

Surgical Treatment for Type 2 Diabetes

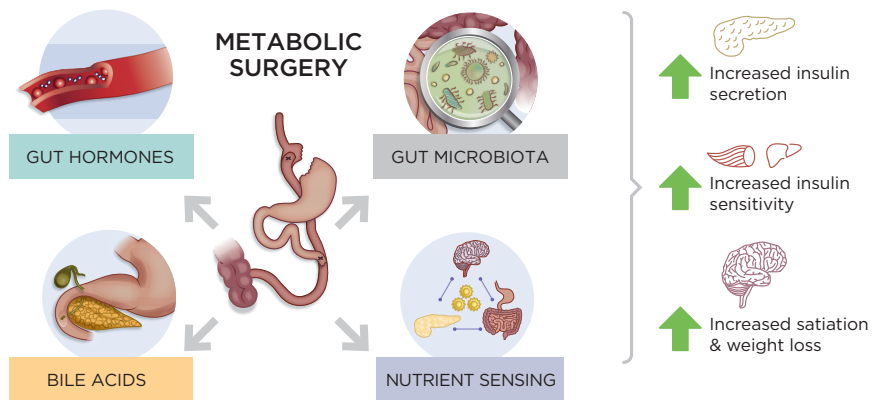


Metabolic surgery is now among the recommended treatment options for Type 2 diabetes among select obese individuals

- American Diabetes Association-Standards of Care 2017 ⁽¹⁾

How does surgery improve diabetes

Metabolic surgery changes various mechanisms of GI physiology involved in metabolic regulation ^(3,4)



Indications for Surgical Treatment

There is now sufficient clinical and mechanistic evidence to support inclusion of metabolic surgery among antidiabetes interventions for people with Type 2 diabetes (T2D) and obesity.” DSS-11 ⁽²⁾

- “Metabolic surgery should be a recommendation option to treat T2D in appropriate surgical candidates with class III obesity (BMI ≥ 40 kg/m², regardless of the level of glycemic control or complexity of glucose-lowering regimens, as well as in patients with class II obesity (BMI 35.0-39.9kg/m²) with inadequately controlled hyperglycemia despite lifestyle and optimal medical therapy.” DSS-II ⁽²⁾
- “Metabolic surgery should also be considered to be an option to treat T2D in patients with class 1 obesity (BMI 30.0-39.9 kg/m²) and inadequately controlled hyperglycemia despite optional medical treatment by either oral or injectable medications (including insulin).” DSS-II ⁽²⁾
- “All BMI thresholds should be reconsidered depending on the ancestry of the patient. For example, patients of Asian descent, the MBI values above should be reduced by 2.5 kg/m².” DSS-II ⁽²⁾

