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Beyond BMI: the need for new guidelines governing the use of bariatric and metabolic surgery

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Abstract

Bariatric surgery use is largely governed worldwide by a 1991 National Institutes of Health consensus statement that advocates BMI as the primary operative criterion and restricts surgery to severely obese patients. These guidelines have been enormously valuable in standardising practice, thereby facilitating accumulation of a copious database of information regarding long-term surgical benefits and risks, from vast clinical experience and research. However, the National Institutes of Health recommendations had important limitations from the outset and are now gravely outdated. They do not account for remarkable advances in minimally invasive surgical techniques or the development of entirely new procedures. In the two decades since they were crafted, we have gained far greater understanding of the dramatic, weight-independent benefits of some operations on metabolic diseases, especially type 2 diabetes, and of the inadequacy of BMI as a primary criterion for surgical selection. Furthermore, there is now a substantial and rapidly burgeoning body of level-1 evidence from randomised trials comparing surgical versus non-surgical approaches to obesity, type 2 diabetes, and other metabolic diseases, including among only mildly obese or merely overweight patients. Herein, we present arguments to impel the development of new guidelines for the use of bariatric and so-called metabolic surgery to inform clinical practice and insurance compensation.

Introduction

In combating the twin pandemics of obesity and type 2 diabetes, bariatric surgery is the most effective long-term intervention for both disorders. Despite recent dramatic surgical advances, including development of several novel operations and devices, and an exploding database to justify revising patient selection criteria, global bariatric surgery practice

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Contributors
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Conflicts of interest
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remains largely dictated by a seriously outdated set of recommendations from the US National Institutes of Health (NIH). Herein, we present a case to impel development of new guidelines for the use of surgery to treat metabolic disease.

Limitations and advantages of bariatric surgery recommendations

Use of bariatric surgery worldwide is largely governed by an NIH consensus statement published 22 years ago.[1] This statement restricts surgery to patients with BMI greater than 40 kg/m^2, or greater than 35 kg/m^2 with serious comorbidities such as type 2 diabetes. Although these recommendations were carefully written in good conscience and have been clinically valuable, they are outdated and have important limitations. For example, only open operations were considered, whereas most procedures are now undertaken laparoscopically, a far safer approach with ten-times lower operative mortality.[2,3] The NIH statement provided only moderate recommendations for diabetes, but since then it has become clear that several of the most commonly undertaken operations exert dramatic effects on type 2 diabetes[4–7] through mechanisms beyond just reducing food intake and bodyweight.[8] Surgical options have evolved enormously since the NIH recommendations were written, further limiting the present-day relevance of those suggestions. One of the two operations approved in 1991, vertical-banded gastroplasty, disappeared from clinical practice more than a decade ago. Conversely, several new procedures—most notably laparoscopic adjustable gastric banding (LAGB) and vertical sleeve gastrectomy (VSG)—have since come into common use. Moreover, the other NIH-approved procedure, Roux-en-Y gastric bypass (RYGB), has been refined, rendering it safer and more effective than it was two decades ago.[9–11] Operative mortality is now lower for laparoscopic RYGB than cholecystectomy.[2,12]

The NIH itself acknowledges the limitations of its 1991 recommendations and posts the following forthright concession prominently atop its related website:[13] “This statement is more than five years old and is provided solely for historical purposes. Due to the cumulative nature of medical research, new knowledge has inevitably accumulated in this subject area in the time since the statement was initially prepared. Thus, some of the material is likely to be out of date, and at worst simply wrong.” Nevertheless, no alternative recommendations have since been provided by the NIH to guide clinical practice and insurance compensation, which thus remain governed by an admittedly outdated set of guidelines.

