






# International consensus position statement on the role of obesity management medications in the context of metabolic bariatric surgery: expert guideline by the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO)

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Members of the International Consensus on the Role of Obesity Management Medications in the Context of Metabolic Bariatric Surgery are co-authors of this study and are listed under the heading Collaborators.

## Introduction

Metabolic bariatric surgery (MBS) is the most effective long-term treatment option for clinical obesity and its complications<sup>1</sup>. Nonetheless, modern pharmacotherapy involving intestinal hormonal analogues, such as semaglutide and tirzepatide, have shown good weight loss outcomes in the short and medium term<sup>2-4</sup>. Potentially, such obesity management medications (OMMs) may be synergistic with or additive to MBS for selected patients before and/or after MBS regarding improved outcomes.

The impact of pharmacotherapy before surgery is unclear, with a lack of high-level evidence regarding the efficacy of preoperative OMMs in reducing intraoperative risks and complications<sup>5</sup>. Similarly, the evidence is scarce for the use of OMMs as an adjunct therapy to MBS or in patients with a suboptimal initial clinical response or with recurrent weight gain after surgery<sup>6-8</sup>. For these reasons, the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) asked a multidisciplinary group of international experts in obesity management to develop evidence-based recommendations to serve as a global reference for using OMMs before and after MBS. These recommendations were developed through a Delphi process, identifying areas of expert consensus after a systematic review of the published literature and highlighting areas warranting further research<sup>9</sup>.

## Methods

### Definitions and nomenclature

Clinical obesity is a condition in which the risk to health associated with excess adiposity has already materialized and can be objectively documented by specific signs and symptoms reflecting biological alterations of tissues and organs that are consistent with extant illness<sup>10</sup>. In 2023, IFSO created a global consensus to standardize MBS outcomes<sup>11</sup>, defining a suboptimal initial clinical response and recurrent weight gain as the standard nomenclature. Modern OMMs are the second-generation intestinal hormonal analogues (single or dual analogues), whereas OMMs include all available pharmacotherapy that may be adjunctive to MBS and are not restricted to only modern agents.

### Partner organizations and selection of voting experts

The core scientific committee (R.V.C., G.P., and L.B.) and the partner organizations—the World Obesity Federation (WOF), the European Association for the Study of Obesity (EASO), and the International Diabetes Federation (IDF)—tasked a multidisciplinary group of 40 international authorities to develop evidence-based recommendations. Voting experts were entirely chosen from academia, without representatives from industry. The names and details of these experts, as well as those of an internationally recognized Delphi expert (R.L.), with knowledge of endocrinology

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and metabolism, and a patient representative, are provided in the Collaborators section.

## Review of evidence

The preset research questions for the systematic review of evidence included preoperative and postoperative use of pharmacotherapy, the class of drugs employed, the impact on weight and obesity-related complications, and the effectiveness and complications of using medications before and after MBS. Given the objectives of the consensus conference, the relatively short duration of availability and clinical use of modern pharmacotherapy, and the heterogeneous publications on the use of other OMMs, it was decided to adopt a relatively low threshold for the selection of evidence, including not only RCTs but also published systematic reviews and observational studies. A document with the results of this systematic review was circulated among the whole group in preparation for the Delphi process.

## Delphi process development and in-person meeting framework

The core scientific committee prepared a list of issues for each statement and a first draft of the rationale for each statement was sent to the experts before the start of the Delphi process. Furthermore, each expert was asked to contribute three to four statements within their field of expertise. The statements were then revised by the core scientific committee and by the Delphi expert.

An initial Delphi process, referred to as the online Delphi process, was conducted by e-mail among the full expert panel, beginning on 25 March 2024. The patient representative was not involved in the online Delphi process. Each expert returned their completed questionnaire to the Delphi expert without sharing their votes or comments with the other expert panel members.

