

# CLINICAL PRACTICE GUIDELINES

## AGA Clinical Practice Guidelines on Intra-gastric Balloons in the Management of Obesity



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Obesity is a global pandemic, affecting about 40% of adults in the United States. There is a vast area of unmet need with respect to weight-loss interventions, as only 1.1% of eligible patients with obesity are receiving primary bariatric surgery. Endoscopic bariatric therapies have evolved as an attractive tool for weight loss; however, <5% of patients with obesity seeking a weight-loss therapy are aware of endoscopic weight-loss options. Intra-gastric balloons (IGBs) launched nearly 4 decades ago have recently gained more popularity with multiple new devices introduced into the US market. Although IGBs are a plausible option for patients seeking weight loss, it is essential for providers, patients, and health care teams to understand how IGBs can augment the effect of lifestyle modifications with respect to important patient outcome measures, such as weight loss, improving metabolic parameters, and minimizing comorbid medical conditions. At the same time, it is also important for providers and patients to be aware of the adverse events and tolerability associated with IGBs, given that the devices have evolved over the years and newer models are available in the US market. This guideline can assist both patients and providers in determining whether IGB is a weight-loss option that should be considered and/or pursued in patients with obesity.

### Methods

This guideline on IGBs was developed by the AGA Institute's Clinical Guidelines Committee and approved by the AGA Governing Board. It is accompanied by a technical review that provides a detailed synthesis of the evidence from which these recommendations were formulated. To get a better understanding of these guidelines, we recommend reading the accompanying technical review. Development of this guideline and the accompanying technical review was fully funded by the AGA Institute without additional outside funding.

### Guideline Panel Composition, Funding, and Conflict of Interest

Members of the Guideline Panel and Technical Review Panel were selected by the AGA Governing Board in consultation with the Clinical Guidelines Committee with careful consideration of all Institute of Medicine recommendations for clinical guideline development. A patient representative was also included in the development and review process and had no recommended changes. The guideline and accompanying technical review underwent independent peer review, and a 30-day open public comment period; all comments were collated by the AGA staff and were reviewed and carefully considered by the Guideline Panel and Technical Review teams, respectively. Changes were incorporated in revised documents, and where changes were not accepted, a thoughtful response document was created. In accordance with the Clinical Guidelines Committee policies, all clinical guidelines are reviewed annually at the AGA Clinical Guideline Committee meeting for new information. The next update for these guidelines is anticipated in 3 years from publication (2024).

This guideline was developed using a process outlined previously. The AGA process for developing clinical practice guidelines follows the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach and adheres to best practices in guideline development as outlined by the National Academy of Medicine (formerly Institute of Medicine).

### Formulation of Clinical Questions

A priori, the Guideline Panel (T.M., L.D., E.H., gastroenterologists, and L.T., nutritionist) and a GRADE methodologist (M.H.M), and a GRADE experts (S.S) identified and formulated clinically relevant questions about the use of IGBs in patients with obesity. Each research question identified the population,

**Abbreviations used in this paper:** AGA, American Gastroenterological Association; BMI, body mass index; CI, confidence interval; GI, gastrointestinal; GRADE, Grading of Recommendations Assessment, Development and Evaluation; IGB, intra-gastric balloon; MD, mean difference; PICO, population, intervention, comparison, and patient-important outcomes; PPI, proton pump inhibitor; RCT, randomized controlled trial; RR, relative risk; SOC, standard of care; %TBWL, percent total body weight loss.

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**Table 1.** Interpretation of the Certainty in Evidence of Effects Using the Grading of Recommendations Assessment, Development and Evaluation Framework

Certainty	Description
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very Low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

intervention, comparison, and patient-important outcomes (PICO). The Technical Review Panel initially reviewed and assessed relevant systematic reviews that addressed the clinical questions, updating high-quality systematic reviews through January 2020 to inform the recommendations when possible.<sup>2</sup>

For situations in which there was either no recent systematic review available or the recent systematic review was not deemed to have a credible process, the Technical Review team conducted the systematic review de novo. The findings from each systematic review were assessed using the GRADE approach and presented in an evidence profile. The GRADE approach breaks down the clinically relevant questions into a series of statements phrased in the PICO format that defines the population (P) under study, the intervention (I) under consideration, the comparator (C) against which the intervention is assessed and the outcome (O) worthy of evaluation.<sup>1</sup> It is important to note that if a comparator is not stated, then it is implied that the management strategy is compared against “potentially equivalent strategy” or “do nothing.”

## Development of Recommendations

The Guideline Panel and the authors of the Technical Review met face to face on March 8, 2020, to discuss the findings from the Technical Review. After this meeting, the Guideline Panel (T.M., L.D., L.T., and E.H.) independently formulated the guideline recommendations; the Technical Review Panel was not involved in the formulating or finalizing of the recommendations. The certainty of available evidence and the strength of recommendation are provided with each PICO statement. The certainty of the evidence supporting the PICO statement is described on a 4-point scale from high to very low (Table 1). A very low rating indicates great uncertainty regarding the estimate of effect.