Despite its limitations, the 1991 NIH consensus statement has had enormous clinical impact. Many additional sets of guidelines have subsequently been articulated by medical societies worldwide to restate the same basic suggestions, limiting surgery to persons with BMI greater than 40 kg/m^2, or greater than 35 kg/m^2 with complications such as type 2 diabetes. These newer, but highly reiterative, clinical practice recommendations include those espoused by the American Diabetes Association, the European Association for the Study of Diabetes, the International Federation for the Surgery of Obesity and Metabolic Disorders, the American College of Physicians, the American Society for Metabolic and Bariatric Surgery, the UK’s National Institute for Health and Care Excellence, the Scottish Intercollegiate Guidelines Network, Australia’s National Health and Medical Research

Council, and Brazil's Federal Council of Medicine. Thus, although existing suggestions were spawned by an American institution, they have largely guided global practice in this arena, establishing the current standard of BMI-based criteria for surgical selection.

In general, the NIH is reluctant to consider generating new clinical practice guidelines without a substantive body of relevant level-1 evidence—ie, results of randomised controlled trials (RCTs). Indeed, their 1991 recommendations followed soon after the publication of several bariatric-surgery RCTs.[14–18] All of these trials compared RYGB with gastroplasty; however, the decision regarding which of these two operations to use is no longer clinically germane. Because those studies and several subsequent RCTs[19–21] consistently reported RYGB to be more effective than gastroplasty, the latter procedure largely disappeared from use within several years of the NIH recommendations being published. Those older RCTs do not inform the decision that the 1991 guidelines primarily influence today—ie, when to use surgery rather than conventional medical or lifestyle interventions, or both.

Despite the substantial limitations of the 1991 NIH recommendations, more than two decades of worldwide practice guided by them have provided extensive clinical evidence that has largely validated their use in making management decisions for severely obese patients. Studies examining thousands of participants for up to 20 years show that, among such individuals, bariatric surgery is associated with long-term reductions in virtually all obesity-related comorbidities, including every major cardiovascular disease (CVD) risk factor,[4–6,11,22–26] actual CVD events such as myocardial infarctions and strokes,[27] cancer,[28] and all-cause mortality.[29–31] Benefits on such hard endpoints have never been shown with medical or behavioural interventions for obesity, including the enormous, very-long-term Look AHEAD trial.[32] Although the aforementioned conclusions about surgery stem from non-randomised studies, several RCTs have also helped validate the NIH recommendations, showing superiority of various bariatric operations over medical or lifestyle interventions, or both, for very obese patients, especially those with type 2 diabetes.[33–37] Bariatric surgery is also cost-effective, estimated at US $3200–6300 per quality-adjusted life-year gained, which is well below the widely accepted societal standard of $50 000 per quality-adjusted life-year for affordable healthcare interventions.[38]

"Metabolic surgery": targeting type 2 diabetes and other metabolic diseases rather than BMI

The question now is not whether bariatric surgery is valuable for severely obese (BMI greater than 35 kg/m^2) individuals—it is—but whether it might also benefit people with lower BMIs, especially if they have type 2 diabetes, and whether BMI is an ideal criterion for surgical selection at all. It has become increasingly apparent that bariatric surgery exerts powerful, beneficial effects on type 2 diabetes, especially with intestinal bypass operations such as RYGB. At least in the short to medium term, this procedure yields about 80% remission of type 2 diabetes,[4–7,33] with a remarkable 92% reduction in diabetes-related deaths.[30] Moreover, some bariatric operations ameliorate type 2 diabetes through mechanisms beyond just secondary consequences of reduced food intake and bodyweight.[8,24,33,39–41] Thus, consideration of such procedures to treat diabetes per se,

rather than primarily targeting bodyweight, is logical, including among diabetic patients who are only mildly obese or merely overweight. Accordingly, use of the term metabolic surgery rather than bariatric surgery is steadily increasing, and most bariatric surgical societies worldwide have recently changed their names to include the word metabolic.[41] Mounting evidence suggests that bariatric operations are safe and effective for type 2 diabetes care among patients with a BMI above only 30 kg/m^2, or perhaps even lower.[24,34,35,41–51] Importantly, neither excessive weight loss nor generalised under nutrition has yet been reported with standard operations in these less obese patients.

