyperglycemia in the  
32  
33 perioperative period in noncardiac surgery. *Diabetes Care* 2010;33(8):1783-8 doi: 10.2337/dc10-0304  
34  
35 [published Online First: 2010/05/04]  
36  
37  
38  
39 18. Black S, Kraemer K, Shah A, et al. Diabetes, Depression, and Cognition: a Recursive Cycle of  
40  
41 Cognitive Dysfunction and Glycemic Dysregulation. *Curr Diab Rep* 2018;18(11):118 doi:  
42  
43 10.1007/s11892-018-1079-0 [published Online First: 2018/09/30]  
44  
45  
46  
47 19. Cryer PE. Severe hypoglycemia predicts mortality in diabetes. *Diabetes Care* 2012;35(9):1814-6  
48  
49 doi: 10.2337/dc12-0749 [published Online First: 2012/08/28]  
50  
51  
52  
53 20. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-  
54  
55 analysis protocols (PRISMA-P) 2015 statement. *Systematic reviews* 2015;4(1):1 doi: 10.1186/2046-  
56  
57 4053-4-1  
58  
59  
60

- 1  
2  
3  
4 21. Hutton B, Salanti G, Caldwell DM, et al. The PRISMA extension statement for reporting of  
5  
6 systematic reviews incorporating network meta-analyses of health care interventions: checklist and  
7  
8 explanations. *Ann Intern Med* 2015;162(11):777-84 doi: 10.7326/m14-2385 [published Online First:  
9  
10 2015/06/02]  
11  
12  
13  
14 22. Buse JB, Caprio S, Cefalu WT, et al. How Do We Define Cure of Diabetes? *Diabetes Care*  
15  
16 2009;32(11):2133.  
17  
18  
19 23. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with  
20  
21 evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240(2):205-13.  
22  
23 [published Online First: 2004/07/27]  
24  
25  
26  
27 24. National Cancer Institute Common Terminology Criteria for Adverse Events v5.0 (CTCAE).  
28  
29 Available:  
30  
31 [https://ctep.cancer.gov/protocoldevelopment/electronic\\_applications/docs/CTCAE\\_v5\\_Quick\\_Referen](https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf)  
32  
33 [ce\\_8.5x11.pdf](https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf)  
34  
35  
36  
37 25. American Diabetes Association. Standards of medical care in diabetes—2016. *Diabetes Care*  
38  
39 2016;39(suppl 1):S1-S106.  
40  
41  
42 26. Polovina S. Management of obesity related conditions through weight. *Obesity Facts* 2018;11:20  
43  
44 doi: 10.1159/000489691  
45  
46  
47 27. Vest AR, Heneghan HM, Agarwal S, et al. Bariatric surgery and cardiovascular outcomes: A  
48  
49 systematic review. *Heart* 2012;98(24):1763-77 doi: 10.1136/heartjnl-2012-301778  
50  
51  
52  
53 28. Rubino F, Nathan DM, Eckel RH, et al. Metabolic Surgery in the Treatment Algorithm for Type 2  
54  
55 Diabetes: a Joint Statement by International Diabetes Organizations. *Surgery for obesity and related*  
56  
57 *diseases* 2016;12(6):1144-62 doi: 10.1016/j.soard.2016.05.018  
58  
59  
60