## Evidence Review

Although the certainty of evidence was a key factor in determining the strength of the recommendations (Table 2), the Panel also considered the balance between the benefits and harms of the interventions, as well as patients' values and preferences, resource use (ie, cost), health equity, acceptability, and feasibility (Evidence to Decision Framework; Supplementary Appendix). A “strong” recommendation supports a clinical decision that should apply to most patients most of the time, whereas a “conditional” (also called “weak”

in some settings) recommendation implies that the decision is more nuanced and that some patients could be managed with a different approach. The recommendations, certainty of evidence, and strength of recommendations are summarized in Table 3.

## External Review

The guideline and technical review went through a 30-day public comment period between September 8, 2020 and October 8, 2020. AGA staff collated the comments. The Guideline Panel deliberated on its response and, when appropriate, modified the guideline. We hope to provide clinicians with clear guidance regarding IGB use in the management of patients with obesity. The target audience for this guideline includes health care providers and patients. In addition, we were not able to assess non-endoscopic balloons as a weight-loss intervention, as these devices are still not available in the United States.

## Recommendations

A summary of all of the recommendations in this guideline is provided in Table 3.

### *Intragastric Balloon Therapy as a Weight-Loss Intervention*

**Recommendation 1. In individuals with obesity seeking a weight-loss intervention who have failed a trial of conventional weight-loss strategies, AGA suggests the use of IGB therapy with lifestyle modification over lifestyle modification alone. (Conditional recommendation, moderate certainty)**

Implementation remark: Trials in the United States were limited to a body mass index (BMI) range between 30 and 40 kg/m<sup>2</sup>. Individuals with BMI values outside this range were sometimes included in international trials.

Implementation remark: Fluid-filled balloons may be associated with more weight loss, lower tolerability, and less favorable safety profile, than gas filled balloons. Shared decision-making is suggested for determining device choice.

**Table 2.** Interpretation of Strong and Conditional Recommendations Using the Grading of Recommendations Assessment, Development and Evaluation Framework

Implications	Strong recommendation	Conditional recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Different choices will be appropriate for individual patients consistent with their values and preferences. Use shared-decision making. Decision aids may be useful in helping patients make decisions consistent with their individual risks, values and preferences.
For policy makers	The recommendation can be adapted as policy or performance measure in most situations	Policy making will require substantial debate and involvement of various stakeholders. Performance measures should assess whether decision making is appropriate.

NOTE. Strong recommendations are indicated by statements that lead with “we recommend,” while conditional recommendations are indicated by statements that lead with “we suggest.”

**Rationale.** IGB as a weight loss therapy for individuals with obesity were examined across a number of important clinical outcomes that focused on weight loss, improving metabolic parameters and medical co-morbidities and the overall safety of the devices. First, across 4 important outcome measures related to weight loss, IGBs perform better than lifestyle modifications or standard of care (SOC) for individuals seeking to lose weight. With respect to weight loss, IGBs led to greater weight loss at 6, 9, and 12 months after initial balloon placement compared with patients treated with SOC alone; however, the amount of weight loss incrementally decreased for each successive time period. For example, pooled data from 7 randomized controlled trials (RCTs) showed IGBs resulted in patients losing an average of 15.46 lbs (95% confidence interval, 10.42–20.51 lbs) at 6 months, 3 RCTs illustrated that IGBs led to an average of 13.12 lbs of weight loss (95% CI, 10.53–15.70 lbs) at 9 months and 2 RCTs reported an average weight loss of 9.76 lbs (95% CI, 6.38–13.14 lbs) compared with patients using only using SOC/lifestyle modifications. Similarly, percent total body weight loss (%TBWL) improved at 6 to 8, 9, and 12 months for patients who received IGB therapy vs those undergoing SOC with the greatest %TBWL observed at 6–8 months (mean difference [MD], 6.89%; 95% CI, 4.09%–9.70%). Also, IGBs were more effective than SOC at all 3 time periods when examining percent excess weight loss with the 9-month time frame, demonstrating the greatest benefit (MD, 20.43%; 95% CI, 16.09%–24.77%). Finally, patients with obesity who received IGB therapy had a significantly greater response of attaining both 5% and 10% TBWL as opposed to those who underwent SOC interventions only for weight loss. Three RCTs showed 85.1% of individuals who received IGB therapy achieved 5% TBWL (vs 34.6% for SOC) (relative risk [RR], 2.44; 95% CI, 2.05–2.91), whereas 4 RCTs demonstrated that 61.9% of patients with an IGB realized 10% TBWL compared with just 13.7% for SOC therapy (RR, 4.31%; 95% CI, 3.21%–

5.80%) over a 6- to 8-month period. Similar trends, although to a smaller degree, were noted at 9 and 12 months for achieving 5% and 10% TBWL in patients with obesity using IGBs. Patients who use an IGB for weight-loss therapy attain greater weight loss across several parameters than SOC/lifestyle modification therapy over a 6- to 12-month time frame.