Comparing surgical versus non-surgical approaches to obesity and type 2 diabetes

As mentioned, the NIH is hesitant to contemplate new guidelines without relevant level-1 evidence, but in the face of convincing clinical findings, are RCTs really needed to establish when to use bariatric surgery rather than conventional care? Some might argue that, for example, use of surgery to treat patients with BMI less than 35 kg/m^2 and poorly controlled type 2 diabetes is reasonable already, on the basis of compelling data from clinical experience and non-randomised studies. Indeed, newer consensus guidelines[40,41,52,53] based on expert opinion recommend considering RYGB or LAGB for people with a BMI as low as 30 kg/m^2 if they have inadequately controlled type 2 diabetes. These suggestions, based primarily on evidence in white patients, include guidelines from the Diabetes Surgery Summit[40,41] and International Diabetes Federation.[52,53] The Diabetes Surgery Summit recommends surgery for patients with class 1 obesity (BMI 30–35 kg/m^2) only in cases where all medical and lifestyle interventions for type 2 diabetes have failed.[40,41] By contrast, the International Diabetes Federation deems surgery reasonable for patients with class 1 obesity and type 2 diabetes who have failed to respond adequately to just lifestyle changes and two oral antidiabetic drugs, placing surgery on the same algorithmic level as thiazolidinediones, dipeptidyl peptidase-4 inhibitors, acarbose, and basal insulin.[52,53] Similar guidelines from expert opinion have been published specifically for Asian patients,[54] who are especially vulnerable to development of type 2 diabetes at low BMIs relative to white individuals.[46] Thought leaders have recommended that in this population surgery can be regarded as a non-primary alternative to treat inadequately controlled type 2 diabetes among patients with BMI as low as 27·5 kg/m^2.[54]

In view of such guidelines by several different groups of experts on the basis of their best judgment, are RCTs of surgical versus non-surgical care needed to contemplate updating the influential 1991 NIH statement to consider surgery in patients with type 2 diabetes and BMI less than 35 kg/m^2, or even just to verify with level-1 data the existing recommendations for more obese patients? Despite compelling findings regarding the safety and efficacy of surgery from non-randomised studies, including in patients without severe obesity, the answer is assuredly yes.

Medical research is replete with cautionary tales wherein conventional wisdom based on non-randomised data was swiftly reversed by even a single, definitive RCT. For example, before the Women's Health Initiative,[55] a prevailing view was that the premenopausal hormonal milieu reduced CVD risk, on the basis of decades of epidemiological evidence

showing fewer CVD events in premenopausal women than in men, with risk equalisation after menopause. Hence, the assumption was that postmenopausal hormone-replacement therapy would reduce CVD incidence in women. However, despite the seemingly convincing evidence supporting this assertion, when put to the test with a definitive RCT—the Women's Health Initiative[55]—the opposite case was shown, and women on postmenopausal hormone replacement had more CVD events than did those not on such treatment. Almost overnight, routine use of postmenopausal hormone replacement for cardioprotection ceased.

Another longstanding conventional assumption before relevant level-1 evidence was available was that intensive glycaemic control in patients with diabetes would reduce macrovascular disease (ie, CVD), and therefore mortality, because such treatment was clearly shown in definitive RCTs to reduce microvascular disease.[56,57] However, again this view was severely challenged when findings from three RCTs comparing intensive versus routine glycaemic control surprisingly showed that the former intervention was either not different or even worse than the latter for prevention of CVD events and death.[58–60]

In bariatric surgery research, the Swedish Obese Subjects (SOS) study[75] has generated the foremost evidence base in the specialty, but conclusions from even this exemplary work are constrained because the study is not an RCT. The SOS study is a prospective, non-randomised examination of obese patients, 2010 of whom chose to undergo bariatric surgery versus 2037 who selected routine non-surgical care and were well matched with the surgical group at baseline. The cohorts have been followed up with extraordinary retention rates for up to 20 years, and high-profile resulting publications have reported that surgery is associated with major reductions in all classical CVD risk factors,[22,23] actual CVD events,[27] cancer,[28] and overall mortality.[29] However, despite the superb quality of this landmark study, all of its conclusions can be questioned on the basis of the potential for a systematic allocation bias in this non-randomised investigation. Perhaps participants who actively selected surgery were more motivated overall to improve their health, so they may have also achieved better lifestyles and medical compliance.