The second part of the Delphi process was conducted as a 2-day in-person meeting, with the full voting expert panel and the patient representative, without voting capacity, but actively involved in the discussions, from 30 April 2024 to 1 May 2024, in Vienna, Austria. The first day consisted of expert presentations and a discussion of the available evidence on using OMMs and MBS. All experts who submitted statements for the Delphi voting presented the topics related to their statements to the entire group before the open discussion. The voting took place on the second day of the in-person meeting. The core scientific committee divided the topics for discussion and voting into three modules: module 1, common understanding of obesity as a disease, the benefits of the extent of weight loss on obesity-related health risks, and the use of OMMs before MBS; module 2, use of OMMs after MBS; and module 3, future perspectives.

## Online and in-person Delphi processes

The Delphi expert counted the votes for each statement to discern the percentage consensus support for each statement. Statements that received 100% consensus support were considered grade A+, statements that received 90–99.9% consensus support were considered grade A, statements that received 80–89.9% consensus support were considered grade B, statements that received 70–79.9% consensus support were considered grade C, and statements that received 66–69.9% consensus support were considered grade D. Statements that received less than 66% consensus support were considered to have failed consensus<sup>12</sup>.

After the initial round of the online Delphi process, statements that were considered grade A or higher were closed for further

voting. Statements that were considered less than grade A, but for which the expert feedback was conflicting or insufficient to suggest a means to edit the statement to achieve higher consensus, were tabled for further discussion during the in-person Delphi process. The Delphi expert edited the remaining statements, incorporating the feedback from the expert panel, and a new questionnaire was distributed to each expert panel member. In total, three rounds of the online Delphi process were conducted.

During the in-person Delphi voting, each statement, including the revised versions developed during the online Delphi process, was presented to the expert panel for further discussion. Each statement considered grade A+ or A during the online Delphi process was individually discussed and edited by the Delphi expert, considering the comments raised by the panel experts. After each set of discussions, a new vote was taken for the statement using a smartphone app to maintain the confidentiality of the vote. When a revised statement did not receive grade A support, discussion regarding further edits took place and a new vote was taken. During the in-person Delphi voting, 12 of the original statements were voted to be deleted by the expert panel due to redundancy with other statements, due to a lack of relevance regarding the aims of the consensus document, or due to conflicts with other statements.

Furthermore, five new statements were added and voted on during the in-person Delphi voting. Due to various valid circumstances, not every expert panel member voted for every statement during the online or in-person Delphi process. Thus, the percentage consensus and the number of total votes are indicated for each statement in each module.

## Results

The statements from the Delphi process and the consensus grade, percentage consensus, number of voting rounds, and number of total votes are reported in detail in [Table 1](#) (module 1), [Table 2](#) (module 2), and [Table 3](#) (module 3).

## Discussion

The aim of this initiative was to inform stakeholders involved in obesity care about the role of adjunctive pharmacotherapy strategies, either before or after MBS. The expert group reached grade A or A+ consensus for the following main statements: first, OMMs after MBS result in weight loss that is similar to that achieved for non-surgical patients and OMMs should be considered for treating a suboptimal initial clinical response or recurrent weight gain after MBS; second, for patients requiring OMMs to maintain a healthy weight after MBS, OMMs should be withheld until the achievement of a weight plateau; and third, OMMs should be considered before revisional surgery. The main areas identified for further research included postoperative intermittent use of OMMs and the long-term safety, efficacy, and cost-effectiveness of combined strategies.

Data on the advantages of preoperative weight loss regarding perioperative outcomes (mortality and surgical complications) are conflicting. Some data show early postoperative mortality benefits<sup>13</sup>, whereas other data show no significant benefits<sup>5</sup>. So, although preoperative weight loss programmes may have beneficial effects on perioperative (surgical) performance, it is important to highlight that most studies have not used modern OMMs but rather other medications (for example orlistat, phentermine/topiramate, or liraglutide). Still, there is insufficient

**Table 1 Delphi results, module 1: common understanding of obesity as a disease, the benefits of different extents of weight loss on obesity-related complications, and the use of obesity management medications before metabolic bariatric surgery**