- 1  
2  
3  
4 29. Deeks JJ, Higgins JPT, Altman DG (editors) on behalf of the Cochrane Statistical Methods Group.  
5  
6 Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Churchill R, Chandler J,  
7  
8 Cumpston MS (editors), *Cochrane Handbook for Systematic Reviews of Interventions* version 5.2.0  
9  
10 (updated June 2017), Cochrane, 2017  
11  
12  
13  
14 30. Furukawa TA, Barbui C, Cipriani A, et al. Imputing missing standard deviations in meta-analyses  
15  
16 can provide accurate results. *J Clin Epidemiol* 2006;59(1):7-10 doi: 10.1016/j.jclinepi.2005.06.006  
17  
18 [published Online First: 2005/12/20]  
19  
20  
21  
22 31. van Valkenhoef G, Lu G, de Brock B, et al. Automating network meta-analysis. *Research synthesis*  
23  
24 *methods* 2012;3(4):285-99 doi: 10.1002/jrsm.1054 [published Online First: 2012/12/01]  
25  
26  
27 32. van Valkenhoef G, Dias S, Ades AE, et al. Automated generation of node-splitting models for  
28  
29 assessment of inconsistency in network meta-analysis. *Research synthesis methods* 2016;7(1):80-93  
30  
31 doi: 10.1002/jrsm.1167 [published Online First: 2015/10/16]  
32  
33  
34  
35 33. Kessler TM, Bachmann LM, Minder C, et al. Adverse event assessment of antimuscarinics for  
36  
37 treating overactive bladder: a network meta-analytic approach. *PLoS One* 2011;6(2):e16718. doi:  
38  
39 10.1371/journal.pone.0016718 [published Online First: 2011/03/05]  
40  
41  
42  
43 34. König J, Krahn U, Binder H. Visualizing the flow of evidence in network meta-analysis and  
44  
45 characterizing mixed treatment comparisons. *Statistics in medicine* 2013;32(30):5414-29 doi:  
46  
47 10.1002/sim.6001 [published Online First: 2013/10/15]  
48  
49  
50 35. Krahn U, Binder H, König J. A graphical tool for locating inconsistency in network meta-analyses.  
51  
52 *BMC medical research methodology* 2013;13:35 doi: 10.1186/1471-2288-13-35 [published Online  
53  
54 First: 2013/03/19]  
55  
56  
57  
58 36. Singh GM, Danaei G, Farzadfar F, et al. The age-specific quantitative effects of metabolic risk  
59  
60

1  
2  
3  
4 factors on cardiovascular diseases and diabetes: a pooled analysis. *PLoS One* 2013;8(7):e65174 doi:  
5  
6 10.1371/journal.pone.0065174 [published Online First: 2013/08/13]  
7

8  
9 37. Ponce J, Nguyen NT, Hutter M, et al. American Society for Metabolic and Bariatric Surgery  
10  
11 estimation of bariatric surgery procedures in the United States, 2011-2014. *Surgery for obesity and*  
12  
13 *related diseases : official journal of the American Society for Bariatric Surgery* 2015;11(6):1199-200  
14  
15 doi: 10.1016/j.soard.2015.08.496 [published Online First: 2015/10/20]  
16  
17

18  
19 38. Imbus JR, Voils CI, Funk LM. Bariatric surgery barriers: a review using Andersen's Model of  
20  
21 Health Services Use. *Surgery for obesity and related diseases : official journal of the American Society*  
22  
23 *for Bariatric Surgery* 2018;14(3):404-12 doi: 10.1016/j.soard.2017.11.012 [published Online First:  
24  
25 2017/12/19]  
26  
27  
28  
29  
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## Supplementary material 1

### **Preliminary Search Strategy in Medline (Ovid interface) for Comparative long-term effectiveness and safety of primary bariatric surgeries in treating type 2 diabetes mellitus in adults: a protocol for systematic review and network meta-analysis of randomized controlled trials**

#1 exp obesity/

#2 exp type 2 diabetes mellitus/

#3 exp weight loss/

#4 obes\*.ti,ab.

#5 over?weight.ti,ab.

#6 diabetes.ti,ab.

#7 T2D\*.ti,ab.

#8 NIDDM.ti,ab.

#9 or/1-8

#10 obesity/su

#11 exp Obesity, Morbid/su

#12 exp bariatric surgery/

#13 (surg\* adj5 bariatric).ti,ab.

#14 anti?obesity adj5 surg\*.ti,ab.

#15 malabsorptive adj5 procedure\*.ti,ab.

#16 (obes\* adj5 surg\*).ti,ab.

#17 (metaboli\* adj5 surg\*).ti,ab.

#18 exp gastric bypass/

#19 (gastroplast\* or gastrogastrostom\* or gastro?gastrostom\* or gastroenterostom\* or (gastric bypass) or (gastric surger\*) or (restrictive surger\*)).ti,ab.

#20 ((one Anastomosis) or (one-Anastomosis) or mini or (single Anastomosis)) adj5 (bypass or switch).ti,ab.

#21 ((greater curvature) or (gastric\*)) adj5 plicat\*.ti,ab.

1  
2  
3  
4 #22 gastrectom\*.ti,ab.

5 #23 LSG.ti,ab.

6  
7 #24 VSG.ti,ab.

8  
9 #25 gastrointestinal adj5 surg\*.ti,ab.

10  
11 #26 gastrointestinal diversion\*.ti,ab.

