Metabolic Surgery in the Treatment Algorithm for Type 2 Diabetes: A Joint Statement by International Diabetes Organizations

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BACKGROUND

Despite growing evidence that bariatric/metabolic surgery powerfully improves type 2 diabetes (T2D), existing diabetes treatment algorithms do not include surgical options.

AIM

The 2nd Diabetes Surgery Summit (DSS-II), an international consensus conference, was convened in collaboration with leading diabetes organizations to develop global guidelines to inform clinicians and policymakers about benefits and limitations of metabolic surgery for T2D.

METHODS

A multidisciplinary group of 48 international clinicians/scholars (75% nonsurgeons), including representatives of leading diabetes organizations, participated in DSS-II. After evidence appraisal (MEDLINE [1 January 2005–30 September 2015]), three rounds of Delphi-like questionnaires were used to measure consensus for 32 data-based conclusions. These drafts were presented at the combined DSS-II and 3rd World Congress on Interventional Therapies for Type 2 Diabetes (London, U.K., 28–30 September 2015), where they were open to public comment by other professionals and amended face-to-face by the Expert Committee.

RESULTS

Given its role in metabolic regulation, the gastrointestinal tract constitutes a meaningful target to manage T2D. Numerous randomized clinical trials, albeit mostly short/midterm, demonstrate that metabolic surgery achieves excellent glycemic control and reduces cardiovascular risk factors. On the basis of such evidence, metabolic surgery should be *recommended* to treat T2D in patients with class III obesity (BMI ≥40 kg/m^2) and in those with class II obesity (BMI 35.0–39.9 kg/m^2) when hyperglycemia is inadequately controlled by lifestyle and optimal medical therapy. Surgery should also be *considered* for patients with T2D and BMI 30.0–34.9 kg/m^2 if hyperglycemia is inadequately controlled despite optimal treatment with either oral or injectable medications. These BMI thresholds should be reduced by 2.5 kg/m^2 for Asian patients.

CONCLUSIONS

Although additional studies are needed to further demonstrate long-term benefits, there is sufficient clinical and mechanistic evidence to support inclusion of metabolic surgery among antidiabetes interventions for people with T2D and obesity. To date, the DSS-II guidelines have been formally endorsed by 45 worldwide medical and scientific societies. Health care regulators should introduce appropriate reimbursement policies.

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F.R. and D.E.C. chaired the writing committee for this report.

**The 2nd Diabetes Surgery Summit voting delegates are listed in Table 2.*

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See accompanying articles, pp. 857, 878, 884, 893, 902, 912, 924, 934, 941, 949, and 954.

Several gastrointestinal (GI) operations, including partial gastrectomies (1,2) and bariatric procedures (Fig. 1) (3–5), promote dramatic, durable improvement of type 2 diabetes (T2D). Given the magnitude and rapidity of the effect of GI surgery on hyperglycemia, along with experimental evidence that rearrangements of GI anatomy similar to those in some bariatric procedures directly affect glucose homeostasis (6), GI interventions have been suggested as a treatment for T2D (7).

In 2007, the delegates from the 1st Diabetes Surgery Summit (DSS-I), an international consensus conference, reviewed available clinical and mechanistic evidence and recommended expanding the use and study of GI surgery to treat diabetes, including for individuals with only mild obesity (5,8). In the ensuing years, the concept of "metabolic surgery" or "diabetes surgery" has become widely recognized in academic circles, and, accordingly, most major worldwide bariatric surgery societies have changed their names to include the word "metabolic" (9).

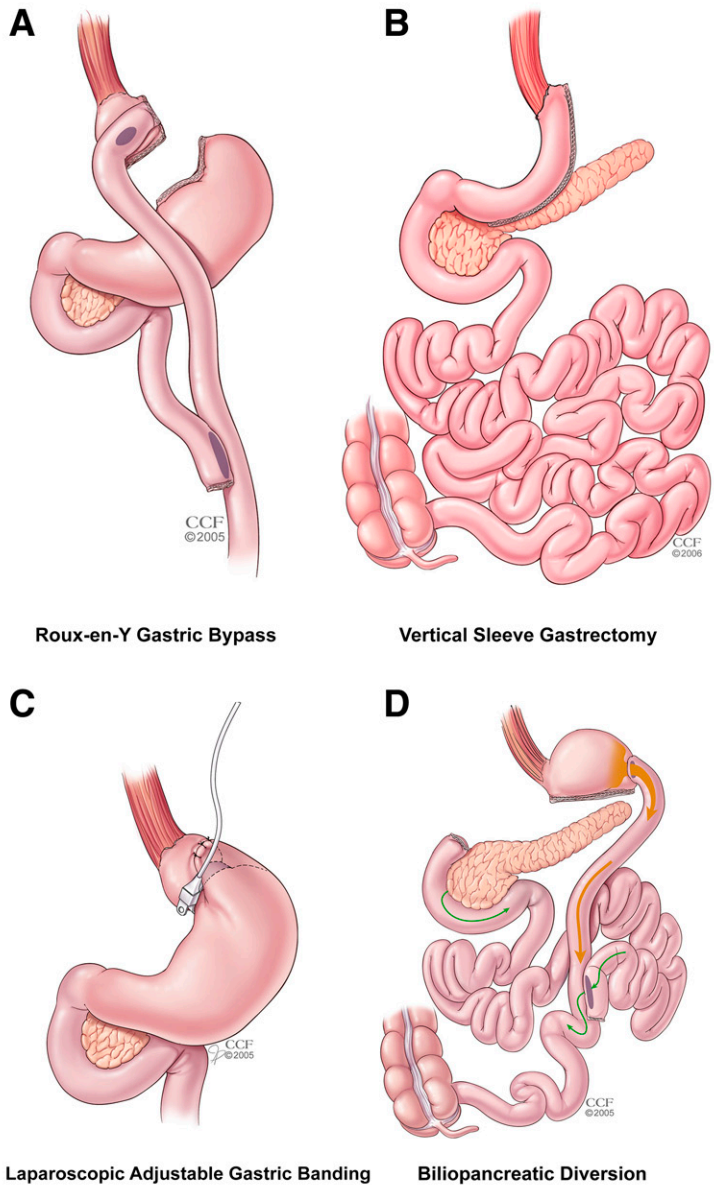

Figure 1—Diagrams of the four bariatric/metabolic operations currently in common clinical use. BPD can be performed as the classic type (shown) or with the duodenal switch variant. Reprinted with permission from the Cleveland Clinic Foundation (CCF).

Since DSS-I, a substantial body of additional evidence has accumulated, including from numerous randomized clinical trials (RCTs), demonstrating that bariatric/metabolic surgery achieves superior glycemic control and reduction of cardiovascular risk factors in obese patients with T2D compared with various medical/lifestyle interventions (10–25). Further research on mechanisms of action of these procedures (5,6,26–34) has corroborated evidence in animal studies demonstrating an important role for the GI tract in glucose homeostasis (35), providing a biological rationale for the use of GI-based interventions to treat T2D. Available data, based predominantly on modeling studies, suggest that bariatric/metabolic surgery is also cost-effective, especially in patients with diabetes (36,37).

On the basis of this mounting evidence, several international professional organizations and government agencies have recently suggested expanding the indications for bariatric/metabolic surgery to include patients with inadequately controlled T2D and BMI as low as 30 kg/m^2, and down to 27.5 kg/m^2 for Asians (8,9,38,39).

However, whereas obesity guidelines by national and international societies and government agencies recommend the use of bariatric surgery in individuals with T2D (9,40), clinical guidelines for diabetes care paradoxically provide little or no mention of a role for surgical interventions for T2D, even in patients with severe obesity (41). Despite the growing popularity of this topic in scientific communities (9) and the media (42), most diabetes care providers and patients are still inadequately informed about the indications, benefits, and potential risks of surgical treatments for diabetes. Moreover, insurance reimbursement policies for bariatric/metabolic surgery continue to reflect only body weight–centric criteria and do not include diabetes-related metrics or cost-effectiveness. Consequently, access to surgery for patients with diabetes is not adequately prioritized. In fact, no existing treatment algorithm for T2D includes a role for surgical intervention.

Using surgery as a diabetes intervention, however, implies conceptual and practical differences from the traditional practice of bariatric surgery for obesity. For instance, the criteria currently used to select candidates for bariatric/metabolic

surgery do not include metrics of metabolic disease severity, predictors of success of treatment, or an evaluation of risks and benefits of surgery as contrasted to those of alternative diabetes treatment options. In addition, preoperative diagnostics, perioperative management, and postoperative follow-up of traditional bariatric surgery are not consistent with the need to identify and monitor diabetes-related parameters and complications. Furthermore, there are no strategies yet for integrating complementary pharmaceutical and surgical therapies to optimize outcomes of diabetes management.

Whereas selection criteria for bariatric surgery have been standardized worldwide for many years through an influential National Institutes of Health (NIH) consensus statement (43), that document is now conspicuously outdated, and there is no reference for surgical treatment of diabetes to globally raise the standards of such practice.