Second, several metabolic parameters and medical comorbidities are improved in the short-term in patients who use IGBs compared with noninvasive measures for weight loss. Data from 5 RCTs and 18 observational studies illustrated that IGB therapy significantly lowers both hemoglobin A1c and fasting blood glucose levels more so than noninvasive therapy alone. In particular, improved laboratory profiles were observed in patients using IGBs who had a fasting blood glucose level >100 mg/dL, hemoglobin A1c >6.5%, and in patients with a BMI >40 kg/m<sup>2</sup>. Mixed results were shown with respect to improving patients’ lipid profiles; although no benefit was realized in reducing triglycerides for those patients that used IGB therapy, there was a trend of decreasing low-density lipoproteins in patients with obesity using IGBs. Improvement in liver function test abnormalities was also observed in patients who used IGBs for weight loss, with alanine aminotransferase values decreasing by 9 U/L and aspartate aminotransferase values lowering by 3 U/L. Finally, diabetes, hypertension, and dyslipidemia all achieved remission to a statistically significant greater degree in patients who used an IGB for weight loss as opposed to those patients who pursued a noninvasive approach. Likewise, patients with obesity who used IGBs, on average, were able to reduce their waist circumference by 4.1 cm compared with patients who used noninvasive approaches. Taken together, current data suggest that IGB therapy improves laboratory abnormalities and accomplishes greater rates of remission for several medical diseases associated with obesity than SOC alone.

**Table 3.** American Gastroenterological Association Recommendations on Intra-gastric Balloon Therapy in the Management of Obesity

Recommendation	Strength of recommendation	Quality of evidence
1. In individuals with obesity seeking a weight-loss intervention who have failed a trial of conventional weight-loss strategies, AGA suggests the use of IGB therapy with lifestyle modification over lifestyle modification alone. <sup>a,b</sup>	Conditional	Moderate
2. In individuals with obesity undergoing IGB therapy, AGA recommends moderate- to high-intensity concomitant lifestyle modification interventions to maintain and augment weight loss.	Strong	Moderate
3. In individuals undergoing IGB therapy, AGA recommends prophylaxis with PPIs.	Strong	Moderate
4. In individuals undergoing IGB therapy, AGA suggests using the intraoperative anesthetic regimens associated with the lowest incidence of nausea along with perioperative antiemetics. AGA suggests a scheduled antiemetic regimen for 2 week after IGB placement. <sup>c</sup>	Conditional	Low
5. In individuals undergoing IGB therapy, AGA suggests against perioperative laboratory screening for nutritional deficiencies.	Conditional	Low
6. AGA suggests daily supplementation with 1–2 adult dose multivitamins after IGB placement.	Conditional	Very low
7. After IGB removal, AGA suggests subsequent weight-loss or maintenance interventions that include dietary interventions, pharmacotherapy, repeat IGB, or bariatric surgery. The choice of weight-loss or maintenance method after IGB is determined based on patient's context and comorbidities following a shared decision-making approach.	Conditional	Low

**Implementation remark:**

<sup>a</sup>Trials in the United States were limited to a BMI range between 30 and 40 kg/m<sup>2</sup>. Individuals with BMI values outside this range were sometimes included in international trials.

<sup>b</sup>Fluid-filled balloons may be associated with more weight loss, lower tolerability, and less favorable safety profile than gas fluid balloons. A shared decision-making is suggested for determining device choice.

<sup>c</sup>Evidence is insufficient to recommend a specific antiemetic regimen. The choice of regimen is based on institutional policy, clinical context, and availability.

Third, early IGBs were associated with a number of devastating adverse events<sup>3,4</sup> that resulted in their removal from the US market in the 1980s and 1990s. Therefore, it is crucial to better understand adverse events associated with newer versions of IGBs introduced in the last 2 decades. Examination of data on newer models of IGB reveals important

information on their tolerability and safety. Early removal of IGBs was noted in 9.4% of patients, with the most common reasons being device intolerance (eg, sense of fullness) and symptomatic intolerance (eg, epigastric pain, reflux, nausea, and emesis). Seven RCTs were examined to assess the outcomes of serious adverse events associated with intra-gastric

balloon therapy after 6–8 months. More serious adverse outcomes were observed in patients who received IGB therapy (5.6%) compared with those in the SOC groups (1.1%) (RR, 3.07; 95% CI, 1.16–8.11). Yet, serious adverse events were relatively rare in patients receiving IGB treatment, and mostly included injury to the gastrointestinal (GI) tract, such as perforation (0.3%), esophageal mucosal injury (0.8%), gastric ulcer/bleeding (0.76%), and gastric outlet/bowel obstruction (0.12%). During a 6- to 8-month period in patients with an IGB in place, no deaths were reported among these 7 RCTs. More recently, post-marketing surveillance of IGB has reported additional rare adverse events of hyperinflation, acute pancreatitis, and death. IGBs appear to be associated with both a favorable adverse event and patient tolerability profile.