	Grade	Percentage consensus	Number of total voting rounds	Number of total votes
1 Clinical obesity is a disease that requires treatment	A+	100	2	39
2 Patients should be informed of the risks and benefits of evidence-based treatment options for obesity	A+	100	1	37
3 A minimum of 5% weight loss has shown metabolic improvements; however, greater weight loss is associated with broader clinical benefits, including a reduction in mortality	A	97	3	39
4 There is insufficient high-level evidence to recommend the routine use of OMMs for weight loss before MBS	A+	100	2	37
5 The decision to use OMMs before MBS should be personalized to determine the most appropriate strategy for each patient's circumstances	A+	100	2	38
6 Future research is needed to explore the value of using OMMs before MBS to assess their benefits, risks, and clinical outcomes	A+	100	2	37
7 Healthy nutrition, including adequate protein consumption, as well as resistance exercise, is recommended for those treated with OMMs before MBS	A	97	2	36
8 In general, preoperative treatment with OMMs should be discontinued before MBS to minimize perioperative risk	A	94	3	35

OMMs, obesity management medications; MBS, metabolic bariatric surgery.

**Table 2 Delphi results, module 2: use of obesity management medications after metabolic bariatric surgery**

	Grade	Percentage consensus	Number of total voting rounds	Number of total votes
9 Treatments with OMMs after MBS should generally be withheld until the achievement of a weight plateau unless there is a compelling clinical need for earlier initiation	A+	100	3	33
10 Future research is needed to identify predictors of which patients are likely to derive substantial benefit from combined pharmaco-surgical therapy for obesity and its complications	A+	100	3	35
11 MBS is strongly associated with reduced adverse cardiovascular events and GLP1RA agonists have been shown to reduce such events; future research is required to determine the benefits of combination treatment for these outcomes	A+	100	3	34
12 Both MBS and GLP1RA agonists reduce chronic kidney disease; future research is required to determine the benefits of combination treatment for these outcomes	A+	100	3	36
13 In patients with a suboptimal initial clinical response after MBS, the addition of OMMs can improve metabolic outcomes	A+	100	1	34
14 For patients requiring OMMs to maintain a healthy weight after MBS, the ongoing use of the medications is likely needed	A	94	2	36
15 Research on the intermittent use of OMMs and/or their dose adjustment after MBS with a suboptimal initial clinical response is needed	A	94	3	36
16 The benefit of endoscopic therapies for obesity can be enhanced by combination with OMMs	C	74	2	35
17 Patients with a suboptimal initial clinical response or recurrent weight gain after MBS should be informed of all available evidence-based treatments, including their benefits and risks	A	100	1	34
18 In patients with a suboptimal initial clinical response or recurrent weight gain after MBS, different options, including OMMs, endoscopic therapies, and revisional and conversion surgery, can be considered	A	94	2	35
19 Emerging evidence indicates that the weight loss induced by OMMs is similar among people who have or have not undergone MBS	A+	100	2	36
20 When used after MBS, there appears to be no increased incidence of side effects of OMMs compared with non-surgical cohorts	A	97	3	34

OMMs, obesity management medications; MBS, metabolic bariatric surgery; GLP1RA, glucagon-like peptide-1 receptor agonists.

evidence to recommend OMMs routinely before MBS. Although there is very low evidence<sup>14</sup>, OMMs, mainly the modern ones, should be stopped before MBS to decrease potential anaesthetic complications.

OMMs produce similar weight loss in patients with or without previous MBS and operated patients may have fewer side effects<sup>15</sup>. The timing for starting OMMs after MBS was exhaustively discussed. The experts agreed that OMMs should be generally withheld until the achievement of a weight

plateau, allowing the assessment of the effect of MBS alone, before starting OMMs. However, there may be some patients who may benefit from early concomitant OMMs and MBS. Hence, the experts agreed that research is needed to identify predictors of which patients will likely substantially benefit from combined pharmaco-surgical therapy for obesity and its complications.