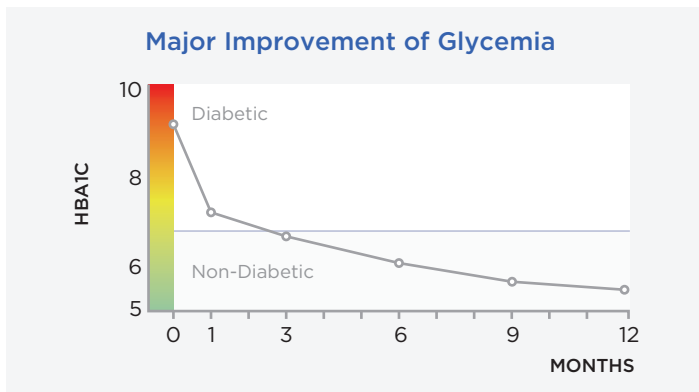
Algorithm for patients with Type 2 Diabetes																									
Non-Obese BMI < 30kg/m ² or 27.5 for Asians	Obese BMI ≤ 30kg/m ² or 27.5 for Asians																								
	<table border="1"> <tr> <th>Class I</th> <th>Class II</th> <th>Class III</th> </tr> <tr> <td> </td> <td> </td> <td> </td> </tr> <tr> <td>Optimal lifestyle & Medical Rx (including injectable meds & insulin)</td> <td>Optimal lifestyle & Medical Rx</td> <td>Expedited Assessment for Metabolic Surgery</td> </tr> <tr> <td> <table border="1"> <tr> <td> Good Glycemia Control </td> <td> Poor Glycemia Control </td> </tr> </table> </td> <td> <table border="1"> <tr> <td> Good Glycemia Control </td> <td> Poor Glycemia Control </td> </tr> </table> </td> <td></td> </tr> <tr> <td colspan="2" style="text-align: center;"> Nonsurgical Treatment </td> <td style="text-align: center;"> Consider Metabolic Surgery </td> <td style="text-align: center;"> Recommend Metabolic Surgery </td> </tr> <tr> <td> Class I BMI ≥ 30-34.9 kg/m² or 27.5-32.4 for Asians </td> <td> Class II BMI ≥ 35-39.9 kg/m² or 32.5-37.4 for Asians </td> <td> Class III BMI ≥ 40 kg/m² or 37.4 for Asians </td> <td></td> </tr> </table>	Class I	Class II	Class III				Optimal lifestyle & Medical Rx (including injectable meds & insulin)	Optimal lifestyle & Medical Rx	Expedited Assessment for Metabolic Surgery	<table border="1"> <tr> <td> Good Glycemia Control </td> <td> Poor Glycemia Control </td> </tr> </table>	Good Glycemia Control	Poor Glycemia Control	<table border="1"> <tr> <td> Good Glycemia Control </td> <td> Poor Glycemia Control </td> </tr> </table>	Good Glycemia Control	Poor Glycemia Control		Nonsurgical Treatment		Consider Metabolic Surgery	Recommend Metabolic Surgery	Class I BMI ≥ 30-34.9 kg/m ² or 27.5-32.4 for Asians	Class II BMI ≥ 35-39.9 kg/m ² or 32.5-37.4 for Asians	Class III BMI ≥ 40 kg/m ² or 37.4 for Asians	
	Class I	Class II	Class III																						
Optimal lifestyle & Medical Rx (including injectable meds & insulin)	Optimal lifestyle & Medical Rx	Expedited Assessment for Metabolic Surgery																							
<table border="1"> <tr> <td> Good Glycemia Control </td> <td> Poor Glycemia Control </td> </tr> </table>	Good Glycemia Control	Poor Glycemia Control	<table border="1"> <tr> <td> Good Glycemia Control </td> <td> Poor Glycemia Control </td> </tr> </table>	Good Glycemia Control	Poor Glycemia Control																				
Good Glycemia Control	Poor Glycemia Control																								
Good Glycemia Control	Poor Glycemia Control																								
Nonsurgical Treatment		Consider Metabolic Surgery	Recommend Metabolic Surgery																						
Class I BMI ≥ 30-34.9 kg/m ² or 27.5-32.4 for Asians	Class II BMI ≥ 35-39.9 kg/m ² or 32.5-37.4 for Asians	Class III BMI ≥ 40 kg/m ² or 37.4 for Asians																							

Clinical Evidence ^(2,5)

Observations that Type 2 Diabetes (T2D) can be improved or even resolved by surgical operation have been reported for almost a century. Since the 2000's experimental evidence that changes in GI anatomy can directly influence glucose homeostasis provided a mechanistic rationale for the use of surgery as an intentional treatment of diabetes. DSS-I and DSS-II assessed clinical evidence, including numerous Randomized Clinical Trials (RCTs) performed over the last decade, leading to current guidelines.

11 randomized trials (RCTs - Level 1 evidence) as well as large, long-term case controlled studies (Level 2 evidence) comparing surgery in overweight/obese people with Type 2 diabetes show that metabolic surgery results in:

- **Greater improvement of glycemic control (Level 1 evidence)**
- **Reduction of medication usage (Level 1 evidence)**
- **Reduction of cardiovascular disease (CVD) risk (Level 1 evidence)**
- **Reduction of heat attacks, strokes, cancer and overall mortality (Level 2 evidence)**
- **Greater weight loss (Level 1 evidence)**
- **Better quality of life (Level 1 evidence)**