Lastly, various models of IGBs are available and can vary by filling medium (ie, gas or liquid). A meta-analysis of 22 RCTs showed that fluid-filled IGBs were associated with nearly 3% more weight loss compared with gas-filled balloons. In particular, all 3 current models of the fluid-filled balloons were demonstrated to be better than controls, whereas only 1 of the 2 gas-filled balloon models was better than controls in achieving 6-month %TBWL. Overall, fluid-filled IGBs were more likely to be associated with more weight loss than gas-filled IGBs at 6 months. At the same time, the systematic review referenced above showed numerically higher rates of adverse events with fluid-filled balloons than with gas-filled balloons, suggesting better tolerability and safety of gas-filled balloons for patients. Consequently, providers and patients together should assess the best available evidence, balance risk and harms, and include patient preferences when determining whether to use a fluid- or gas-filled IGB. Overall, the panel rated the quality of evidence in this area as moderate due to serious imprecision in the included studies.

**Recommendation 2. In individuals with obesity undergoing IGB therapy, AGA recommends moderate- to high-intensity concomitant lifestyle modification interventions to maintain and augment weight loss.** (Strong recommendation, moderate certainty)

**Rationale.** Few studies have examined lifestyle modifications to maintain and/or enhance weight loss in patients with obesity who have had an IGB placed. In the available literature, diets were the primary lifestyle modification examined with respect to improving weight loss once an IGB was placed and to maintain weight loss once the balloon was removed. One RCT randomized 80 patients with obesity to a moderate-intensity low-calorie diet vs a high-intensity very-low-calorie ketogenic diet after having had an IGB in place for 4 months with patients being followed for an additional 2 months after the IGB had been removed (total 6-month treatment period). After 6 months, the high-intensity, very-low-calorie ketogenic diet cohort experienced a greater mean weight loss and percent excess weight loss than the low-calorie diet cohort (MD, 7.1 kg; 95% CI, 6.30–7.90 kg and MD, 12%; 95% CI, 10.66%–13.34%, respectively). Examining the data only in the period after the IGB was removed

confirmed that the high-intensity, very-low-calorie ketogenic diet continued to be superior to the low-calorie diet with respect to losing weight. In addition, patients who underwent IGB placement for weight loss and continued with a moderate- to high-intensity diet for an additional 6 months after therapy were noted to have ongoing weight loss (17 kg) and BMI reduction (6 kg/m<sup>2</sup>); moreover, there was progressive weight loss through the 6 months of treatment even after the IGB was removed. Overall, the quality of evidence for this recommendation was rated as moderate, as a result of the small number of patients included in these trials. Although diet does augment and sustain weight loss in patients receiving IGB therapy, it is unclear whether other lifestyle modifications (eg, exercise) would have the same impact and is an area that deserves further investigation.

**Recommendation 3. In individuals undergoing IGB therapy, AGA recommends prophylaxis with proton pump inhibitors.** (Strong recommendation, moderate certainty)

**Rationale.** Given that the mucosa of the GI tract can be eroded and potentially bleed during and after the placement of IGBs, questions have arisen around the prophylactic administration of proton pump inhibitors (PPIs) in individuals undergoing IGB therapy. Unfortunately, no RCTs have directly assessed patient outcomes with respect to PPI use in patients with IGB placement. However, indirect evidence suggests that: PPIs reduce the risk of rebleeding in patients with high-risk bleeding stigmata in the upper GI tract<sup>5,6</sup> and in 4 RCTs in which patients received an IGB and were administered PPI therapy, there were lower device/non-procedure-related serious adverse events, especially as it pertained to upper GI bleeding. PPIs are postulated to have risks of their own both in the short term (eg, enteric infections including *Clostridium difficile*, community-acquired pneumonia) and long term (eg, increased bone fracture risks, kidney disease, and micronutrient deficiencies)<sup>7–9</sup>; it is therefore imperative that the lowest dose, frequency, and duration of PPIs be used in patients undergoing IGB therapy. Overall, the quality of evidence was deemed moderate for concomitant PPI prophylaxis due to a lack of comparative outcome data being available in the studies. Future studies that include a comparator group and assess the optimal dosing, frequency, and duration of PPI administration in patients with obesity receiving IGB therapy are warranted.

**Recommendation 4. In individuals undergoing IGB therapy, AGA suggests using the intraoperative anesthetic regimens associated with the lowest incidence of nausea along with perioperative antiemetics. AGA suggests a scheduled antiemetic regimen for 2 weeks after IGB placement.** (Conditional recommendation, low certainty)

Implementation remark: Evidence is insufficient to recommend a specific antiemetic regimen. The choice of regimen is based on institutional policy, clinical context, and availability.