Both modern OMMs and MBS have shown cardiovascular and renal benefits<sup>4,16,17</sup>, significant control of type 2 diabetes, and

Table 3 Delphi results, module 3: future perspectives

	Grade	Percentage consensus	Number of total voting rounds	Number of total votes	Observations
21 As the long-term efficacy and safety of OMMs after MBS is unknown, studies are needed to understand the value and limitations of such combination therapy	A+	100	3	34	–
22 Endpoints of future clinical trials of existing and/or novel obesity management interventions (behavioural, pharmacological, endoscopic, and surgical) should focus on improvement, remission, and prevention of clinical manifestations and complications of obesity, in addition to weight loss	A+	100	3	35	–
23 Studies are needed to define stage-specific therapeutic protocols that integrate surgical intervention and adjuvant pharmacotherapy to achieve improvement (or remission when possible) of clinical obesity	A	95	1	38	95% after first round of online Delphi—no voting in person
24 Further investigation of the mechanisms of action of distinct MBS procedures is an important research priority to understand the additive versus synergistic effects of different possible combinations of surgical and drug-based therapies; this knowledge is necessary to optimize the safety and efficacy of adjuvant pharmacotherapy for obesity	A	95	2	35	95% after first round of online Delphi—no voting in person
25 For patients with recurrent weight gain, treatment with available OMMs should be considered before revisional surgery	A	92	1	38	92% after first round of online Delphi—no voting in person
26 When treatment with OMMs after MBS results in a suboptimal initial clinical response or when there is an inability to continue medications (for example due to cost or an adverse reaction), then endoscopic, revisional, or conversion surgery should be considered	A+	100	3	35	–
27 People living with obesity need access to all evidence-based treatments, including MBS and OMMs, as part of standard healthcare services	A	95	1	38	95% after first round of online Delphi—no voting in person
28 Health systems need to support the long-term management of obesity, as they do for other chronic diseases (for example diabetes or cardiovascular disease)	A	95	1	38	95% after first round of online Delphi—no voting in person
29 All healthcare providers need a basic understanding of the complex aetiology, pathophysiology, and evidence-based management of obesity	A+	100	–	38	100% after first round of online Delphi—no voting in person
30 Studies on the cost-effectiveness of the association of modern pharmacotherapy and MBS are essential to determine the role of preoperative and postoperative OMMs	A+	100	–	38	100% after first round of online Delphi—no voting in person
31 Similar benefit–risk and benefit–cost considerations, and therefore willingness to pay, should be applied to the treatment of obesity, as they are to other chronic diseases	A+	100	3	35	–

OMMs, obesity management medications; MBS, metabolic bariatric surgery.

significant weight loss<sup>2,3,18</sup>. However, there is a need for studies on the eventual additive effects of both treatments on these outcomes.

There was broad agreement regarding the effectiveness of adjunctive pharmacotherapy in patients with a suboptimal initial clinical response or recurrent weight gain after MBS, as there is good quality of evidence of additional weight loss when adding OMMs to MBS<sup>15,19</sup>.

Even though studies of patients who did not undergo MBS show that withdrawing OMMs leads to weight gain<sup>20</sup>, there are no data on the safety of and the need for continuous or intermittent use of OMMs after MBS. Grade A+ consensus was reached regarding the need for studies to assess these issues. The concept of ‘treatment to target’ is emerging in managing obesity and its complications<sup>21</sup>, as well as tailoring OMMs after MBS to meet individual needs. For example, some patients may be able to taper off semaglutide after recurrent weight gain and use other strategies to maintain their improved health status. Others may need to continue with a lower dose or a different drug. No single pathway will work for every person, as clinical obesity is chronic and heterogeneous.

Revisional/conversion surgery is highly technical and complex, and carries a higher risk of complications than primary MBS<sup>22,23</sup>. In addition, solid data on its safety and efficacy are lacking<sup>24</sup>. There was grade A consensus for using modern OMMs and endoscopic therapies before offering revisional/conversion surgery, which may be a safer and more effective strategy. However, further research is needed.

Recently introduced endoscopic procedures<sup>25</sup> may lead to improved weight loss when concomitant OMMs are used; however, consensus among the experts was low (grade C) on the potential added benefits of endoscopic procedures regarding the outcomes of OMMs.

This work has several limitations. Every expert consensus survey has the potential for bias and relies on opinions. In the present study, the impact of bias was mitigated in numerous ways. A thorough systematic review was performed, the results of which were sent to all of the experts before the first round of Delphi voting. Also, multidisciplinary experts from every continent and a patient representative were included. Finally, a recognized Delphi expert was utilized to balance all statements during the Delphi process.