Recognizing the need to inform diabetes care providers about the benefits and limitations of metabolic surgery, the 2nd Diabetes Surgery Summit (DSS-II) was convened in collaboration with six leading international diabetes organizations: the American Diabetes Association, International Diabetes Federation, Chinese Diabetes Society, Diabetes India, European Association for the Study of Diabetes, and Diabetes UK. The overarching aim of this consensus conference was to review available evidence and to develop global recommendations that integrate medical and surgical therapies in a rational treatment algorithm for T2D. Specific goals included providing guidance for selection of surgical candidates and use of diabetes-specific measures in the preoperative workup and postoperative follow-up of patients.

At the time this article went to press, the DSS-II consensus statements and guidelines had been officially endorsed by 45 leading professional societies across the globe, of which 30 are primarily medical (diabetes, endocrinology, and gastroenterology) and 15 are primarily surgical organizations (Table 1). Additional medical and scientific societies are currently considering endorsing these results as well.

These recommendations reflect currently available data and will need to be updated as new evidence is developed in the future.

Here we report the methods for DSS-II, the resulting recommendations, and their supporting evidence.

Executive Summary

T2D is associated with complex metabolic dysfunctions, leading to increased morbidity, mortality, and cost. Although population-based efforts through lifestyle interventions are essential to prevent obesity and diabetes, people who develop this disease should have access to all effective treatment options.

Given its role in metabolic regulation, the GI tract constitutes a clinically and biologically meaningful target for the management of T2D.

A substantial body of evidence has accumulated, including numerous, albeit mostly short/midterm RCTs, demonstrating that metabolic surgery—defined here as the use of GI surgery with the intent to treat T2D and obesity—can achieve excellent control of hyperglycemia and reduce cardiovascular risk factors.

Although additional studies are needed to further demonstrate long-term benefits, there is now sufficient clinical and mechanistic evidence to support inclusion of metabolic surgery among antidiabetes interventions for people with T2D and obesity.

Complementary criteria to the sole use of BMI, the traditional criterion used to select candidates for bariatric surgery, need to be developed to achieve a better patient selection algorithm for metabolic surgery.

Metabolic surgery should be a *recommended* option to treat T2D in appropriate surgical candidates with class III obesity (BMI $\geq$40 kg/m^2), regardless of the level of glycemic control or complexity of glucose-lowering regimens, as well as in patients with class II obesity (BMI 35.0–39.9 kg/m^2) with inadequately controlled hyperglycemia despite lifestyle and optimal medical therapy.

Metabolic surgery should also be *considered* to be an option to treat T2D in patients with class I obesity (BMI 30.0–34.9 kg/m^2) and inadequately controlled hyperglycemia despite optimal medical treatment by either oral or injectable medications (including insulin).

All BMI thresholds should be reconsidered depending on the ancestry of the patient. For example, for patients of Asian descent, the BMI values above should be reduced by 2.5 kg/m^2.

Metabolic surgery should be performed in high-volume centers with multidisciplinary teams that understand and are experienced in the management of diabetes and GI surgery.

Ongoing and long-term monitoring of micronutrient status, nutritional supplementation, and support must be provided to patients after surgery, according to guidelines for postoperative management of bariatric/metabolic surgery by national and international professional societies.

Metabolic surgery is a potentially cost-effective treatment option in obese patients with T2D. The clinical community should work together with health care regulators to recognize metabolic surgery as an appropriate intervention for T2D in people with obesity and to introduce appropriate reimbursement policies.

METHODS

DSS-II Partners and Selection of Voting Delegates

The DSS-II organizing committee and the partner diabetes organizations tasked a multidisciplinary group of 48 international authorities to develop a set of evidence-based recommendations. This DSS-II Expert Committee included scholars representing diabetology, endocrinology, internal medicine, cardiology, gastroenterology, primary care, nutrition, and surgery, including official representatives of partner diabetes organizations (Table 2). To ensure maximum scholarship, voting delegates were chosen entirely from academicians, with no representatives from industry. To further minimize potential conflicts of interest, nonsurgeons were purposefully overrepresented (75%) and were complemented by academic surgeons with relevant publication records. Two independent, nonvoting moderators/adjudicators developed

Table 1—International societies that have ratified and/or endorsed the DSS-II consensus statements and guidelines

Partner diabetes organizations that helped develop and have ratified the DSS-II consensus statements and guidelines:	Country
American Diabetes Association (ADA)	USA
International Diabetes Federation (IDF)	International
Diabetes UK (DUK)	UK
Chinese Diabetes Society (CDS)	China
Diabetes India (DI)	India
Other organizations that formally endorse the DSS-II consensus statements and guidelines (to date):	
American Association of Clinical Endocrinologists (AACE)	USA
American College of Surgeons (ACS)	USA
American Gastroenterological Association (AGA)	USA
American Society for Metabolic and Bariatric Surgery (ASMBS)	USA
Argentinian Society of Diabetes (SAD)	Argentina
Argentinian Society for Bariatric and Metabolic Surgery (SACO)	Argentina
Asia-Pacific Bariatric and Metabolic Surgery Society (APBMSS)	International
Association of British Clinical Diabetologists (ABCD)	UK
Australian Diabetes Society (ADS)	Australia
Belgian Diabetes Association (ABD)	Belgium
Brazilian Society of Diabetes (SBD)	Brazil
Brazilian Society of Bariatric and Metabolic Surgery (SBCBM)	Brazil
British Obesity and Metabolic Surgery Society (BOMSS)	UK
Czech Society for the Study of Obesity (CSSO)	Czech Republic
Chilean Society of Endocrinology and Diabetes (SCED)	Chile
Chilean Society for Bariatric and Metabolic Surgery (SCCBM)	Chile
Endocrine Society	USA
European Association for the Study of Obesity (EASO)	International
French Society of Diabetes (SFD)	France
French Society of Bariatric and Metabolic Surgery (SOFFCO)	France
German Diabetes Society (DDG)	Germany
German Society for Obesity Surgery (CA-ADIP)	Germany
Hellenic Diabetes Association (HDA)	Greece
International Federation for the Surgery of Obesity & Metabolic Disorders (IFSO)	International
Israel Diabetes Association (IDA)	Israel
Italian Society of Bariatric & Metabolic Surgery (SICOB)	Italy
Italian Society of Diabetology (SID)	Italy
Japan Diabetes Society (JDS)	Japan
Latin American Association of Diabetes (ALAD)	International
Mexican College of Bariatric and Metabolic Surgery (CMCOEM)	Mexico
Mexican Society of Nutrition and Endocrinology (SMNE)	Mexico
Qatar Diabetes Association (QDA)	Qatar
Saudi Diabetes and Endocrine Association (SDEA)	Saudi Arabia
Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)	USA
Society for Endocrinology (SfE)	UK
Society for Surgery of the Alimentary Tract (SSAT)	USA
South African Society for Surgery Obesity and Metabolism (SASSO)	South Africa
Spanish Society for Bariatric and Metabolic Surgery (SECO)	Spain
Spanish Society of Diabetes (SED)	Spain
The Obesity Society (TOS)	USA

This table indicates the societies that, at the time this article went to press, had officially ratified and/or endorsed the DSS-II consensus statements and guidelines. Additional international medical and scientific societies are currently considering endorsing these results as well.

and administered questionnaires for the Delphi process and chaired the face-to-face meeting of voting delegates (vide infra).

Methods for Collection and Evaluation of Evidence

Criteria used for evidence searching were based on methods used in previous consensus development conferences and systematic reviews of evidence (44,45), adapted to serve the DSS-II objectives. We used a highly selective, diabetes-focused approach (only level-1 evidence from RCTs) to assess comparative effectiveness of surgery versus nonsurgical therapies for T2D and to compare the glycemic effects of different operations. A broader evidence base was used (RCTs plus high-quality observational studies) for matters such as durability of glycemic control, surgical safety, and cardiovascular disease (CVD) risk reduction. Economic implications of bariatric/metabolic surgery were assessed using available studies of cost-effectiveness and systematic reviews with specific reference to patients with T2D.

Questions for evidence assessment included the following: *1*) long-term effects of surgery on glycemic control in patients with T2D; *2*) effectiveness of surgery compared with medical/lifestyle interventions on glycemic control; *3*) comparative effectiveness of different procedures on T2D; *4*) effects of surgery on microvascular complications of diabetes, CVD risk, CVD events, and mortality; *5*) short- and long-term surgical safety; and *6*) comparative safety profile of different operations.

MEDLINE from 1 January 2005 through 15 June 2015 was searched to generate the first draft of the consensus document. New evidence published by 30 September 2015 was available for discussion in face-to-face DSS-II meetings and is incorporated into this document, using the same inclusion/exclusion criteria for evidence evaluation as in the initial draft.

Studies considered to appraise the evidence included RCTs and observational studies (case-control and case-series), as appropriate for specific questions (vide infra). For both RCTs and observational studies, only reports documenting at least 1-year follow-up and with 80% retention at 2 years and 70% beyond 2 years were included. These criteria are adapted from the methods of recent systematic reviews of bariatric surgery (46).