**Rationale.** In individuals undergoing IGB therapy, the panel suggests using the intraoperative anesthetic regimens associated with the lowest incidence of nausea in conjunction with perioperative antiemetics. After IGB placement, the panel suggests a scheduled antiemetic regimen for 2 weeks. The specific antiemetic regimen should be based on institutional policy, clinical context, and availability. Two RCTs assessing antiemetic efficacy after IGB placement were identified. The first study compared a therapeutic regimen of midazolam and ondansetron vs ondansetron alone for preventive treatment of nausea/vomiting and found that combination therapy of midazolam and ondansetron trended toward outperforming ondansetron alone (RR, 0.57; 95% CI, 0.32–1.02).<sup>10</sup> Further, early balloon removal rate was lower in the midazolam and ondansetron arm compared with the ondansetron-alone arm (0 of 29 and 3 of 28, respectively; RR, 0.14; 95% CI, 0.01–2.56). The second study compared mean vomiting incidence among alizapride, tropisetron, and tropisetron with droperidol, but due to limited availability of these agents in the United States, it was not applied to this recommendation.<sup>11</sup> Due to limited direct evidence, RCTs assessing efficacy of antiemetics in any restrictive bariatric surgery were considered.

Overall, the quality of evidence for this recommendation was low for antiemetic treatment of nausea in IGB. The 2 studies specific to this recommendation in IGB were found to have a serious risk of bias, indirectness, and imprecision. In addition, when the search was expanded to include antiemetic therapy across bariatric surgery interventions, the quality of evidence was found to be low to very low quality.

**Recommendation 5. In individuals undergoing IGB therapy, AGA suggests against perioperative laboratory screening for nutritional deficiencies.** (Conditional recommendation, low certainty)

**Rationale.** The panel suggests against perioperative screening for nutritional deficiencies in individuals undergoing IGB therapy. No direct evidence was identified on perioperative laboratory screening for nutritional deficiencies in individuals undergoing IGB placement for weight loss. In addition, no indirect evidence from other restrictive bariatric procedures was identified regarding perioperative laboratory screening for nutritional deficiencies.

A number of perioperative deficiencies have been identified in observational sleeve gastrectomy or gastric bypass surgery studies to date: thiamine, folate, and magnesium deficiencies have been reported. Five studies identified report a prevalence of thiamine deficiency in perioperative IGB ranging from 0%–29%.<sup>2</sup> Four studies identified report a prevalence of perioperative folate deficiency ranging from 0% to 24%.<sup>2</sup> In 3 pre-laparoscopic sleeve gastrectomy procedure cohorts, no patients were found to have hypomagnesemia.<sup>2,12–14</sup>

Overall, the quality of evidence for this recommendation was low for perioperative laboratory screening for

nutritional deficiencies. Observational studies suggest a potential for perioperative nutritional deficiencies, however, and clinical judgment should be used on an individual basis regarding perioperative screening for nutritional deficiencies.

**Recommendation 6. AGA suggests daily supplementation with 1–2 adult dose multivitamins after IGB placement.** (Conditional recommendation, very low certainty)

**Rationale.** The panel suggests daily supplementation with 1–2 adult dose multivitamins after IGB placement. No direct evidence was identified for prophylactic dosing of multivitamin supplements post IGB. Therefore, the panel evaluated the role of prophylactic dosing of multivitamins after IGB placement or similar restrictive gastric bypass procedures on a number of specific nutrient deficiencies: thiamine, folate, magnesium, and potassium. Among 3 studies reporting a preoperative thiamine deficiency prevalence of 0%–29%, prophylactic dosing of 1–3 multivitamin tablets/day resulted in postoperative thiamine deficiency prevalence of 0%–9%.<sup>2,12,15,16</sup> In addition, a single study reported maintenance of a normal preoperative thiamine level at 3 months postoperatively with a daily multivitamin regimen.<sup>17</sup> Two studies in restrictive bariatric surgery cohorts, demonstrate maintenance of a normal preoperative folate level for 3–12 months after surgery with 1 multivitamin/d prophylaxis.<sup>14,18</sup> Furthermore, there appears to be potential for de novo development of a folate deficiency if no prophylaxis is given in a subset of patients (6%–9.2%).<sup>19,20</sup> In 3 post-laparoscopic sleeve gastrectomy procedure cohorts, in which 1–2 multivitamins with minerals were recommended, no patients (n = 205) were found to have hypomagnesemia up to 5 years after the procedure.<sup>2,12–14</sup> Two single-arm cohort studies provide evidence for the potential development of asymptomatic hypokalemia from vomiting 1-week post-IGB placement (6.8%–8.5%).<sup>21,22</sup> Whether or not these patients were on a multivitamin was not reported.<sup>2</sup>

Overall, the quality of evidence for this recommendation was very low for prophylactic use of 1–2 adult-dose multivitamins after IGB placement. Observational studies suggest a potential for postoperative nutritional deficiencies that may be preventable with multivitamin therapy.