Hence, for good reason, the NIH is unlikely to consider revising its 1991 guidelines without relevant level-1 evidence to inform its decisions. Diabetes policy makers are accustomed to proposing clinical practice guidelines on the basis of results from large, long-term RCTs, which are often powered to measure hard microvascular or macrovascular endpoints, or both. For example, regarding just the question of whether intensive glycaemic control is superior to routine control, thought leaders can turn to such mega-RCTs as DCCT-EDIC (Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications),[56,61] UKPDS (UK Prospective Diabetes Study),[57] ACCORD (Action to Control Cardiovascular Risk in Diabetes),[58] ADVANCE (Action in Diabetes and Vascular Disease: preterAx and diamicroN-MR Controlled Evaluation),[59] VADT (Veterans Affairs Diabetes Trial),[60] and Steno-2.[62] Similarly, for type 2 diabetes treatment algorithms, large RCTs support recommendations for each treatment step, including lifestyle modification,[63–65] oral pharmaceutical monotherapy,[57,66,67] oral drug combinations,[68] oral drugs plus basal insulin,[69] and several daily insulin injections.[70]

Unfortunately, it is extremely difficult to recruit and retain participants for the most important RCTs needed to generate solid guidelines regarding when to use surgery—ie, those comparing surgical versus non-surgical interventions. Most RCTs in health-care research involve interventions that are not particularly disparate with one another from the patients' perspective, such as comparing various doses of a drug, one drug versus another, or even different operations. By contrast, the most pressing RCTs needed to advance metabolic surgery research would need participants to be randomly allocated to undergo either a major surgical procedure, or a medical or lifestyle intervention, or both. Surgery carries a small risk of immediate mortality and a reasonable chance of substantial morbidity,[2] but it also offers major potential benefits of massive weight loss, type 2 diabetes remission, and improvements in other comorbidities.[6,22] By contrast, medical and lifestyle interventions are perceived as safe, but are far less effective regarding these endpoints, and in many cases represent extensions of strategies that patients have already attempted for years. Unfortunately, finding candidates who are genuinely in equipoise regarding interventions as diverse as these is extremely difficult.

Despite such herculean challenges, five excellent RCTs comparing various bariatric operations with non-surgical care have recently been published, with consistent results. They showed that each of the four bariatric operations commonly used at the time of writing (RYGB, LAGB, VSG, and biliopancreatic diversion [BPD]) is substantially more effective than medical or lifestyle interventions in terms of weight loss, glycaemic control, type 2 diabetes remission, and improvements in CVD risk factors, with acceptable rate of complications, for 1–2 years (table).[33–37,71] The findings apply not only to severely obese individuals but also to those with BMI as low as 27 kg/m^2, and surgical benefits for type 2 diabetes were especially dramatic. Several similar RCTs are also underway (eg, NCT01295229, NCT01073020, NCT01047735, NCT01667783, NCT01040468, NCT1821508, NCT1257087, and others), thanks in part to generous NIH funding dedicated to this endeavour.

Unanswered questions

Numerous questions remain to be answered by future research efforts. What is the proper timing of surgery relative to other type 2 diabetes therapies? Because long diabetes duration is the strongest predictor of postoperative non-remission,[41] surgery could be considered earlier in the disease, rather than only as salvage therapy.[53]

How do various operations compare with one another? Available evidence suggests that by engaging weight-independent anti-diabetes effects,[8,24,33,39–41] intestinal bypass operations such as RYGB and BPD ameliorate type 2 diabetes more effectively for a given amount of weight loss than do LAGB or VSG.[41,71,72] Hence, RYGB and BPD are logical operations for patients with type 2 diabetes. The order of weight-loss effectiveness is BPD>RYGB>VSG>LAGB. This order can be considered when choosing among operations for patients with varying degrees of obesity, while taking into consideration that the rank order for safety is opposite to that of weight-loss effectiveness.[41] However, optimum procedure selection for individual patients ultimately needs evidence from RCTs powered to see small differences between one operation and another, and several are underway (eg,

NCT247377, NCT1581801, NCT540462, NCT1486680, NCT1778738, NCT793143, NCT356213, NCT1806506, and NCT840736).