Table 2—The DSS-II voting delegates

DSS-II delegate	Affiliation	Nationality	Specialty
K. George M.M. Alberti*	Imperial College London	U.K.	Diabetology
Nizar Albache	Aleppo University	Syria	Endocrinology
Stephanie A. Amiel*	King's College London	U.K.	Diabetology
Rachel L. Batterham	University College London	U.K.	Endocrinology
Deepak L. Bhatt	Harvard Medical School	U.S.	Cardiology
Camilo Boza	Clínica Las Condes	Chile	Surgery
William T. Cefalu	Pennington Biomedical Research Center, Louisiana State University	U.S.	Diabetology
Ricardo V. Cohen*	Oswaldo Cruz Hospital	Brazil	Surgery
Anita P. Courcoulas	University of Pittsburgh	U.S.	Surgery
David E. Cummings*†	University of Washington	U.S.	Endocrinology
Stefano Del Prato	University of Pisa	Italy	Diabetology
Sean F. Dinneen	Galway University Hospitals	Ireland	Endocrinology
John B. Dixon*	Baker IDI Heart and Diabetes Institute	Australia	General Medicine
Robert H. Eckel	University of Colorado Anschutz Medical Campus	U.S.	Endocrinology
Ele Ferrannini	University of Pisa	Italy	Diabetology
Paola Fioretto	University of Padova	Italy	Endocrinology
Gema Frühbeck	University of Navarra, CIBERobn	Spain	Endocrinology
Michel Gagner	Florida International University and Hôpital du Sacré-Coeur de Montréal	U.S. and Canada	Surgery
Richard W. Grant	Kaiser Permanente Division of Research	U.S.	Internal Medicine
William H. Herman	University of Michigan	U.S.	Endocrinology
Sayeed Ikramuddin	University of Minnesota	U.S.	Surgery
Linong Ji*	Peking University	China	Diabetology
Desmond G. Johnston	Imperial College London	U.K.	Diabetology
Lee M. Kaplan*†	Harvard Medical School	U.S.	Gastroenterology
Sangeeta R. Kashyap	Cleveland Clinic	U.S.	Endocrinology
Tracy Kelly	Diabetes UK	U.K.	Nutrition
Tomasz Klupa	Jagiellonian University	Poland	Diabetology
Judith Korner	Columbia University	U.S.	Endocrinology
Blandine Laferrère	Columbia University	U.S.	Endocrinology
Harold E. Lebovitz	State University of New York	U.S.	Diabetology
Wei-Jei Lee	Min-Sheng General Hospital	Taiwan	Surgery
Carel W. le Roux*	University College Dublin	Ireland	Metabolic Medicine
Jeffrey I. Mechanick	Icahn School of Medicine at Mount Sinai	U.S.	Endocrinology
Geltrude Mingrone*	Catholic University of Rome	Italy	Internal Medicine
John M. Morton	Stanford University	U.S.	Surgery
David M. Nathan	Harvard Medical School	U.S.	Diabetology
Walter J. Pories	East Carolina University	U.S.	Surgery
Robert E. Ratner*	American Diabetes Association, Chief Scientific and Medical Officer	U.S.	Diabetology
Gerry Rayman	Ipswich Hospital NHS Trust	U.K.	Diabetology
Francesco Rubino*†	King's College London and King's College Hospital	U.K.	Surgery
Shaukat M. Sadikot*	Diabetes India	India	Diabetology
Philip R. Schauer*†	Cleveland Clinic	U.S.	Surgery
Harvey J. Sugerman	Virginia Commonwealth University	U.S.	Surgery
Luc Van Gaal	University of Antwerp	Belgium	Endocrinology
Josep Vidal	Hospital Clinic	Spain	Endocrinology
Jianping Weng	Sun Yat-sen University	China	Diabetology
Bruce M. Wolfe*	Oregon Health & Science University	U.S.	Surgery/Nutrition
Paul Z. Zimmet*	Monash University	Australia	Diabetology

†DSS-II conference codirectors. *DSS-II conference organizing committee.

Question-Specific Inclusion Criteria

- For evidence related to the effectiveness of surgery versus medical/lifestyle interventions to control T2D, only RCTs were considered. A comprehensive algorithm was used to identify all RCTs published by 30 September 2015 reporting the effects of bariatric/metabolic surgery in patients with diabetes. Evidence listed includes studies of patients with BMI $\geq$35 kg/m^2 and $<$35 kg/m^2. A simple meta-analysis was performed to present an integrated picture of existing evidence.
- For evidence regarding comparative effectiveness of different surgical procedures on T2D, data were obtained only from RCTs in which different procedures were used expressly to treat diabetes.
- For evidence regarding the effect of GI surgery on CVD events and CVD risk reduction, data were obtained from RCTs when available, as well as from long-term case-control studies, and from the most recent relevant meta-analyses.
- For evidence regarding the durability of postoperative glycemic control, surgical safety in general, and comparative safety profiles of different operations, data were obtained from RCTs when available, from longitudinal case-series and case-control studies, and from the most recent relevant meta-analyses.

Descriptors of Level of Evidence

Herein we use standard level of evidence (LoE) descriptors, defined as follows: IA, evidence from meta-analysis of RCTs; IB, evidence from at least one RCT; IIA, evidence from at least one controlled study without randomization; IIB, evidence from at least one other type of quasi-experimental study; III, evidence from nonexperimental descriptive studies (e.g., comparative, correlation, or case-control); IV, evidence from expert committee reports, opinions or clinical experience of respected authorities, or both.

Consensus Development Process

After review and appraisal of evidence, two independent moderators developed online Delphi-like questionnaires (47,48) to measure the degree of consensus for a set of statements and recommendations that were believed to summarize and reflect available evidence. For each of these, we sought to achieve consensus, defined as agreement by a supermajority ($\geq$67%) of voting delegates, consistent with other medical consensus conferences (49). DSS-II delegates who did not agree with proposed statements were asked to state their reasons and propose amendments. Three rounds of questionnaires were administered to test various amendments to the original statements that could increase consensus levels from the group. Draft conclusions generated through this iterative process were presented at the combined DSS-II and 3rd World Congress on Interventional Therapies for Type 2 Diabetes (WCITD 2015, London, U.K., 28–30 September 2015). Proceedings were open to public comment by other experts in the field (members of the Faculty of WCITD) and by the entire audience through opinion polls, using real-time electronic voting. Approximately 630 professionals and stakeholders from 50 nations on five continents contributed to those discussions.

Finally, on 30 September 2015, voting DSS-II delegates met face-to-face to define a final consensus document. Several relevant professional organizations and stakeholders were invited to observe the proceedings by sending official representatives to WCITD 2015/DSS-II (Supplementary Table 1). The document with conclusions reached by the experts underwent a final review by DSS voting delegates and was then submitted to the appropriate committees and executive boards of partner organizations for formal approval (Table 1).

Grade of Consensus

We used a supermajority rule to define consensus. Consistent with other studies (8,50), consensus was considered to have been reached when $\geq$67% of the experts agreed on a given topic. However, language was iteratively modified to maximize agreement, and the degree of consensus for each statement was graded according to the following scale: grade U = 100% agreement (unanimous); grade A = 89–99% agreement; grade B = 78–88% agreement; grade C = 67–77% agreement (Table 3). This grading scale is meant to indicate statements that reflect unanimous or near-unanimous opinions (grade U and grade A), strong agreement with little variance (grade B), or a consensus statement that reflects an averaging of more and possibly extremely diverse opinions (grade C). We report here both the grade of consensus and the exact percentage of agreement for each statement.

SUMMARY OF EVIDENCE: CLINICAL AND BIOLOGICAL RATIONALE FOR SURGICAL TREATMENT OF T2D

Evidence Supporting Surgical Treatment of T2D

The GI tract is an important contributor to normal glucose homeostasis (35), and mounting evidence, especially over the past decade, has demonstrated benefits of bariatric/metabolic surgery to treat and prevent T2D (3,5,10–25,51–53). Beyond inducing weight loss–related metabolic improvements, some operations engage mechanisms that improve glucose homeostasis independent of weight loss (6), such as changes in gut hormones, bile acid metabolism, microbiota, intestinal glucose metabolism, and nutrient sensing (5,6,26–34). Bariatric/metabolic surgery confers sustained favorable effects on glycemia—up to 20 years in one observational study (52)—although benefits can decrease over time, with or without weight regain (3,51,52,54–56).

Data from a growing number of recent RCTs in patients with T2D (10–25), including mainly individuals with BMI $\geq$35 kg/m^2 (the most commonly used threshold for traditional bariatric surgery) as well as some patients with BMI $<$35 kg/m^2 (range 25–35 kg/m^2), consistently demonstrate superior efficacy of bariatric/metabolic surgery in reducing weight and lowering glycemia compared with a variety of medical/lifestyle interventions (LoE IA) (Fig. 2*A*). Although the antidiabetes benefits of surgery often wane over time, the relative superiority of surgery over medical/lifestyle interventions in RCTs is similar throughout a range of 1–5 years (Fig. 2*B*). Our analysis of these trials shows a median HbA_{1c} reduction of 2.0% for surgery versus 0.5% for conventional therapies ($P < 0.001$) (Figs. 2*C* and 3*A*). Each of the 11 existing surgery-versus-medicine/lifestyle RCTs reported greater HbA_{1c} reduction following surgery (Figs. 2*C* and 3*B*). In all of these trials, final HbA_{1c} in the surgical groups was near 6.0%, regardless of the level of baseline HbA_{1c} (Fig. 3*C*). However, the majority of these RCTs have only examined 1- to 2-year results, and only a handful of them have examined results for 3–5 years.