**Recommendation 7. After IGB removal, AGA suggests subsequent weight loss or maintenance interventions that include dietary interventions, pharmacotherapy, repeat IGB or bariatric surgery. The choice of weight loss or maintenance method after IGB is determined based on patient's context and comorbidities following a shared decision-making approach.** (Conditional recommendation, low certainty)

**Rationale.** Having an open discussion with patients about the risks, benefits, and alternatives of each weight-loss management strategy is required for clinical practice. In patients who have had their IGB removed, the panel

suggests subsequent weight-loss or maintenance therapies that include dietary interventions, pharmacotherapy, sequential IGB, or bariatric surgery. The choice of therapy is based on open discussions with patients about their clinical status, their value and preferences, and safety profile of various strategies in a shared decision-making approach.

Two randomized controlled clinical trials provided evidence with respect to pharmacotherapy in addition to IGB therapy. One RCT studied sibutramine 10 mg/day vs moderate-/high-intensity diet as maintenance therapy for 6 months after IGB removal. At the end of the study at 1 year, both groups reported significant, progressive weight loss of 17 kg and  $>6$  kg/m<sup>2</sup> decrease in BMI. Pharmacotherapy fared slightly better than moderate-/high-intensity diet (total weight loss  $>10\%$ : relative risk [RR], 1.50; 95% CI, 0.81 to 2.78; weight loss in kg: MD, 0.20 kg loss; 95% CI, 2.01 gain to 2.41 lost; decrease in BMI: MD, 0.30 kg/m<sup>2</sup> decrease; 95% CI, 0.55 increase to 1.15 decrease).<sup>23</sup> A second RCT studied liraglutide 3 mg/d in addition to IGB vs IGB alone for 6 months. This study showed that the pharmacotherapy arm performed better than IGB alone (total weight loss 10%: MD, 14.72%; 95% CI, 8.81 to 21.26; WL in kg: MD, 3.8 kg loss; 95% CI, 2.43–5.17 kg loss; decrease in BMI: MD, 1.32 kg/m<sup>2</sup> decrease; 95% CI, 0.92 kg/m<sup>2</sup> increase to 1.72 kg/m<sup>2</sup> decrease) (evidence profile: medication).<sup>2</sup>

Evidence regarding sequential IGB therapy was based on 2 RCTs,<sup>2</sup> which evaluated sequential IGB vs IGB for 6 months followed by low-calorie diet for 7 months. When the study ended at 13 months, patients who underwent a second IGB experienced a greater BMI reduction compared with individuals without a second IGB (BMI MD, 5.49 kg/m<sup>2</sup> decrease; 95% CI, 4.82–6.16 kg/m<sup>2</sup>). Non-RCT studies also demonstrated a trend toward greater BMI reduction favoring sequential IGB. However, risks and complications tend to be more frequent in patients with a second IGB or prolonged IGB use.

One observational comparative cohort study served as the primary source of evidence regarding bariatric surgery as a weight-loss maintenance method after IGB therapy. Comparing patients who underwent bariatric surgery (lap-band, laparoscopic adjustable gastric banding, or duodenal switch) after IGB with patients who refused any weight-loss maintenance strategy, the bariatric surgery group reported a delta of 16.6 kg/m<sup>2</sup> reduction in BMI and a delta of 42.5% excess weight loss at 12 months.<sup>24</sup> One RCT and 3 observational studies offered evidence for effectiveness and safety of IGB before laparoscopic gastric band placement. A small benefit was seen using IGB before surgery in reducing length of hospitalization stay by 1 day, lowering the risk of intraoperative risks and moderate to severe postoperative complications.

Overall, the panel rated the quality of evidence as low. Although RCTs involving dietary intervention, pharmacotherapy, and sequential IGB were well conducted, the quality of evidence was rated lower due to the imprecision as a result of a small number of subjects and a short follow-up period. Furthermore, the efficacy and safety of sequential IGB and bariatric surgery strategies were informed by observational studies.

## Implementation Considerations

IGB therapy can be an effective tool in the management of obesity and our goal is to provide clinicians and patients with clear guidance regarding its use. Successful implementation of IGBs during the active weight-loss phase and maintenance phase often occurs with concomitant therapy, such as lifestyle modifications, pharmacologic agents, sequential IGBs, or bariatric surgery. These strategies implemented in conjunction with IGBs lowers the risk of weight-gain recidivism.

The panel acknowledges that fluid-filled balloons may be associated with greater weight loss and lower tolerability and a less favorable safety profile than air fluid balloons (Recommendation 1); however, the panel makes no recommendations on specific IGB devices. In fact, the quality of the evidence to support this recommendation was based on moderate evidence as a result of serious imprecision and a very small number of included studies and patients. Future, larger studies that directly compare these 2 IGB models with respect to a number of patient outcomes is needed before making a definitive statement on the superiority of one IGB over another. This determination is best made in a shared decision-making approach while considering the patient's values and preferences, balancing benefits and harms within the patient's clinical and behavioral context, cost, and availability. Likewise, these factors are also critical in guiding the appropriate selection for concomitant lifestyle modifications, pharmacotherapy, or sequential procedures.