12  
13 #27 exp biliopancreatic diversion/  
14

15 #28 biliopancreatic diversion.ti,ab.

16  
17 #29 biliopancreatic bypass.ti,ab.

18  
19 #30 gastric adj5 stapl\*.ti,ab.

20  
21 #31 duodenal adj5 switch\*.ti,ab.

22  
23 #32 gastric band\*.ti,ab.

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25 #33 silicon band\*.ti,ab.

26  
27 #34 exp gastroenterostomy/  
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29 #35 gastroplasty/  
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31 #36 LAGB.ti,ab.

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33 #37 stomach adj5 stapl\*.ti,ab.

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35 #38 laparoscop\* adj5 band\*.ti,ab.

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37 #39 lap?band\*.ti,ab.

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39 #40 malabsorptive adj5 surg\*.ti,ab.

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41 #41 mason\* adj5 procedure.ti,ab.

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43 #42 Roux-en-Y.ti,ab.

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45 #43 anastomosis, Roux-en-Y/  
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47 #44 or/12-43

48 #45 9 and 44

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50 #46 10 or 11 or 45

51  
52 #47 limit 46 to yr=2004 - 2018

53  
54 #48 limit 47 to (clinical trial, phase iii or clinical trial, phase iv or clinical trial

55  
56 or comparative study or controlled clinical trial or evaluation studies or

57  
58 guideline or meta analysis or multicenter study or practice guideline or

59  
60 randomized controlled trial or scientific integrity review or technical report or

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4 twin study or validation studies or systemic review)

5 **#49** randomized controlled trial.pt

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7 **#50** controlled clinical trial.pt

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9 **#51** randomized.ab

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11 **#52** placebo.ab

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13 **#53** clinical trials as topic.sh.

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15 **#54** randomly.ab

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17 **#55** trial.ti

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19 **#56** groups.ti,ab

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21 **#57** or/49-56

22  
23 **#58** exp animals/ not humans.sh.

24  
25 **#59** 57 NOT 58

26  
27 **#60** 47 and 59

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29 **#61** 48 or 60

30 ab=abstract; adj = adjacent; exp =exploded; pt=publication type; sh = MeSH

31 (Medical subject heading); su=surgery; ti=title; the asterisk (\*) substitutes

32 one or no characters; the question mark (?) substitutes one character.  
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## Supplementary material 2

### Preliminary Screening questions and Data Extraction Form for Comparative long-term effectiveness and safety of primary bariatric surgeries in treating type 2 diabetes mellitus in adults: a protocol for systematic review and network meta-analysis of randomized controlled trials

Reference code \_\_\_\_\_

Basic information			
Code of Original study		Code of Report	
Code of Valuator		Date of Evaluation	
Contact info of Author			
Quotation format(author, study title, journal, Year of publication, volume)			
Inclusion and exclusion criteria			
Inclusion criteria	<p><b>Participants</b></p> <p>① Include overweight or obese adults with type 2 diabetes mellitus yes <input type="checkbox"/> no <input type="checkbox"/></p> <p><b>Interventions and control</b></p> <p>② Procedures and/or controls involved  <i>Roux-en-Y gastric bypass</i> <input type="checkbox"/> <i>sleeve gastrectomy</i> <input type="checkbox"/>  <i>adjustable gastric banding</i> <input type="checkbox"/>  <i>biliopancreatic diversion with duodenal switch</i> <input type="checkbox"/>  <i>greater curvature plication</i> <input type="checkbox"/> <i>one-anastomosis gastric bypass</i> <input type="checkbox"/>  <i>single anastomosis duodenal-ileal bypass with sleeve gastrectomy</i> <input type="checkbox"/>  <i>Other surgical procedure(s) except procedures no longer performed, (including biliopancreatic diversion without duodenal switch, jejunoileal bypass, horizontal or vertical gastroplasty, and banding that is not adjustable)</i> _____ <input type="checkbox"/>  <i>non-surgical treatments</i> <input type="checkbox"/></p> <p><b>Comparisons</b></p> <p>③ Includes comparisons of at least two of the items above yes <input type="checkbox"/> no <input type="checkbox"/></p> <p><b>Study designs</b></p> <p>④ Randomized controlled trial yes <input type="checkbox"/> no <input type="checkbox"/></p> <p>⑤ Duration of follow-up <math>\geq 3</math> years yes <input type="checkbox"/> no <input type="checkbox"/></p>		
Exclusion criteria	<p><b>Participants</b></p> <p>① Restrict participants to specific diseases other than type 2 diabetes mellitus yes <input type="checkbox"/> no <input type="checkbox"/></p> <p>② Do not include adults yes <input type="checkbox"/> no <input type="checkbox"/></p> <p>③ Do not include participants with type 2 diabetes mellitus</p> <p><b>Interventions and comparison</b></p>		