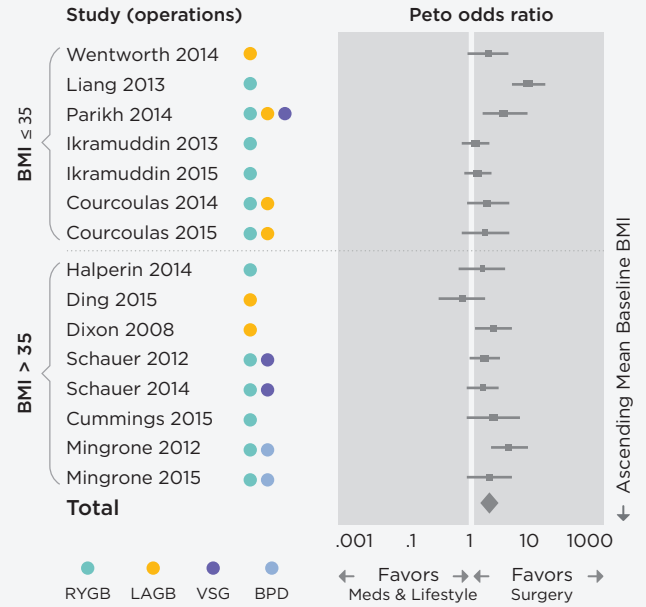
Chance of Disease Remission: A substantial proportion of patients (between 30% and 60%, depending on the procedure) experience durable (≥ 5 year) normalization of blood sugar levels without the need for ongoing pharmacologic treatment (disease remission)

Cost Effectiveness: Economic analyses have also shown that surgical treatment for diabetes are cost-effective. Cost per quality adjusted life-year (QALY) is approximately \$3,200-\$6,500, well below \$50,000/QALY (which is deemed appropriate for coverage).

References

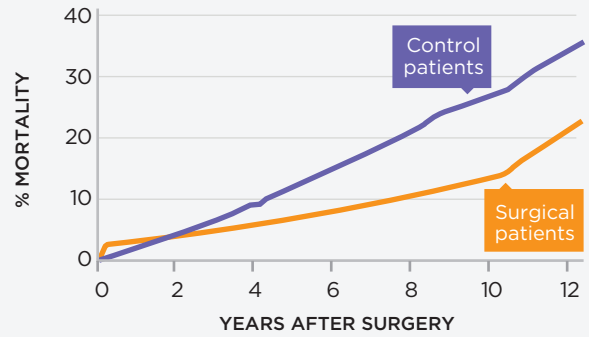
- (1) ADA Standards of Medical Care in Diabetes 2017 Diabetes Care; Jan. 2017; vol. 40 Issue Suppl. 1
- (2) Rubine F. et al. Diabetes Care Diabetes Care 2016; Jun. 39 (6): 861-877
- (3) Rubine F. Nature 2016; 533(7604)459-61
- (4) Evers SS et al. Annu Rev Physiol. 2017 Feb 10; 79:313-334
- (5) Cummings DE and Cohen R. Diabetes Care 2016 Jun; 39 (6): 924-933

Randomized Clinical Trials - Level 1 Evidence Surgery vs Lifestyle & Pharmacotherapy



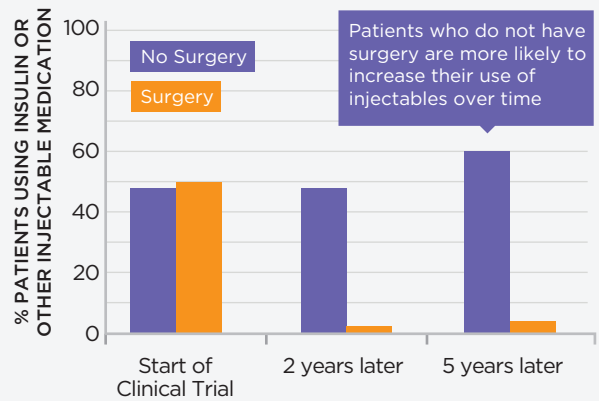
Based on Rubino F. et al. Diabetes Care 2016; 39, 861-877

Reduction of CVD & Mortality Risk



Based on Arterburn D. et al; JAMA. 2015; 313 (1): 62-70

Reduction of Medication Usage



Based on Mingrone G. et al; Lancet 2015; 386 (9997): 964-973