## Discussion

The role of gastroenterologists in the management and treatment of weight loss in patients with obesity has evolved over the last 4 decades. Part of this changing role has been driven by the advancement of IGBs, which are devices placed endoscopically in the outpatient setting and serve as a restrictive form of weight-loss therapy for patients. Therefore, it is imperative that gastroenterologists understand the growing body of literature surrounding these devices; in particular, it is essential to understand not only the role that providers play in choices for weight-loss therapy, but also the effectiveness, safety, and patient and provider experiences with these devices. A better understanding of this information will allow gastroenterologists to create a more patient-centered approach whereby providers and patients collaboratively reach evidence-based and value-congruent decisions on the use of IGBs in patients with obesity.

Significant improvements have been observed in patients with obesity using IGBs with respect to a number of critical weight-loss outcomes. IGBs lead to greater weight loss, improve metabolic laboratory abnormalities, and change the trajectory of several medical comorbidities associated with obesity; clearly IGB therapy (with lifestyle modification) is superior to lifestyle modifications alone at initial and maintenance of weight loss for patients in the short term (within at least 12 months of initial IGB placement). Although many questions surrounding IGBs have been answered, studies involving IGBs reveal many

shortcomings; many conclusions were drawn as a result of indirect evidence, a number of studies lack a comparator group, small sample sizes were included, selection bias was present in several studies, and there was a low reporting of several important outcomes across many of the studies. Future work in this area needs to focus on larger RCTs that examine the short- and long-term efficacy of IGBs with respect to obesity-related medical comorbidities (eg, hypertension, diabetes, nonalcoholic steatohepatitis, and cardiovascular disease), the long-term impact of single IGB implantation, predictive modeling for patients who may be nonresponders or at higher risk of having adverse events, and comparing IGB efficacy with other short-term weight loss devices/procedures. Finally, cost-effectiveness studies of IGBs are necessary to more fully understand the entirety of the impact of these devices. One question that remains open is where IGB therapy falls in the algorithm for patients with obesity seeking to lose weight. More information is required to better understand whether IGBs alone, sequentially, and/or with concomitant therapies may be sufficient for some patients, while in other patients it may serve as a bridge to longer-term weight-loss interventions, such as bariatric surgery.

IGBs have been on the US market since 1982, yet very few guidelines or consensus documents have specifically addressed the efficacy, safety, and role that IGBs play in weight-loss therapy. This guideline incorporates the most recent literature and evidence on IGBs and using GRADE methodology provides several evidence-based recommendations as it pertains to IGBs. One question that arises is how this guideline fits in with other published work on this topic. In the United States, 2 guidelines have been generated: a position statement by the American Society for Metabolic and Bariatric Surgery/Society of American Gastrointestinal and Endoscopic Surgeons (2016),<sup>13</sup> and the American Society for Gastrointestinal Endoscopy<sup>25</sup> systematic review and meta-analysis assessing Preservation and Incorporation of Valuable Endoscopic Innovations thresholds for adopting endoscopic bariatric therapies (2015). The American Society for Gastrointestinal Endoscopy position statement focused only on 1 IGB (ie, ORBERA) and discovered that it resulted in a decrease of the percentage of excess weight loss and percentage of total body weight loss over a 12-month period, serious adverse events were infrequent and most patients tolerated the IGB with a 7% early removal rate. On the other hand, the American Society for Metabolic and Bariatric Surgery/Society of American Gastrointestinal and Endoscopic Surgeons consensus statement examined 2 IGBs (ie, ORBERA and ReShape). Here, they also illustrated that adverse events were rare (eg, bowel obstructions, perforation, and death), there was a voluntary removal rate of 4.2%–7.0%, and both balloons demonstrated efficacy at reducing the percentage of excess weight loss, total body weight loss, and improved liver histology in patients with nonalcoholic steatohepatitis. On the international stage, a Brazilian consensus statement<sup>26</sup> based on the experiences of 40,000 IGB placements provided guidance on indications (ie, age and BMI), contraindications for placement, pre- and post-procedure evaluation

with a multidisciplinary team, medications to use to relieve symptoms (ie, antiemetics, steroids, analgesics, and PPIs) and a review of adverse events. The strength of our guideline is that it rigorously examined all available data and applied a validated tool to synthesize the data, included all current IGBs on the market, and assessed efficacy across a number of areas (laboratory values, metabolic parameters, and medical comorbidities), safety (both major and minor adverse events) and tolerability. This comprehensive guideline validates and expands on the conclusions of previous position statements and provides greater clarity on IGBs with respect to additional areas of concern to patients, providers, and health care teams.

## Future Research Needs and Evidence Gaps

These recommendations highlight the need for additional research on the use of IGBs for the management of obesity. Our Technical Review<sup>2</sup> suggests that IGB therapy with lifestyle modification is an effective weight-loss intervention. Further, IGB therapy seems to result in improvements in metabolic parameters and medical comorbidities. Evidence gaps include long-term efficacy of IGB therapy compared with SOC beyond 1 year. Given the incremental trend toward a decrease in weight loss observed in the period 6–12 months after placement, there is a need to determine the efficacy of IGB therapy beyond 1 year, with regard to weight loss, but also metabolic parameters and medical comorbidities. Consideration should be given to variables such as the filling medium (fluid vs gas) and the potential efficacy of an ongoing dietary intervention, pharmacotherapy, or sequential balloon placement for sustained weight loss. Studies on the role of exercise in weight-loss sustainability after IGB placement are also needed. Although the risk of serious adverse events appears to be relatively low, early removal due to device intolerance seems to be relatively common. Identifying predictors of device intolerance can help inform patient selection by identifying those patients who would be most likely to succeed with IGB therapy.