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		<p>④ Revisional procedures <span style="float: right;">yes <input type="checkbox"/> no <input type="checkbox"/></span>          Comparisons between/among surgical procedure(s) no longer performed (biliopancreatic diversion without duodenal switch, jejunoileal bypass, horizontal or vertical gastroplasty, not adjustable banding, other _____) or between such procedures and non-surgical treatment <span style="float: right;">yes <input type="checkbox"/> no <input type="checkbox"/></span>          Comparisons between different techniques of the same procedure <span style="float: right;">yes <input type="checkbox"/> no <input type="checkbox"/></span></p> <p><b>Study designs</b></p> <p>⑤ Non-RCT, comparative studies <span style="float: right;">yes <input type="checkbox"/> no <input type="checkbox"/></span>          ⑥ Duration of follow-up &lt; 3 year <span style="float: right;">yes <input type="checkbox"/> no <input type="checkbox"/></span>          ⑦ Animal studies. <span style="float: right;">yes <input type="checkbox"/> no <input type="checkbox"/></span></p>
16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	Conclusion of inclusion or exclusion	<input type="checkbox"/> inclusion <input type="checkbox"/> exclusion <input type="checkbox"/> undetermined Support for judgement: _____ _____

<b>Characteristics of Methodology</b>																										
Study design(multiple choice)	<input type="checkbox"/> RCT <input type="checkbox"/> quasi-RCT <input type="checkbox"/> non-RCT <input type="checkbox"/> cluster randomized trial <input type="checkbox"/> cross-over trial Support for judgement: _____																									
Duration of study	Study beginning time: _____ year _____ month Study ending time: _____ year _____ month Mean(±SD) or median[inter-quartile range] follow-up period: _____																									
Sequence generation	randomized <input type="checkbox"/> non-randomized <input type="checkbox"/> quasi-randomized <input type="checkbox"/> undetermined <input type="checkbox"/> Support for judgement: _____																									
allocation concealment	yes <input type="checkbox"/> no <input type="checkbox"/> undetermined <input type="checkbox"/> Support for judgement: _____																									
Blinding participants*	<input type="checkbox"/> patients <input type="checkbox"/> intervenor <input type="checkbox"/> evaluator of all outcomes <input type="checkbox"/> evaluator of some, but not all outcomes <input type="checkbox"/> Statistical analyst comments(if blinding differs among outcomes): _____ Support for judgement: _____																									
Other factors that may introduce bias?	yes <input type="checkbox"/> no <input type="checkbox"/> Support for judgement: _____																									
Intentional analysis	yes <input type="checkbox"/> no <input type="checkbox"/> Support for judgement: _____																									
Other information of study	1. study site: single center <input type="checkbox"/> multi-center <input type="checkbox"/> Location of center(s) _____ 2. early conclusion of study: yes <input type="checkbox"/> no <input type="checkbox"/> 3. funding of study: _____ 4. potential conflict of interest: _____																									
Baseline information	comparable <input type="checkbox"/> ; non-comparable <input type="checkbox"/> ; undetermined <input type="checkbox"/> Support for judgement:( Mean±SD for continuous variables) <table style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th></th> <th style="text-align: center;">intervention 1</th> <th style="text-align: center;">intervention2</th> <th style="text-align: center;">intervention3</th> <th style="text-align: center;">intervention4</th> </tr> </thead> <tbody> <tr> <td>sex(M/F)</td> <td style="text-align: center;">/ /</td> <td style="text-align: center;">/ /</td> <td style="text-align: center;">/ /</td> <td style="text-align: center;">/ /</td> </tr> <tr> <td>Age(year)</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> </tr> <tr> <td>Weight(kg)</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> </tr> <tr> <td>BMI(kg/m<sup>2</sup>)</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> <td style="text-align: center;">±</td> </tr> </tbody> </table>		intervention 1	intervention2	intervention3	intervention4	sex(M/F)	/ /	/ /	/ /	/ /	Age(year)	±	±	±	±	Weight(kg)	±	±	±	±	BMI(kg/m <sup>2</sup> )	±	±	±	±
	intervention 1	intervention2	intervention3	intervention4																						
sex(M/F)	/ /	/ /	/ /	/ /																						
Age(year)	±	±	±	±																						
Weight(kg)	±	±	±	±																						
BMI(kg/m <sup>2</sup> )	±	±	±	±																						
<b>Characteristics of participants</b>																										
Total participants	_____																									
Settings	<input type="checkbox"/> hospital <input type="checkbox"/> community <input type="checkbox"/> nursing home <input type="checkbox"/> outpatient <input type="checkbox"/> chronic care institution Others: _____																									
Type of population	Healthy population: yes <input type="checkbox"/> no <input type="checkbox"/> BMI: BMI _____ to _____ kg/m <sup>2</sup> Or without complication BMI _____ to _____ kg/m <sup>2</sup> with complication BMI _____ to _____ kg/m <sup>2</sup> Type 2 diabetes: _____ Duration of type 2 diabetes: <input type="checkbox"/> unlimited <input type="checkbox"/> more than _____ months																									
Age	_____ to _____ years old   mean _____ SD _____ median _____ interquartile range _____																									
Sex	<input type="checkbox"/> Unlimited <input type="checkbox"/> Male only <input type="checkbox"/> Female only																									
Country	_____																									
Ethnicity	_____																									