Several classic "bariatric" operations cause T2D remission—defined as achieving nondiabetic HbA_{1c} levels off all diabetes medications—in a majority of cases

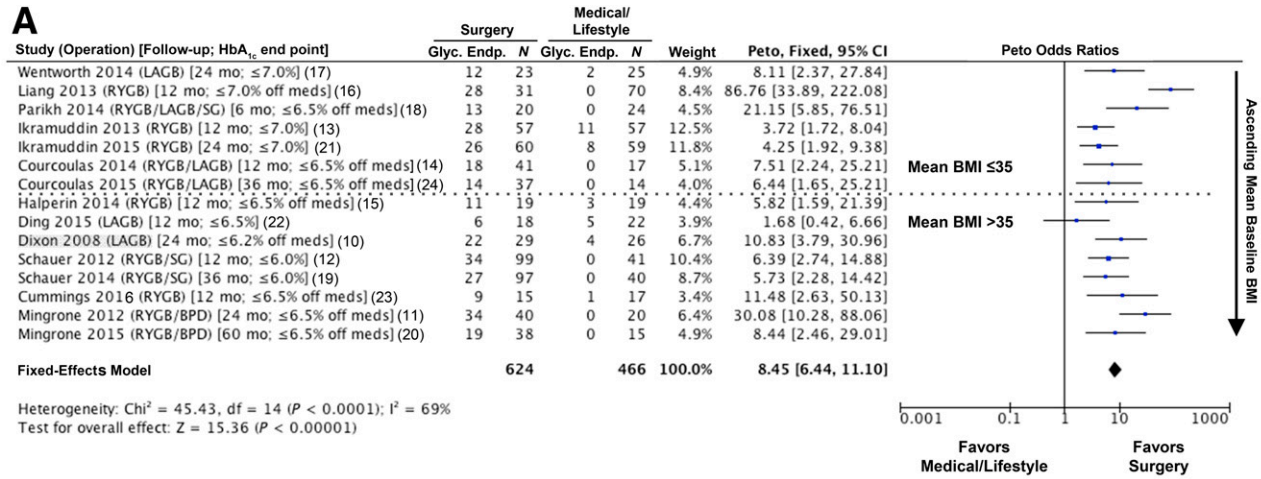

Figure 2—*A*: Forest plot of Peto odds ratios (ORs) of main glycemic end points, as defined in each trial, from published RCTs of bariatric/metabolic surgery compared with medical/lifestyle treatments for diabetes. Data are arranged in order of ascending mean baseline BMI; the dotted line separates trials performed with cohorts exhibiting an average baseline BMI above or below 35 kg/m^2. Study duration and HbA_{1c} end point thresholds are shown in brackets in column 1, where "off meds" indicates a threshold achieved off all diabetes medications; otherwise, end points represent HbA_{1c} thresholds achieved with or with such medications. ORs >1 indicate a positive effect of surgery compared with medical/lifestyle treatment. For each study, the OR is shown with its 95% CI. The pooled Peto ORs (95% CI) for all data were calculated under the assumption of a fixed-effects model. Weights represent inverse variance of ORs (or mean differences [MDs]) and provide an indirect measure of the relevance of each study within the meta-analysis, as a function of individual study size and variance. *B*: Forest plot of the trials depicted in Fig. 2*A*, with data arranged in order of increasing length of follow-up. *C*: Forest plot of MDs of HbA_{1c} serum levels after bariatric/metabolic surgery compared with medical/lifestyle treatments in published RCTs related to diabetes. Data are arranged in order of increasing follow-up time. Negative MDs denote lower HbA_{1c} levels following surgery than medical/lifestyle treatment. Data for each study are shown as the MD with its 95% CI. A random-effects model was used to calculate the pooled standardized MD. Glyc. Endp., glycemic end point; mo, month; SG, sleeve gastrectomy.

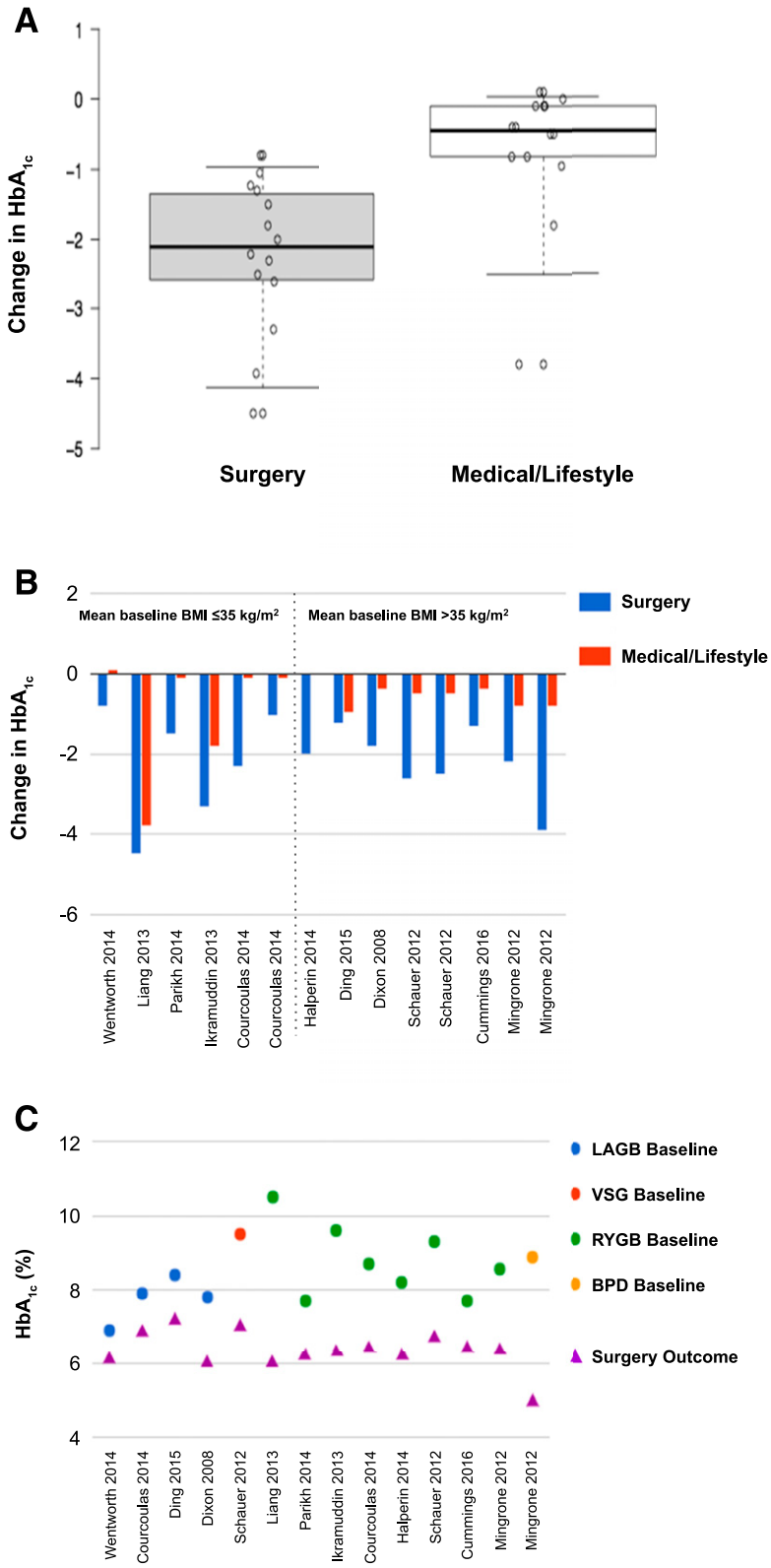

Figure 3—*A*: Box plot comparing the average changes in HbA_{1c} between surgery and medical/lifestyle treatments in the first reports of the 11 RCTs published to date. The plot shows 15 sample points because some RCTs reported results from two different surgical arms separately. Center lines show medians; box limits indicate the 25th and 75th percentiles, as determined by R software; whiskers extend 1.5 times the interquartile range from the 25th and 75th percentiles. Data points are plotted as open circles. *B*: Change from baseline HbA_{1c} in each of the 11 RCTs displayed in Fig. 3*A*. In trials where more than one type of surgery was studied, each operation is displayed separately, compared with the medical/lifestyle group. *C*: Dot plot comparing baseline with final HbA_{1c} levels following surgery in each of the 11 RCTs displayed in Fig. 3*A*.