What is the proper role for bariatric operations that are now being undertaken in clinical practice that were not considered in the 1991 NIH statement (eg, LAGB, VSG, BPD, and duodenal switch)? Is there any utility outside clinical trials for new experimental procedures that replicate subcomponents of standard operations (eg, duodenal-jejunal bypass, ileal interposition, endoluminal sleeves, and gastric plication)? What is the full risk:benefit ratio of classical operations in less obese patients with type 2 diabetes, and how low a BMI might we contemplate? Should we consider ethnic origin, since populations such as Asians develop type 2 diabetes at lower BMI values than do white populations?

What about long-term effects? Although several types of bariatric surgery are associated with high rates of type 2 diabetes remission and reductions in the incidence of newly diagnosed diabetes over periods of 6–15 years,[4,11,22–26] there is no level-1 evidence comparing surgery versus non-surgery for more than 2 years. Emerging data suggest that rates of diabetes recurrence after initial postoperative remission can sometimes be high;[73] however, even a transient disease-free period might confer longlasting benefits as a result of the effects of metabolic memory.[74] Glycaemic control is almost universally improved long after bariatric surgery, even if diabetes does not completely resolve. RCTs measuring important clinical endpoints, such as CVD events, would be preferable to existing studies of surrogate endpoints such as HbA_{1c}. However, such trials need thousands of participants. Given the difficulties of randomly allocating people into surgical versus non-surgical interventions, novel methods to recruit participants in equipoise are needed, and relevant efforts are underway (eg, NCT01295229).

A key unanswered question is what are the optimum criteria for surgical selection? Although BMI is the established standard,[1] substantial evidence indicates that it is an inadequate primary criterion. The SOS study has shown that baseline BMI does not predict the benefits of bariatric surgery pertaining to development of diabetes, cancer, myocardial infarctions, stroke, or death.[23,27–29] Although BMI is associated with these outcomes, it is not related to the treatment effects of surgery on them (ie, the differences in incidence between surgical and non-surgical groups). Surgical advantages for these endpoints are similar across a wide range of baseline BMI values. By contrast, surgical benefits for almost all of these outcomes are clearly predicted by high preoperative fasting insulin or glucose concentrations, or both, presumably as a result of insulin resistance.[75] Overall, surgical value seems more related to improved glucose homoeostasis than weight loss.[23,24,27,29,33,34,43] Available evidence suggests that fasting insulin or glucose concentrations, or both, would constitute better surgical criteria than BMI, and these metrics could provide the gatekeeping function that BMI has traditionally subserved to prioritise and limit surgery, in view of limited health-care budgets.

Conclusion

The 1991 NIH recommendations for bariatric surgery use have been enormously influential and clinically useful worldwide, but they are woefully outdated and crying out for revision.

New consensus guidelines are needed to give due consideration to many novel operations and devices, increasingly safe minimally invasive techniques, and the remarkable effect of some procedures on metabolic diseases such as type 2 diabetes, through mechanisms beyond just weight loss.[8] Helping to inform policy decisions, a wealth of new data has been generated since 1991 regarding the safety and efficacy of surgical versus non-surgical approaches to obesity and type 2 diabetes, including from very large, long-term observational studies[22,23,25,27–30] and several RCTs,[33–37] with many more well underway.

Search strategy and selection criteria

We searched PubMed and the Cochrane Library (all dates for both), using the search terms “gastric bypass” or “sleeve gastrectomy” or “gastric banding” or “biliopancreatic diversion” or “duodenal-jejunal bypass” or “ileal interposition” or “ileal transposition” or “bariatric surgery” or “metabolic surgery”, in combination with the terms “guidelines” or “recommendations” or “consensus” or “suggestions”. No language limitations were set. Additionally, we combined the same set of surgical terms listed above with “diabetes”. We largely selected publications within the past 5 years, along with commonly referenced and highly regarded older papers. We also searched the reference lists of articles identified by this strategy and selected those we judged relevant.