Attrition (year 3)	Lost to follow-up at year 3: Number of participants lost to follow-up: Group 1 _____, reason _____ Group 2 _____, reason _____ Group 3 _____, reason _____ Group 4 _____, reason _____		
	Drop-out at year 3: Number of drop-out participants: Group 1 _____, reason _____ Group 2 _____, reason _____ Group 3 _____, reason _____ Group 4 _____, reason _____		
Attrition (year 5)	Lost to follow-up at year 5: Number of participants lost to follow-up: Group 1 _____, reason _____ Group 2 _____, reason _____ Group 3 _____, reason _____ Group 4 _____, reason _____		
	Drop-out at year 5: Number of drop-out participants: Group 1 _____, reason _____ Group 2 _____, reason _____ Group 3 _____, reason _____ Group 4 _____, reason _____		
<b>Intervention</b>			
Group	Number of Participants	Intervention	Description of intervention(intensity, frequency and duration etc.)
Group 1			
Group 2			
Group 3			
Group 4			
Integrity of interventions			
<b>Outcome Data</b>			
Planned outcomes	Planned: _____ Difference between report and plan: _____		
Planned time of Observation	Plan: _____ Difference between report and plan: _____		
Outcome data	Definition Diagnosis or evaluation: criteria for diagnosis or evaluation; Laboratory examination; assay method, unit, reference range; Scale: name, score range, state if higher or lower value is favorable If the evaluation time doesn't concord with the follow-up time, the time point of evaluation should be specified If number of missing data doesn't concord with attrition, the reason should be specified		
Full diabetes remission	Evaluation criteria: _____ Evaluation time (if not consistent) _____		

	Reason for extra missing data _____
Partial diabetes remission	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Major adverse event	Evaluation criteria: _____ Criteria of major adverse effect: _____ Evaluation time (if not consistent) _____ early complication: post-op _____ day; late complication: post-op _____ day- _____ year Reason for extra missing data _____
Diabetes management goal including HbA1c, BP and LDL-C	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Percentage excess weight loss (% EWL)	Definition: _____ Unit: <input type="checkbox"/> % <input type="checkbox"/> Other _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Body mass index (BMI) at follow-up	Definition: _____ Unit: <input type="checkbox"/> kg/m <sup>2</sup> <input type="checkbox"/> Other _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Weight (Wt) at follow-up	Definition: _____ Unit: <input type="checkbox"/> kg <input type="checkbox"/> Other _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Cardiovascular risk score	Scale name: _____ Score range: _____ which value is favorable <input type="checkbox"/> high score <input type="checkbox"/> low score Evaluation time (if not consistent) _____ Reason for extra missing data _____
Glycated hemoglobin (HbA1C)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
Fasting blood glucose (FBG)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
total cholesterol (TC)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
low-density lipoprotein cholesterol (LDL)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
high-density lipoprotein cholesterol (HDL)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
triglyceride (TG)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____