(LoE IA) (Fig. 2*A*). Numerous RCTs with postoperative follow-up ranging between 1 and 5 years have consistently documented sustained diabetes remission in 30–63% of patients (LoE IB) (10–25). Available data suggest an erosion of diabetes remission over time: 35–50% or more of patients who initially achieve remission of diabetes eventually experience recurrence. However, the median disease-free period among such individuals with Roux-en-Y gastric bypass (RYGB) is 8.3 years (52,56). With or without diabetes relapse, the large majority of patients who undergo surgery maintain substantial improvement of glycemic control from baseline for at least 5 (LoE IB) (20) to 15 (LoE IIA) (52,55–59) years.

Baseline duration of diabetes (e.g., >8 years) (LoE IB) (19), use of insulin, and poorer glycemic control (LoE IIA) are consistently associated with lower rates of diabetes remission and/or higher risk of recidivism (19,52,58). Baseline visceral fat area may also help to predict postoperative outcomes, especially among Asian patients with T2D, who typically have more visceral fat compared with Caucasians with diabetes of the same BMI (60).

Beyond improving glycemia, bariatric/metabolic surgery has been shown to confer additional health benefits in RCTs, including greater reductions compared with medical/lifestyle interventions in other CVD risk factors (10–25), and enhancements in quality-of-life measures (LoE IB) (15,19,20). Improvements in other critical outcomes, such as micro- and macrovascular complications of diabetes, CVD, cancer, and death, have been observed only in nonrandomized studies (LoE IIA) (3,52,57,61–65).

Small retrospective analyses and a recent prospective multicenter nonrandomized study (LoE IIA) (66) suggest that bariatric/metabolic surgery may induce similar benefits in obese adolescents with T2D. Teenagers appear to experience similar degrees of weight loss, diabetes remission, and improvement of cardiometabolic risk factors for at least 3 years after surgery (66). No randomized trials, however, have yet compared the effectiveness and safety of surgery to those of conventional treatment options in adolescents.

Available data from economic analyses, albeit predominantly based on modeling

studies, support cost-effectiveness of bariatric/metabolic surgery, especially in patients with T2D (37). Cost per quality-adjusted life-year (QALY) of bariatric/metabolic surgery in general is approximately $3,200–$6,300, well below the range of $50,000/QALY deemed appropriate for coverage (36,67). In a U.S. study of obese patients, RYGB had incremental cost-effectiveness ratios (ICERs) of $7,000/QALY for newly diagnosed diabetes and $12,000/QALY for established diabetes (68). As a comparison, other treatments for diabetes, such as intensive glycemic and lipid control, have ICERs of $41,384/QALY and $51,889/QALY, respectively (69). Although some models have suggested that bariatric surgery may even be cost-saving, direct measurements of health care costs from clinical studies have not demonstrated that surgery decreases overall health care expenditures.

A long-term assessment of health care costs in subjects enrolled in the Swedish Obese Subjects (SOS) study was performed according to diabetes status at baseline, providing a comparison of drug-related and total health care expenditure for patients who undergo bariatric surgery versus matched control participants over 15 years (37). Drug costs were lower for the surgery patients who started with prediabetes ($3,329 less per patient) or diabetes ($5,487 less per patient). Although total health care costs for the surgery group were higher for patients with euglycemia or prediabetes, there was no difference between the surgery and conventional treatment groups for patients with diabetes at baseline. These findings further support the economic value of bariatric/metabolic surgery, specifically in patients with obesity and T2D. There are, however, several limitations of economic studies in this field, warranting further research (vide infra).

Safety of Bariatric/Metabolic Surgery

Procedures used in bariatric/metabolic surgery are characterized by distinct anatomic rearrangements (Fig. 1). This implies differences in technical complexity, mechanisms of action, clinical outcomes, and safety profiles. Safety of bariatric/metabolic surgery also varies across hospitals and surgeons. Empirical data suggest that proficiency of the operating surgeon is an important factor determining mortality, complications, reoperations, and readmissions (70).

Safety of bariatric/metabolic surgery in general has improved significantly over the last two decades, with continued refinement of minimally invasive approaches (laparoscopic surgery), enhanced training and credentialing, and involvement of multidisciplinary teams. Mortality rates with bariatric/metabolic operations are typically 0.1–0.5%, similar to cholecystectomy or hysterectomy (71–75). Morbidity has also dramatically declined with laparoscopic approaches. Major complications rates are 2–6%, with minor complications in up to 15% (71–79), comparing favorably with other commonly performed elective operations (75).

There are, however, still complications of surgery that may require reoperations and rehospitalizations. A recent multicenter study showed early reoperation and readmission rates after laparoscopic operations of 2.5% and 5.1% for RYGB, versus 0.6% and 2.0% for laparoscopic adjustable gastric banding (LAGB), versus 0.6% and 5.5% for vertical sleeve gastrectomy (VSG), after a median 3-year follow-up (76). Long-term studies (>5 years) demonstrate low rates of reoperation after most bariatric/metabolic procedures except LAGB, which is associated with removal or revision rates of >20% over 5–10 years (72,77–79). Biliopancreatic diversion (BPD), classic type or duodenal switch (BPD-DS), is the most complex procedure, requires longer operative time, and is associated with the highest perioperative mortality and morbidity rates (80). Compared with RYGB, BPD results in more surgical complications and greater incidence of GI side effects (81), as well as nutritional deficiencies (20) (LoE IB).

Long-term nutritional and micronutrient deficiencies with related complications, such as anemia, bone demineralization, and hypoproteinemia, may occur with variable frequency depending on the type of procedure, requiring lifelong vitamin/nutritional supplementation (82,83). Iron deficiency after bariatric surgery, with or without clinical anemia, has been observed in 5–64% of adults (84). One study reported iron deficiency in up to 50% of operated adolescents (66). Of note, iron deficiency has been observed in up to 44% of adults prior to bariatric surgery (85). Hence, differences in baseline iron status may explain the large variability in reported rates of postoperative iron deficiency.

Nutritional complications, as well as bone demineralization, are more likely with intestinal bypass operations, particularly BPD (20), and less common/severe with standard RYGB, LAGB, and VSG. Risk of bone fractures after surgery is unclear. One retrospective cohort study showed no increased fracture risk, whereas another reported a 1.2-fold increase in the surgery versus control groups (86,87). Postprandial hypoglycemia can also occur, especially with RYGB (83,88). The exact prevalence of symptomatic hypoglycemia is unknown. In one study, it affected 11% of 450 patients who had undergone RYGB or VSG (88). Severe hypoglycemia resistant to conservative therapy, however, is rare (89).

Novel Device-Based Interventions for Diabetes

There has recently been increased interest in device-based GI interventions designed to reproduce some of the benefits of metabolic surgery. Small human studies have examined numerous approaches, including space-occupying endoluminal devices (90), gastric electrical stimulation (91), duodenal and gastroduodenal endoluminal barriers (92,93), and duodenal mucosal resurfacing (clinical trial reg. no. NCT01927562, clinicaltrials.gov). Preliminary short-term results show variable degrees of efficacy, depending on the device, in improving glycemic and metabolic control in patients with obesity and T2D. Because of limitations in sample size and/or relatively short-term follow-up of existing studies, however, the current LoE for these devices was not yet deemed sufficient for formal recommendation.

Knowledge Gaps

Available RCTs do not allow an assessment of the relative role of surgery versus conventional therapies in many clinical scenarios, including the long-term effects of the most commonly performed current procedure (VSG), or of the effectiveness of surgery in different stages of disease severity. Factors predicting glycemic control after surgery

are incompletely characterized, and there is insufficient evidence from RCTs to clearly define cutoffs in diabetes duration and/or laboratory markers that could quantitatively predict the success of treatment over time. Furthermore, the number of patients with BMI <35 kg/m^2 studied in RCTs is still modest, and there are even fewer patients with BMI <30 kg/m^2. Few RCTs have compared surgical procedures head-to-head, specifically to treat T2D. Further studies are needed to understand the roles of different operations in specific clinical scenarios, especially in adolescents and patients with BMI <35 kg/m^2, and to determine what exactly constitutes failure of medical/lifestyle management before surgery is considered. The current LoE is not sufficient to determine the role of surgery as a first-line treatment in most clinical scenarios, especially in mildly obese or merely overweight patients.

Although it is likely that major glycemic improvements and/or prolonged diabetes remission after bariatric/metabolic surgery lead to reductions in diabetes-related complications, data regarding micro- and macrovascular events, cancer, and mortality can be extrapolated only from nonrandomized trials (3,52,57,61–65,94). There are no available long-term RCTs directly comparing surgery versus modern pharmacological therapies with diabetes complications or CVD events as primary end points, or with sufficient size, duration, and completeness of follow-up to conclusively determine the effects of surgery on these hard outcomes. Such trials, which are clearly warranted, should ideally be randomized, with adequate power and follow-up to examine microvascular and CVD outcomes as primary end points.

Although long-term safety and efficacy of metabolic surgery have been demonstrated in several studies (20,52,55–59), investigations with follow-up beyond 5 years are limited. This is particularly relevant for some procedures such as VSG because of their relatively recent introduction into clinical practice. Further evaluation of long-term outcomes of bariatric/metabolic surgery, particularly in comparison with available alternative treatments of diabetes, should be pursued. The surgeon's experience appears to influence outcomes (70), and there is a need to identify effective strategies for assessing the expertise of teams/centers providing metabolic surgery to increase standardization of outcomes across hospitals and geographic areas.