The use of several medications both peri- and post-IGB placement requires further investigation. Indirect evidence suggests that the prophylactic use of PPI therapy with IGB placement can protect against upper GI bleeding-related complications. RCTs that directly assess patient outcomes with PPI use after IGB placement are still needed. In addition, studies are needed to determine the optimal dosing, frequency, and duration of PPI administration. To date, there is a dearth of literature on the use of intraoperative anesthetic regimens and antiemetic regimens both pre- and postoperatively in IGB patients. Given the frequency of nausea reported by patients after IGB placement, this is an important area of research that can help improve IGB tolerance.

Throughout creation of these guidelines, an emphasis was placed on ensuring that they accommodate a broad audience to address health care disparities. Another gap in



the literature is an absence of research examining disparities that may persist in terms of weight-loss treatments offered to patients, including IGB. In the vast majority of studies included in the Technical Review,<sup>2</sup> patients were either White with little inclusion of individuals from other racial and ethnic backgrounds, or there was no reporting of race or ethnicity within the studies. Future research must concentrate on studying a more diverse patient population, identifying whether disparities exist in weight-loss treatment interventions offered to patients and assessing whether such disparities affect outcomes of weight-loss interventions.<sup>27</sup> Evidence suggests that IGBs are an effective weight-loss option for patients with obesity, but their use has historically been limited to certain medical centers. As the number of IGB devices available on the US market continues to expand, however, it is important to ensure guidance is available that allows for their application in a diverse range of health care settings.

Lastly, the micronutrient management of individuals who undergo IGB placement requires additional research. Limited research is available about the need for perioperative laboratory screening for nutritional deficiencies or micronutrient needs after IGB placement. However, the Technical Review<sup>2</sup> did not find any supporting evidence for the replacement of potassium, vitamin D, or additional micronutrients in the IGB population. Ultimately, more research is needed to determine the optimal protocol for IGB placement, maintenance, and sustainability of metabolic improvements. There are several limitations associated with these recommendations. Some of the recommendations are based heavily on indirect or imprecise evidence at this time due to the limited literature available. In particular, recommendations on micronutrient monitoring and management of IGB placement, as well as subsequent weight loss or maintenance interventions after removal, all received conditional recommendations with low to very low certainty. Therefore, it is distinctly possible that future research may alter future recommendations regarding IGB therapy in the management of obesity.

In conclusion, the AGA suggests IGB therapy with moderate- to high-intensity lifestyle therapy as a weight-loss intervention over lifestyle interventions alone. In addition, the AGA recommends prophylaxis with PPI therapy to prevent upper GI bleeding, but the lowest and least frequent dosing regimen should be used. In the context of limited evidence, the AGA suggests using the intraoperative anesthetic regimens associated with the lowest incidence of nausea and a scheduled antiemetic regimen for 2 weeks after IGB placement. In addition, the AGA recommends against perioperative laboratory screening for nutritional deficiencies, but does suggest daily supplementation with 1–2 adult dose multivitamins after IGB placement. After IGB removal, the AGA recommends subsequent weight-loss or maintenance interventions that include dietary interventions, pharmacotherapy, repeat IGB, or bariatric surgery, and that a strategy be determined based on a shared decision-making approach. The AGA acknowledges the limitations of the available evidence on this topic as well as the

potential confounding based on IGB characteristics, RCT design, and geographic variations of included studies; however, a rigorous review of current data supports the efficacy and safety of IGBs for patients with obesity. The AGA recognizes that new evidence may emerge in the future that might strengthen or modify some of the recommendations for the use of IGB in management of obesity.

### Plans for Updating This Guideline

Guidelines are living products. To remain useful, they need to be updated regularly as new information accumulates. This document will be updated when major new research is published. The need for an update will be determined no later than 2022.

### Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at [www.gastrojournal.org](http://www.gastrojournal.org), and at <https://doi.org/10.1053/j.gastro.2021.03.003>.

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**Conflicts of interest**

All members were required to complete the disclosure statement. These statements are maintained at the American Gastroenterological Association (AGA) headquarters in Bethesda, Maryland, and pertinent disclosures are published with this report. These authors disclose the following: Lukejohn W. Day served as Chair of the Quality Assurance in Endoscopy Committee at the American Society for Gastrointestinal Endoscopy, member of the Minority Affairs and Cultural Diversity Committee at the American College of Gastroenterology and a Board member of the Association of American Indian Physicians. Levi M Teigen served as a consultant for Nestle Health Sciences. The remaining authors disclose no conflicts.