1 2 3 4 5 6 7	Systolic blood pressure	Method: _____ Model _____ Unit: _____ Reference: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
8 9 10 11	Diastolic blood pressure	Method: _____ Model _____ Unit: _____ Reference: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
12 13 14 15	Requirement of less anti-diabetic drugs at follow-up	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
16 17 18	discontinuation of insulin	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
19 20 21	Progression of diabetic retinopathy	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
22 23 24	Progression of diabetic nephropathy	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
25 26 27	Progression of diabetic neuropathy	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
28 29 30	Number of pts experiencing myocardial infarction	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
31 32 33	Number of pts experiencing stroke	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
34 35 36	Number of pts experiencing amputation of at least one digit	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
37 38 39	Number of pts experiencing ischemic limb disease	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
40 41 42	Number of pts experiencing heart failure	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
43 44 45	urine albumin/creatinine ratio (ACR)	Method: _____ Reagent info _____ Unit: _____ Reference range: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
46 47 48	All-cause mortality	Evaluation criteria: _____ Evaluation time (if not consistent) _____ Reason for extra missing data _____
49 50 51 52	<b>Other information</b>	
53 54	Key conclusion of authors	
55 56 57 58 59 60	Correspondence required	Study author contacted: yes <input type="checkbox"/> no <input type="checkbox"/> Study author replied: yes <input type="checkbox"/> no <input type="checkbox"/> Information asked: _____ Information provided: _____

**Outcome data (year 3)-Continuous data-1**

	Group 1 (Intervention_____)				Group 2 (Intervention_____)								
	Total number of participants	Reported cases for each outcome	mean	SD	Total amount	Case number	mean	SD	p-value	Estimate of effect	95%CI Lower limit	95%CI Upper limit	Comments (e.g., if the results shown in median and quartile range)
percentage excess weight loss													
BMI at follow-up													
Weight at follow-up													
Cardiovascular risk score													
Glycated hemoglobin (HbA1C)													
Fasting blood glucose (FBG)													
total cholesterol (TC)													
low-density lipoprotein													

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cholesterol (LDL)														
high-density lipoprotein cholesterol (HDL)														
triglyceride (TG)														
Systolic blood pressure (SBP)														
Diastolic blood pressure (DBP)														
urine albumin/creatinine ratio														
<b>Outcome data-Continuous data (year 3)-2 (when applicable, i.e. more than 2 comparative arms involved)</b>														
	Group 3 (Intervention_____)				Group 4 (Intervention_____)									
	Total number of participants	Reported cases for each outcome	mean	SD	Total amount	Case number	mean	SD	p-value	Estimate of effect	95%CI Lower limit	95%CI Upper limit	Comments (e.g., if the results shown in median and quartile range)	
percentage excess weight loss														
BMI at follow-up														
Weight at follow-														

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Cardiovascular risk score													
Glycated hemoglobin (HbA1C)													
Fasting blood glucose (FBG)													
total cholesterol (TC)													
low-density lipoprotein cholesterol (LDL)													
high-density lipoprotein cholesterol (HDL)													
triglyceride (TG)													
Systolic blood pressure (SBP)													
Diastolic blood pressure (DBP)													
urine albumin/creatinine ratio													

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Outcome data (year 3)-dichotomous data-1											
	Group 1 (Intervention_____)			Group 2 (Intervention_____)							
	Total number of participants	Reported participants for each outcome	Case number	Total number of participants	Reported participants for each outcome	Total number of participants	p-value	Estimate of effect	95%CI Lower limit	95%CI Upper limit	Comments
Full remission of type 2 diabetes mellitsu											
Full or partial remission of type 2 diabetes mellitsu											
Achieve treatment goals with regard to blood glucose, blood pressure and lipids											
Requirement of less anti-diabetic drugs at follow-up											
Discontinuation of insulin											
Progression of diabetic retinopathy											
Progression of diabetic											

nephropathy											
Progression of diabetic neuropathy											
Number of patients experiencing myocardial infarction											
Number of patients experiencing stroke											
Number of patients experiencing amputation of at least one digit											
Number of patients experiencing ischemic limb disease											
Number of patients experiencing heart failure											
All-cause mortality											
<b>Outcome data-dichotomous data (year 3)-2 (when applicable, i.e. more than 2 comparative arms involved)</b>											
	Group 3 (Intervention_____)			Group 4 (Intervention_____)							
	Total number of participants	Reported participants for each	Case number	Total number of participants	Reported participants for each	Total number of participants	p-value	Estimate of effect	95%CI Lower limit	95%CI Upper limit	Comments