There is also limited evidence regarding the appropriate frequency of monitoring of nutritional status and the effectiveness of different types and dosage of nutritional and vitamin supplementations. The exact prevalence and causes of severe hypoglycemia after bariatric/metabolic surgery remain unknown (89); hence, studies investigating the best means of preventing and treating this condition are warranted.

There is a paucity of studies investigating the role of multimodality therapy with integration of pharmaceutical and surgical treatment to optimize outcomes of diabetes management. In particular, little is known about the role of complementary postoperative lifestyle and pharmaceutical interventions to increase and maintain diabetes remission or enhance glycemic control and lower the risk of diabetes complications.

Although available data suggest that metabolic surgery may be as effective in adolescents as in adults (66), there is presently no level-1 evidence to assess the effectiveness of surgery compared with conservative treatment in this population. In particular, there are minimal long-term data regarding the safety of metabolic surgery and the potential negative impact of nutritional deficits on growth.

Although preliminary clinical evidence for some device-based GI interventions is promising, appropriate RCTs with adequate end points, sample size, and follow-up are necessary for formal consideration of such approaches in the treatment algorithm for T2D. Studies should investigate the role of these approaches in specific clinical scenarios, alone or in combination with medications and/or lifestyle interventions, and their potential value to predict surgical outcomes (e.g., screening of surgical candidates).

Although most studies suggest a significant positive economic impact of bariatric/metabolic surgery, especially in patients with T2D, current evidence has limitations. Most assessments of the economic impact of bariatric/metabolic surgery derive from modeling studies rather than from direct measurements of economic costs from clinical trials. Modeling studies are prone to risks of overestimating cost-savings because they make assumptions about the durability of clinical benefits from metabolic surgery. For instance, weight regain and diabetes relapse have not been properly accounted for in many economic analyses. Variations in nonsurgical treatments of obesity and diabetes, plus costs across different types of payers (private versus public) and across countries, also are likely to determine different levels of return on investment. Uncertainty also exists about the cost-effectiveness or savings of bariatric/metabolic surgery for patients with lower BMIs. On the other hand, most studies so far examined patients receiving bariatric surgery primarily for severe obesity and with a relatively low prevalence of diabetes; these studies might underestimate economic value of surgery because cost-effectiveness appears to be greater in obese patients with diabetes at baseline compared with those without diabetes (37). Additional cost-effectiveness studies of specific metabolic surgery procedures in different clinical scenarios, and based on RCT data, would greatly facilitate the decision-making process of policymakers determining insurance coverage for surgical treatment of T2D.

Finally, although numerous physiological consequences of GI operations appear to contribute to the antidiabetes and weight-reducing benefits of bariatric/metabolic surgery (5,6,26,28–34), the exact mechanisms mediating diabetes remission after various procedures are not fully known. Studies designed to further elucidate these mechanisms represent an important research priority. Such knowledge holds promise to inform decisions regarding the choice of procedures for individual patients, to optimize surgical design, and hopefully to provide targets for novel device-based and/or pharmaceutical approaches to T2D.

STATEMENTS AND RECOMMENDATIONS

(See Table 3.)

Metabolic Surgery Versus Traditional Bariatric Surgery

Although obesity and T2D are often associated with one another, T2D is a disease entity with significant heterogeneity

that presents distinct challenges for clinical care. Therefore, the traditional model of bariatric surgery practice, which is shaped around the goal to induce weight loss and treat severe obesity, is not consistent with the principles and standards of modern diabetes care. A few examples below provide an idea of the conceptual and practical ramifications of using a disease-specific model of care when surgery is used specifically to treat T2D.

Offering GI surgery with the primary intent to treat T2D, instead of just as a weight reduction therapy, can influence the demographic characteristics and baseline disease states of patients who elect to undergo surgery. Patients choosing bariatric surgery are typically young, predominantly female, with relatively low prevalence of T2D for their BMI (3,4,95). In contrast, a study comparing patient populations in a "metabolic surgery" program versus a traditional "bariatric surgery" program within the same academic center showed that despite being similarly obese, patients who sought metabolic surgery were older, were more often male, and had more severe T2D and CVD at baseline (95). Although not surprising, these differences can significantly influence the outcomes of surgery (e.g., rates of diabetes remission/control, cost-effectiveness, etc.), and they have important ramifications for all aspects of patient care. These implications, rather than the BMI of the target population, represent the fundamental distinction between bariatric and metabolic surgery, necessitating the development of a new, disease-based model of practice.

Traditional bariatric surgery is primarily conceived of as an intervention that reduces the risk of future disease (i.e., to prevent metabolic or CVD complications of severe obesity) rather than as an approach to treat established disease. Such (mis)conception is reflected in the fact that most guidelines and criteria for coverage of bariatric surgery today make no recommendation for early intervention and often delay access to surgery. However, T2D is a progressive disease associated with increased risk for CVD and microvascular complications. Furthermore, evidence shows that metabolic improvement following surgery in patients with T2D correlates with shorter diabetes duration at baseline, possibly reflecting more preserved β-cell function (19,52,96). This suggests that unnecessarily delaying access to surgery might reduce health benefits and cost-effectiveness of surgery in patients with diabetes. Moreover, existing criteria used for coverage of bariatric surgery are of low relevance for metabolic surgery. For example, because BMI is not a standard diagnostic parameter or a measure of severity of T2D, using BMI thresholds as stand-alone criteria for metabolic surgery does not allow health care providers to appropriately select candidates for such operations or to define criteria for prioritization of this type of approach.

Defining Goals and Success of Metabolic Surgery

The loss of 50% of excess body weight (a somewhat arbitrary metric) is considered to be a successful outcome of traditional bariatric surgery. T2D, however, describes a continuum of hyperglycemic states, is a heterogeneous disorder, and is associated with complex metabolic dysfunctions that increase CVD risk, as well as morbidity and mortality. Thus, it is necessary to define meaningful definitions of goals and successful treatment when surgery is used with the primary intent to treat T2D. Because even temporary (months to years) normalization of glycemic control or major long-term improvement of glycemia without remission confers potential benefits for patients with T2D, remission of diabetes, although desirable, should not be regarded as the only goal of metabolic surgery or the only measure of success. The success of metabolic surgery needs to be defined in the larger context of comprehensive diabetes care plans. Metabolic surgery should be considered a means to achieve the glycemic control necessary to reduce risk of microvascular complications and CVD. To date, no high-quality (RCT) data have directly demonstrated reductions in microvascular complications or CVD events, compared with standard therapy.

An ADA expert panel in 2009 defined partial and complete remission of T2D as achievement of HbA_{1c} $<6.5\%$ and $<6.0\%$, respectively, off all diabetes medications, and maintenance of these glycemic levels for at least 1 year (97). Although these definitions have helped to improve standardization of reporting outcomes, their applications in routine clinical practice and research are problematic. The DSS delegates felt that remission as currently defined should not be considered to be the sole clinical benefit justifying metabolic surgery usage, especially since remission requires removal of all diabetes medications, and metformin is often used in individuals without diabetes. Furthermore, complementary pharmaceutical therapies such as metformin should not be discontinued simply to meet the definition of remission, and metformin as well as ACE inhibitors and statins should be maintained as needed to sustain adequate glycemic control and prevent diabetes complications. Additional studies are warranted to identify more reliable biological and/or clinical markers for an exact definition of remission and/or cure in diabetes.

Patient Selection

Patient selection for metabolic surgery should be based on balancing surgical and other long-term risks with potential long-term benefits to individual patients, as with any operation (Fig. 4). This trade-off needs to take into account factors such as baseline CVD risk due to metabolic disease and hyperglycemia that do not adequately respond to nonsurgical treatments, as well as conditions that could contraindicate any elective operation, such as prior abdominal surgery, risk of anastomotic dehiscence, or risks of deep vein thrombosis and pulmonary embolism.

In addition, preoperative indicators other than BMI should be established to make patient selection for metabolic surgery diabetes relevant. There are no data showing that baseline BMI predicts metabolic surgery success. Instead, strong evidence indicates that preoperative BMI, at least within the obese range, does not predict the benefits of GI surgery with regard to diabetes prevention (51,57), remission (11,20,52,53,56,98,99), relapse after initial remission (20), or the magnitude of its effects on CVD events (62,100), cancer (61), or death (LoE IIA) (51,53,56,61–63,98). Of note, a recent meta-analysis of all studies reporting diabetes remission rates following bariatric surgery—including 94,579 surgical patients with T2D—showed that the rate of remission was equivalent among the

60 studies in which mean preoperative BMI was ≥35 kg/m^2 compared with the 34 studies with mean preoperative BMI <35 kg/m^2 (71% versus 72%, respectively) (98). Overall, the surgical value seems to be more related to improved glucose homeostasis than weight loss per se (11,12,51,54,55, 61–63).