In the USA, insurance companies are unlikely to pay for bariatric or metabolic surgery that is undertaken outside the dictates of NIH guidelines, and historically in this specialty, clinical practice in most of the rest of the world follows NIH recommendations. Whether or not the NIH intended to influence policy outside the USA, their previous guidelines have done exactly that. Yet, in east Asia, for example, the vast majority of patients with type 2 diabetes cannot benefit from surgery by the 1991 BMI-based criteria, because fewer than 2% of diabetic individuals there have a BMI greater than 35 kg/m^2.[46] Even in the USA, where mean BMI values among patients with type 2 diabetes are much higher than in Asia, lowering the BMI threshold for surgery in patients with type 2 diabetes from 35 to 30 kg/m^2, though a modest numerical change, would affect a very large population because the BMI distribution peak among diabetic patients in the USA lies within this range, representing over a quarter of Americans with diabetes.[76] Thus, even a modest alteration of surgical criteria to include this population would have far-reaching implications for diabetes care.

The NIH is a venerated, responsible health-care leader. The time has come for this storied institution to lead again and generate new consensus guidelines for the use of bariatric, or metabolic, surgery.

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Table

Randomised trials of surgical versus medical or lifestyle interventions, or both, for type 2 diabetes and obesity

	Interventions compared	Number of participants	Baseline BMI (kg/m^2)	Follow-up length	Main findings*
Ikramuddin et al[37]	RYGB *vs* intensive medical and lifestyle care	120 adults with type 2 diabetes	30–40	1 year	Achieved composite goal† for type 2 diabetes, hypertension, and dyslipidaemia: RYGB 49%, medical and lifestyle care 19% (OR 4·8, 95% CI 1·9–11·7)
Schauer et al[34] and Kashyap et al[71]	RYGB *vs* VSG *vs* intensive medical care	150 adults with type 2 diabetes	27–43	1 year	HbA_{1c} <6·0% (42 mmol/mol): RYGB 42%, VSG 37%‡, medical care 12%
Mingrone et al[33]	RYGB *vs* BPD *vs* conventional medical care	60 adults with type 2 diabetes	≥35	2 years	HbA_{1c} <6·5% (48 mmol/mol) without diabetes drugs: RYGB 75% (OR 7·5, 95% CI 2·0–28·6, *vs* medical care), BPD 95% (OR 9·5, 95% CI 2·5–35·5, *vs* medical care), medical care 0%
Dixon et al[35]	LAGB *vs* conventional medical care	60 adults with type 2 diabetes	30–40	2 years	HbA_{1c} <6·2% (44 mmol/mol) without diabetes drugs: LAGB 73%, medical care 13% (OR 5·5, 95% CI 2·2–14·0)§
O'Brien et al[36]	LAGB *vs* supervised lifestyle intervention	50 adolescents without type 2 diabetes	>35	2 years	>50% excess bodyweight loss: LAGB 84%, lifestyle intervention 12%

BPD= biliopancreatic diversion. LAGB= laparoscopic adjustable gastric banding. OR=odds ratio. RYGB=Roux-en-Y gastric bypass. VSG=vertical sleeve gastrectomy.

*All comparisons of surgical *vs* non-surgical interventions are significantly different (p<0·05). All surgical interventions also produced significantly more weight loss than did their respective non-surgical controls (p<0·05).

†Defined as HbA_{1c} <7·0% (53 mmol/mol), LDL cholesterol <100 mg/dL (2·59 mmol/L), and systolic blood pressure <130 mm Hg at 1 year. The benefit of surgery on this triple endpoint was primarily driven by reductions in HbA_{1c}. The RYGB group also used 66% fewer drugs for diabetes, hypertension, and dyslipidaemia at 1 year than did the medical and lifestyle care group (p<0·001).

‡Fewer diabetes drugs, including insulin, were being used at 1 year in the RYGB group compared with the VSG group.

§All participants had mild diabetes (mean HbA_{1c} at baseline 7·7%, 61 mmol/mol) of less than 2 years' duration.