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		outcome			outcome						
Full remission of type 2 diabetes mellitsu											
Full or partial remission of type 2 diabetes mellitsu											
Achieve treatment goals with regard to blood glucose, blood pressure and lipids											
Requirement of less anti-diabetic drugs at follow-up											
Discontinuation of insulin											
Progression of diabetic retinopathy											
Progression of diabetic nephropathy											
Progression of diabetic neuropathy											
Number of patients experiencing											

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myocardial infarction											
Number of patients experiencing stroke											
Number of patients experiencing amputation of at least one digit											
Number of patients experiencing ischemic limb disease											
Number of patients experiencing heart failure											
All-cause mortality											

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Group 3 (if applicable) (Intervention _____) (Lines may be added when necessary)		
Coding of Adverse event	Quotation from report regarding timing, severity, presentation, diagnosis, and management of adverse event	Anologue score of adverse event
Group 4 (if applicable) (Intervention _____) (Lines may be added when necessary)		
Coding of Adverse event	Quotation from report regarding timing, severity, presentation, diagnosis, and management of adverse event	Anologue score of adverse event

**Outcome data (year 5, if applicable)-Continuous data-1**

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	Group 1 (Intervention_____)				Group 2 (Intervention_____)								
	Total number of participants	Reported cases for each outcome	mean	SD	Total amount	Case number	mean	SD	p-value	Estimate of effect	95%CI Lower limit	95%CI Upper limit	Comments (e.g., if the results shown in median and quartile range)
percentage excess weight loss													
BMI at follow-up													
Weight at follow-up													
Cardiovascular risk score													
Glycated hemoglobin (HbA1C)													
Fasting blood glucose (FBG)													
total cholesterol (TC)													
low-density lipoprotein cholesterol (LDL)													

high-density lipoprotein cholesterol (HDL)													
triglyceride (TG)													
Systolic blood pressure (SBP)													
Diastolic blood pressure (DBP)													
urine albumin/creatinine ratio													
<b>Outcome data-Continuous data (year 5, if applicable)-2 (when more than 2 comparative arms involved)</b>													
	Group 3 (Intervention_____)				Group 4 (Intervention_____)								
	Total number of participants	Reported cases for each outcome	mean	SD	Total amount	Case number	mean	SD	p-value	Estimate of effect	95%CI Lower limit	95%CI Upper limit	Comments (e.g., if the results shown in median and quartile range)
percentage excess weight loss													
BMI at follow-up													
Weight at follow-up													

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Cardiovascular risk score														
Glycated hemoglobin (HbA1C)														
Fasting blood glucose (FBG)														
total cholesterol (TC)														
low-density lipoprotein cholesterol (LDL)														
high-density lipoprotein cholesterol (HDL)														
triglyceride (TG)														
Systolic blood pressure (SBP)														
Diastolic blood pressure (DBP)														
urine albumin/creatinine ratio														

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Outcome data (year 5, if applicable)-dichotomous data-1											
	Group 1 (Intervention_____)			Group 2 (Intervention_____)							
	Total number of participants	Reported participants for each outcome	Case number	Total number of participants	Reported participants for each outcome	Total number of participants	p-value	Estimate of effect	95%CI Lower limit	95%CI Upper limit	Comments
Full remission of type 2 diabetes mellitsu											
Full or partial remission of type 2 diabetes mellitsu											
Achieve treatment goals with regard to blood glucose, blood pressure and lipids											
Requirement of less anti-diabetic drugs at follow-up											
Discontinuation of insulin											
Progression of diabetic retinopathy											
Progression of diabetic											

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nephropathy											
Progression of diabetic neuropathy											
Number of patients experiencing myocardial infarction											
Number of patients experiencing stroke											
Number of patients experiencing amputation of at least one digit											
Number of patients experiencing ischemic limb disease											
Number of patients experiencing heart failure											
All-cause mortality											
<b>Outcome data-dichotomous data (year 5, if applicable )-2 (when more than 2 comparative arms involved)</b>											
	Group 3 (Intervention_____)			Group 4 (Intervention_____)							
	Total number of participants	Reported participants for each	Case number	Total number of participants	Reported participants for each	Total number of participants	p-value	Estimate of effect	95%CI Lower limit	95%CI Upper limit	Comments