Although baseline BMI per se does not predict outcomes in metabolic surgery, available evidence, including all existing RCTs, is based on studies that have included BMI ranges among their primary criteria for eligibility. The number of patients with BMI <35 kg/m^2 in such studies is also limited. Inevitably, and until additional studies identify more robust predictors of outcomes, BMI ranges remain necessary to select patients who might benefit from metabolic surgery, based on extant data. However, additional diabetes-specific parameters should help to identify clinical scenarios where surgical treatment of T2D should be prioritized.

Preoperative Workup

Indications for surgical treatment of T2D should be evaluated by a multidisciplinary clinical team following a comprehensive preoperative assessment of diabetes and metabolic health. Exact diagnosis of the type of diabetes, screening for diabetes complications, and measurement of residual insulin secretory reserve have special relevance for the practice of metabolic surgery. This knowledge can inform clinicians about patients' counseling (e.g., the likelihood of diabetes remission after surgery), risks of postoperative diabetic ketoacidosis (for patients with unrecognized type 1 diabetes [T1D]), planning the frequency of postoperative monitoring of glycemic control and diabetes complications, and use of complementary postoperative medical therapy.

Choice of Procedure

The choice of surgical procedure should be based on evaluation of the risk-to-benefit ratio in individual patients, weighing long-term nutritional hazards versus effectiveness on glycemic control and CVD risk.

It is too early to establish a gold standard operation for metabolic surgery because of the paucity of RCTs comparing surgical procedures head-to-head. However, available RCTs and nonrandomized studies specifically designed to compare different procedures against

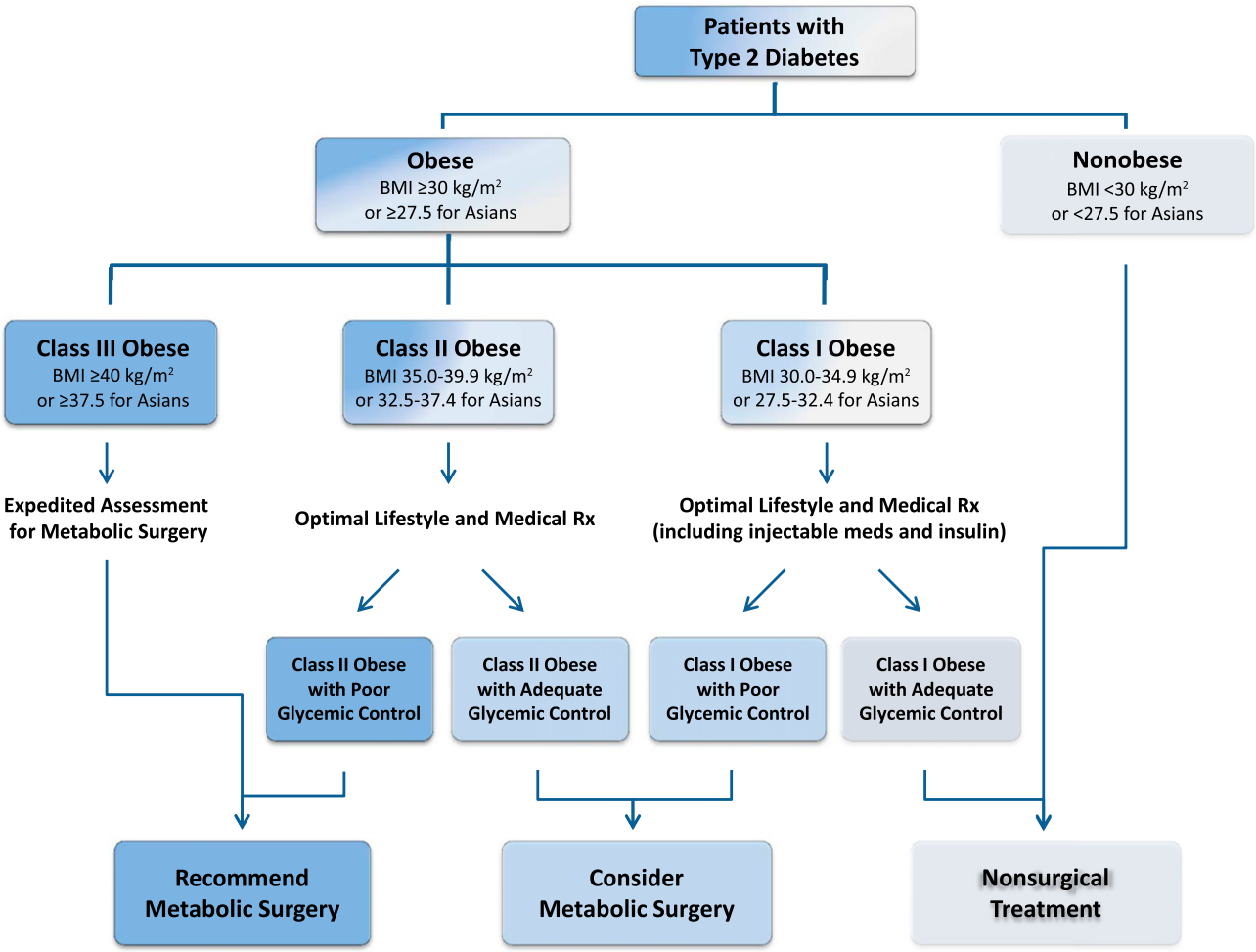

Figure 4—Algorithm for the treatment of T2D, as recommended by DSS-II voting delegates. The indications above are intended for patients who are appropriate candidates for elective surgery. meds, medications.

Table 3—Statements and recommendations

	Grade; LoC
Generalities	
1. Given its role in metabolic regulation, the GI tract constitutes a clinically and biologically meaningful target for the management of T2D.	Grade U; LoC 100%
2. There is now sufficient clinical and mechanistic evidence to support inclusion of GI surgery among antidiabetes interventions for people with T2D and obesity.	Grade A; LoC 97%
3. Algorithms for treating T2D should include specific scenarios in which metabolic surgery is considered to be a treatment option in addition to lifestyle, nutritional, and/or pharmacological approaches.	Grade A; LoC 92%
4. The development of an integrated chronic disease care model of lifestyle, nutritional, pharmacological, and surgical approaches is an important priority for modern diabetes care.	Grade U; LoC 100%
5. The clinical community should work together with health care regulators to recognize metabolic surgery as a valid intervention for T2D in people with obesity and to introduce appropriate reimbursement policies.	Grade U; LoC 100%
Metabolic surgery versus traditional bariatric surgery	
6. Metabolic surgery—defined here as the use of GI surgery with the intent to treat T2D and obesity—requires the development of a diabetes-based model of clinical practice consistent with international standards of diabetes care.	Grade U; LoC 100%
7. Complementary criteria to the sole use of BMI, the traditional criterion used to select candidates for bariatric surgery, need to be developed to achieve a better patient selection algorithm for metabolic surgery.	Grade U; LoC 100%
8. RYGB, VSG, LAGB, and BPD classic or duodenal switch variant (BPD-DS), are common metabolic operations, each with its own risk-to-benefit ratio. All other metabolic operations are considered to be investigational at this time.	Grade A; LoC 91%
9. Metabolic surgery should be performed in high-volume centers with multidisciplinary teams that understand and are experienced in the management of diabetes and GI surgery.	Grade U; LoC 100%
Defining goals and success of metabolic surgery	
10. Although more studies are needed to further demonstrate long-term benefits, evidence exists for GI surgery to be considered as an additional approach beyond lifestyle modifications and current medical therapies to reduce complications of T2D.	Grade A; LoC 97%
11. The aim of metabolic surgery in people with T2D and obesity is to improve their hyperglycemia and other metabolic derangements, while reducing their complications of diabetes, in order to improve their long-term health.	Grade A; LoC 97%
Patient selection	
12. Patients' eligibility for metabolic surgery should be assessed by a multidisciplinary team including surgeon(s), internist(s) or diabetologist(s)/endocrinologist(s), and dietitian(s) with specific expertise in diabetes care. Also, depending on individual circumstances, other relevant specialists could be consulted to evaluate the patient.	Grade B; LoC 85%
13. Contraindications for metabolic surgery include diagnosis of T1D (unless surgery is indicated for other reasons, such as severe obesity); current drug or alcohol abuse; uncontrolled psychiatric illness; lack of comprehension of the risks/benefits, expected outcomes, or alternatives; and lack of commitment to nutritional supplementation and long-term follow-up required with surgery.	Grade A; LoC 93%
14. Metabolic surgery is *recommended* as an option to treat T2D in patients with the following conditions:	
• Class III obesity (BMI $\geq$40 kg/m^2), regardless of the level of glycemic control or complexity of glucose-lowering regimens.	Grade U; LoC 100%
• Class II obesity (BMI 35.0–39.9 kg/m^2) with inadequately controlled hyperglycemia despite lifestyle and optimal medical therapy.	Grade A; LoC 97%
15. Metabolic surgery should also be *considered* to be an option to treat T2D in patients with class I obesity (BMI 30.0–34.9 kg/m^2) and inadequately controlled hyperglycemia despite optimal medical treatment by either oral or injectable medications (including insulin).	Grade B; LoC 87%
16. All BMI thresholds used in these recommendations should be reconsidered depending on the ancestry of the patient. For example, for patients of Asian descent, the BMI values above should be reduced by 2.5 kg/m^2.	Grade B; LoC 86%
17. Given the lack of level-1 evidence involving the effects of metabolic surgery on T2D in adolescent patients, the DSS-II committee feels a recommendation for use of GI surgery in this population is inappropriate at present. However, the committee does consider this a high priority for future research.	Grade U; LoC 100%
Preoperative workup	
18. Preoperative patient evaluation should include assessment of endocrine, metabolic, physical, nutritional, and psychological health.	Grade U; LoC 100%
19. Preoperative evaluation should include a combination of routine clinical tests and diabetes-specific metrics. The following tests are recommended by the DSS-II expert group:	Grade A; LoC 98%
• Standard preoperative tests used for GI surgery at individual providers' institutions.	
• Recent tests to characterize current diabetes status—for example, but not limited to, HbA_{1c}, fasting glucose, lipid profile, and tests for retinopathy, nephropathy, and neuropathy.	
• Tests to distinguish T1D from T2D (fasting C-peptide; anti-GAD or other autoantibodies).	
20. In order to reduce the risk for postoperative infection due to hyperglycemia, an attempt should be made to improve glycemic control before surgery.	Grade A; LoC 95%
Choice of procedure	
21. RYGB is a well-standardized surgical procedure, and among the four accepted operations for metabolic surgery, it appears to have a more favorable risk-benefit profile in most patients with T2D.	Grade U; LoC 100%