Modern pharmacotherapy has changed the landscape of the treatment of clinical obesity and its complications. However, a knowledge gap regarding important points in contemporary obesity treatments remains. Over 15% of total weight loss may be key to halting or preventing obesity complications<sup>19</sup>. However, that was challenged by the SELECT trial<sup>4</sup>, where cardiovascular-related events were lowered by 20%, with approximately 9.4% total weight loss compared with placebo. Future studies need to include weight loss and the remission or improvement of obesity complications as a composite primary outcome, as no robust evidence exists regarding the eventual mechanistic synergy or added benefits for modern pharmacotherapy and MBS. This includes the agents in the pipeline currently under phase 1 and 2 evaluation<sup>26</sup>. The safety and efficacy of newer OMMs should be compared with those of semaglutide and tirzepatide. Moreover, besides the magnitude of weight loss, newer medications must lead to additional benefits regarding obesity complications and quality of life.

Long-term use of medications for several chronic diseases is well accepted by patients and healthcare providers. The recurrence of hypertension after the cessation of antihypertensive agents is expected and not questioned. However, unlike other chronic diseases, healthcare providers, policymakers, payors, and the public, in general, do not regard obesity as a disease that needs lifelong treatment. The stigmatization of obesity may significantly contribute to this view<sup>27</sup>. This is an essential issue that needs to be addressed, with the education of all stakeholders involved in treating obesity and its complications. Finally, consensus was reached regarding the need for studies to determine the mechanisms of action of combined medical and surgical treatments and a better understanding of payors about obesity treatments in equipoise with other chronic diseases<sup>28</sup>.

The only study available on the cost-effectiveness of modern OMMs puts them above the willingness-to-pay threshold in the USA<sup>29</sup>. Patients may benefit from an approach that combines OMMs and MBS for different reasons, but the economic impact of this approach is still unknown, especially the in long-term. Even though MBS is currently the most effective and durable treatment for obesity and its complications, its outcomes are variable. Ultimately, the conclusions of this consensus will guide clinical practice and assist in creating an algorithm to aid clinicians in their decisions when treating patients with a suboptimal initial clinical response or recurrent weight gain after MBS. Furthermore, the need for more research to address the questions generated by this international consensus is highlighted.

## Collaborators

### International Consensus on the Role of Obesity Management Medications in the Context of Metabolic Bariatric Surgery

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## Author contributions

Ricardo V. Cohen (Conceptualization, Formal analysis, Methodology, Project administration, Writing—original draft, Writing—review & editing), Luca Busetto (Conceptualization, Formal analysis, Methodology, Writing—review & editing), Randy Levinson (Data curation, Formal analysis, Methodology, Writing—review & editing), Carel W. Le Roux (Validation, Writing—review & editing), Paulina Salminen (Validation, Writing—review & editing), and Gerhard Prager (Conceptualization, Formal analysis, Methodology, Project administration, Validation, Writing—review & editing)

## Disclosure

R.V.C. has received research grants from Johnson & Johnson MedTech and Medtronic, and has received payment for lectures from Johnson & Johnson MedTech, Medtronic, and Novo Nordisk. L.B. is an advisory board member for Novo Nordisk, Lilly, Pfizer, Boehringer Ingelheim, and Bruno Farmaceutici, and

is a speaker for Rythm Pharmaceuticals and Pronokal. C.W.L.R. has received grants from the Irish Research Council, the Science Foundation Ireland, Anabio, and the Health Research Board, and serves on advisory boards and speaker panels for Herbalife, GI Dynamics, Novo Nordisk, Lilly, Johnson & Johnson MedTech, Glia, Irish Life Health, Boehringer Ingelheim, Currax, Zealand Pharma, and Rhythm Pharmaceuticals. P.S. has received lecture fees from Novo Nordisk and grants from the Academy of Finland, the European Research Council, and the Sigrid Juselius Foundation. G.P. has received educational grants from Novo Nordisk, Johnson & Johnson MedTech, Olympus, and Medtronic, speaker fees from Medtronic, Meril, and Olympus, and serves on scientific advisory boards for Lilly and Novo Nordisk. The authors declare no other conflict of interest.

## Data availability

No data are presented.

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