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		outcome			outcome						
Full remission of type 2 diabetes mellitsu											
Full or partial remission of type 2 diabetes mellitsu											
Achieve treatment goals with regard to blood glucose, blood pressure and lipids											
Requirement of less anti-diabetic drugs at follow-up											
Discontinuation of insulin											
Progression of diabetic retinopathy											
Progression of diabetic nephropathy											
Progression of diabetic neuropathy											
Number of patients experiencing											



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myocardial infarction											
Number of patients experiencing stroke											
Number of patients experiencing amputation of at least one digit											
Number of patients experiencing ischemic limb disease											
Number of patients experiencing heart failure											
All-cause mortality											

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<p align="center"><b>Outcome data-adverse event (year 5, if applicable)</b></p> <p align="center">1. Coding of Adverse event: ###(study code) – ##(group number) – ###(adverse event number)</p> <p align="center">2. After sequence randomization, the adverse event will be re-numbered sequentially before sent for score translation)</p> <p align="center">3. Only adverse events not included in the “Outcome data-adverse event (year 3)” table will be listed.</p>		
<p align="center">Group 1 (Intervention _____) (Lines may be added when necessary)</p>		
Coding of Adverse event	Quotation from report regarding timing, severity, presentation, diagnosis, and management of adverse event	Anologue score of adverse event
<p align="center">Group 2 (Intervention _____) (Lines may be added when necessary)</p>		
Coding of Adverse event	Quotation from report regarding timing, severity, presentation, diagnosis, and management of adverse event	Anologue score of adverse event



# PRISMA-P Checklist for *Comparative long-term effectiveness and safety of primary bariatric surgeries in treating type 2 diabetes mellitus in adults: a protocol for systematic review and network meta-analysis of randomized controlled trials*

This checklist has been adapted for use from Table 3 in Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Systematic reviews. 2015;4:1.

Section/topic	#	Checklist item	Information reported		Page (P) and Line (L) Number(s)
			Yes	No	
<b>ADMINISTRATIVE INFORMATION</b>					
<b>Title</b>					
Identification	1a	Identify the report as a protocol of a systematic review	√		P1, L4-12
Update	1b	If the protocol is for an update of a previous systematic review, identify as such			N/A
<b>Registration</b>	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	√		P2, L58
<b>Authors</b>					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	√		P1, L14-41; P18, L43-54
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	√		P18, L14-25
<b>Amendments</b>	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments			N/A
<b>Support</b>					
Sources	5a	Indicate sources of financial or other support for the review	√		P18, L30-36
Sponsor	5b	Provide name for the review funder and/or sponsor			N/A
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	√		P18, L35-41
<b>INTRODUCTION</b>					
<b>Rationale</b>	6	Describe the rationale for the review in the context of what is already known	√		P3, L43 - P5, L25
<b>Objectives</b>	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	√		P5, L32-46
<b>METHODS</b>					

Section/topic	#	Checklist item	Information reported		Page (P) and Line (L) Number(s)
			Yes	No	
<b>Eligibility criteria</b>	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	√		P6, L17 – P9, L59
<b>Information sources</b>	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	√		P10, L4-49
<b>Search strategy</b>	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	√		Supplementary material 1
<b>STUDY RECORDS</b>					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	√		P10, L53 - P11, L10
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	√		P10, L53 - P11, L12; P11, L22-44
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	√		P10, L53 - P11, L18
<b>Data items</b>	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	√		P11, L45 - P13, L15
<b>Outcomes and prioritization</b>	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	√		P7, L40 – P9, L60; P3, L43 - P5, L25
<b>Risk of bias in individual studies</b>	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	√		P13, L17-46; P16, L14-54
<b>DATA</b>					
<b>Synthesis</b>	15a	Describe criteria under which study data will be quantitatively synthesized	√		P14, L50-60; P16, L4-13
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., $I^2$ , Kendall's tau)	√		P13, L50-P15, L60
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	√		P16, L14-54
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	√		P16, L4-13
<b>Meta-bias(es)</b>	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	√		P16, L56 – P17, L15

Section/topic	#	Checklist item	Information reported		Page (P) and Line (L) Number(s)
			Yes	No	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	√		P17, L17-34

Abbreviations: N/A: not applicable.

For peer review only