Continued on p. 874

Table 3—Continued

	Grade; LoC
22. Although longer-term studies are needed, current data suggest that VSG is an effective procedure that results in excellent weight loss and major improvement of T2D, at least in the short to medium term (1–3 years) in which outcomes have been measured in RCTs. It could be a valuable option to treat diabetes, especially in patients for whom concerns exist about the risk of operations that involve bowel diversion.	Grade B; LoC 80%
23. LAGB is effective in improving glycemia in patients with obesity and T2D, to the degree that it causes weight loss. The procedure, however, is associated with greater risk for reoperation/revision compared with RYGB due to failure or band-related complications, e.g., slippage/migration, erosion, etc.	Grade B; LoC 85%
24. Although clinical evidence suggests that BPD/BPD-DS may be the most effective procedure in terms of glycemic control and weight loss, the operation is associated with significant risk of nutritional deficiencies, making its risk-benefit profile less favorable than that of the other bariatric/metabolic procedures for most patients. BPD/BPD-DS should be considered only in patients with extreme levels of obesity (e.g., BMI >60 kg/m^2).	Grade B; LoC 83%
Postoperative follow-up	
25. After surgery, patients should continue to be managed by multidisciplinary teams including diabetologists/endocrinologists, surgeons, nutritionists, and nurses with specific diabetes expertise.	Grade A; LoC 98%
26. Postoperative follow-up should include surgical and nutritional evaluations at least every 6 months, and more often if necessary, during the first 2 postoperative years and at least annually thereafter.	Grade U; LoC 100%
27. Unless patients have a documented, stable condition of nondiabetic glycemia, glycemic control should be monitored with at least the same frequency as in standard diabetes care of nonoperated patients.	Grade U; LoC 100%
28. In patients who have reached stable normalization of hyperglycemia for at least 6 months, monitoring of glycemic control should be performed with the same frequency as recommended for patients with prediabetes because of the potential for relapse.	Grade A; LoC 95%
29. Patients with a stable condition of nondiabetic glycemia for less than 5 years should be monitored for complications of diabetes at the same frequency as before remission. Once remission reaches the 5-year mark, monitoring of complications can be done at a reduced frequency, depending on the status of each complication. Complete cessation of screening for a particular complication should be considered only if nondiabetic glycemia persists and there is no history of that complication.	Grade B; LoC 85%
30. Within the first 6 months after surgery, patients should be carefully evaluated for glycemic control and antidiabetes medication(s) tapered according to the professional opinion of the physician(s). Further medical treatment of T2D after this initial 6-month period should be dosed accordingly, but not discontinued until laboratory proof of stable glycemic normalization is obtained. Stable nondiabetic glycemia (i.e., HbA_{1c} in the normal range) should be documented for at least two 3-month HbA_{1c} cycles (6 months in total) before considering complete withdrawal of glucose-lowering drugs, although withdrawal of certain frontline medications (e.g., metformin) should be considered more carefully.	Grade B; LoC 82%
31. In the event of plasma glucose levels rapidly approaching the normal range early postoperatively, appropriate adjustments to medical therapy (medication types and dosage) should be implemented to prevent hypoglycemia. Metformin, thiazolidinediones, GLP-1 analogs, DPP-4 inhibitors, α-glucosidase inhibitors, and SGLT2 inhibitors are suitable drugs for early postoperative diabetes management due to their low risk of inducing hypoglycemia.	Grade A; LoC 98%
32. Ongoing and long-term monitoring of micronutrient status, nutritional supplementation, and support must be provided to patients after surgery, according to guidelines for postoperative management of metabolic/bariatric surgery by national and international societies (for example, AACE/TOS/ASMBS, IFSO, BOMSS).	Grade U; LoC 100%

Grade U = 100% agreement (unanimous); grade A = 89–99% agreement; grade B = 78–88% agreement; grade C = 67–77% agreement. AACE, American Association of Clinical Endocrinologists; ASMBS, American Society for Metabolic and Bariatric Surgery; BOMSS, British Obesity & Metabolic Surgery Society; DPP-4, dipeptidyl peptidase 4; GLP-1, glucagon-like peptide 1; IFSO, International Federation for the Surgery of Obesity and Metabolic Disorders; LoC, level of consensus; SGLT2, sodium–glucose cotransporter 2; TOS, The Obesity Society.

medical/lifestyle interventions or other operations in patients with T2D show a gradient of efficacy among the four accepted surgical approaches for weight loss and diabetes remission, as follows: BPD>RYGB>VSG>LAGB. The opposite gradient exists for comparative safety of these operations (10–25,72,76–79,101–104). Evidence from these studies can be summarized as follows:

- RYGB versus BPD: BPD promotes greater T2D remission but more metabolic complications compared with RYGB (LoE IB).
- RYGB versus LAGB: RYGB achieves greater diabetes remission compared with LAGB (LoE IA). RYGB is associated with higher risk of early postoperative complications but lower risk of long-term reoperations (LoE IIA).
- RYGB versus VSG: Compared with VSG, RYGB promotes higher diabetes remission rates (LoE IA), better lipid control (LoE IA), similar risk of reoperation (LoE IA), better quality of life (LoE IB), and higher incidence of postoperative complications (LoE IA).

Postoperative Follow-up

Regardless of the level of diabetes control and/or remission achieved by patients following surgery, diabetes management should include—in addition to optimizing glycemic control—monitoring and ameliorating CVD risk factors, such as hypertension and dyslipidemia, because it is reasonable to assume that these patients remain at higher risk of CVD complications and disease

relapse than does the general population. Thus, until surgery-specific predicting factors of diabetes relapse are better developed, patients should continue to be monitored by primary care physicians, endocrinologists, and internal medicine specialists as appropriate and have regular postoperative screening for development and/or progression of microvascular complications of T2D (e.g., retinopathy, nephropathy, and neuropathy). Because sudden improvement of prolonged hyperglycemia can acutely worsen microvascular disease, particularly intensive early postoperative monitoring is warranted in patients known to be afflicted (Table 3).

Future Research

The DSS delegates identified the following arenas for future research in metabolic surgery:

1. Develop and evaluate criteria for surgery that are more appropriate than BMI alone in people with T2D.
2. Investigate the long-term effect of surgery on microvascular disease and CVD in high-quality studies (RCTs especially and prospective, well-matched case-control studies).
3. Refine the structure of therapeutic algorithms to incorporate metabolic surgery.
4. Establish appropriate national/international registries of metabolic surgery in patients with T2D, especially designed to facilitate standardized collection of quality long-term data about CVD, mortality, and other relevant outcomes.
5. Investigate the long-term effectiveness and safety of metabolic surgery in adolescents as compared with alternative treatment options.
6. Determine which operation is the optimal choice for individual patients.
7. Determine the optimal time to intervene in individual patients.
8. Identify specific clinical scenarios in patients with diabetes that warrant escalation of treatment and earlier consideration of surgery.
9. Define the optimal use of therapies that combine surgical, pharmacological, and postoperative lifestyle-based treatments.
10. Identify optimal definitions of outcome to be used across treatment modalities.
11. Increase understanding of surgical mechanisms, so as to improve use of current treatment options and develop effective, new alternative therapies.
12. Investigate the role of device-based GI interventions ("interventional diabetology") to treat T2D, in combination with lifestyle and/or pharmaceutical approaches.
13. Investigate cost-effectiveness of specific procedures and of the use of surgery in distinct clinical scenarios to inform policymakers about optimal strategies to prioritize surgical access.

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