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Catarina Columbano Paulino da Silva

# GLP-1 analogues in post-operative bariatric surgery patients: a systematic review and meta-analysis

MARÇO, 2024

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# GLP-1 analogues in post-operative bariatric surgery patients: a systematic review and meta-analysis

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Área: Ciências Médicas e da Saúde

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Trabalho efetuado sob a Orientação de:

Doutora Paula Isabel Marques Simões de Freitas

sob a Coorientação de:

Dr. Hugo Santos Sousa

Trabalho organizado de acordo com as normas da revista:

Obesity Surgery

**MARÇO, 2024**

Eu, Catarina Columbano Paulino da Silva, abaixo assinado, nº mecanográfico 201807400, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro ter actuado com absoluta integridade na elaboração do meu trabalho de Dissertação ou Monografia.

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DESIGNAÇÃO DA ÁREA DO PROJECTO

Ciências médicas e da saúde > Medicina clínica

TÍTULO DISSERTAÇÃO/~~MONOGRAFIA~~ (riscar o que não interessa)

GLP-1 analogues in post-operative bariatric surgery patients: a systematic review and meta-analysis

ORIENTADOR

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UC Dissertação - Declaração de Transparência relativamente à utilização de ferramentas de chatbot generativo baseadas em large language models

Eu, Catarina Columbano Paulino da Silva, abaixo assinado, nº mecanográfico 201807400 estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro que:

¾ Não procedi à utilização de ferramentas de chatbox generativo baseadas em large language models para nenhuma das tarefas no contexto do meu trabalho de Dissertação ou Monografia

¾ Procedi à utilização de ferramentas de chatbox generativo baseadas em large language models no contexto do meu trabalho de Dissertação ou Monografia, encontrando-se todas as interacções ( prompts e respostas) transcritas em anexo bem como a indicação das aplicações utilizadas.

Neste sentido, confirmo que a eventual utilização de ferramentas de chatbox generativo baseadas em large language models no contexto do meu trabalho de Dissertação ou Monografia foi exclusivamente descrita na sequência de prompts e respostas transcritos em anexo e nas aplicações indicadas.

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**Dedicatória**

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# GLP-1 analogues in post-operative bariatric surgery patients: a systematic review and meta-analysis

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**Declarations of interest:** none to declare.

**Key-words:** GLP-1 analogues, bariatric surgery, metabolic surgery, weight regain

**Abstract**

Purpose: The objective of this study is to assess the potential benefits of incorporating GLP-1 analogues as an adjuvant treatment in patients after bariatric surgery.

Methods A comprehensive literature review was conducted, accessing MEDLINE (through PubMed), Web of Science and Scopus databases, until October 2023. Studies about the use of postoperative GLP-1 analogues after metabolic surgery were integrated. Data on weight change, total weight loss percentage and body index mass change were extracted.

Results: A total of 12 studies met the eligibility criteria which involved 975 participants. The analysis revealed a significant correlation between the use of GLP-1 analogues and weight reduction, which indicated that GLP-1 analogues might confer advantageous outcomes for weight reduction following bariatric surgery.

Conclusion: This systematic review and meta-analysis demonstrate that the use of GLP-1 analogues in addition to surgical interventions demonstrate potential for favourable outcomes offering a viable option for individuals experiencing suboptimal results following bariatric surgery.

## 1) Introduction

Obesity is chronic relapsing disease with multifactorial aetiology, which constitutes an alarmingly increasing major public health issue. [1]

The rise in the prevalence of obesity is associated with increases in the prevalence of many comorbidities as type 2 diabetes, hyperlipidaemia, hypertension, obstructive sleep apnea, heart disease, stroke, asthma, back and lower extremity weight-bearing degenerative problems, several forms of cancer and depression [2].

Bariatric surgery is a powerful tool not only for weight management but also to improve or resolve obesity-associated comorbidities, thereby reducing mortality. [3] However, a considerable part of patients presents with unsatisfactory response in the long term. Weight regains after bariatric surgery is unfortunately a common occurrence and it´s estimated to occurs in up to a third of patients. Furthermore, it´s proved that consequently reduces treatment-associated health benefits. [4]

Glucagon-like peptide-1 receptor agonists (GLP1-RAs) are the currently most efficacious weight lowering drugs, which make them promising agents for the treatment of obese individuals. [5]

In this way, the combination of these drugs after bariatric surgery could be a strategy to prevent the weight regain as well as promoting additional health benefits. However, their role remains unclear and need to be further investigated.

Therefore, the aim of this systematic review and meta-analysis is to study the possible beneficial effects of using GLP-1 analogues as an addition in adult patients after bariatric surgery.

## 2) Methods

### 2.1) Search Strategy

This systematic review and meta-analysis was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[6]

A systematic review of literature was performed by two authors independently using three different databases: PubMed, Scopus, and Web of Science until October 2023.

The following query was used: bariatric surgery AND GLP-1 AND (weight regain OR insufficient loss); (metabolic surgery OR bariatric surgery) AND (GLP-1 OR semaglutide) AND (weight regain OR insufficient loss); [(metabolic AND surgery) OR (bariatric AND surgery)] AND (GLP-1 OR semaglutide) AND [(weight AND regain) OR (insufficient AND loss)]. A total of 1319 articles were retrieved from the search.

### 2.2) **Study Selection**

The inclusion criteria were defined**:** a) original studies published until October 2023; b) conducted in adults aged 18 or older which had bariatric/metabolic surgery; c) at least one group /subgroup had to have treatment with GLP-1 analogue after previous bariatric/metabolic surgery; and d) studies relevant to the topic, presenting original data: at least include follow up information of the weight evolution.

We excluded a) non original studies; b) studies performed in children or adolescents; c) patients with type 2 diabetes using GLP-1 analogues prior /after surgery; d) patients who underwent revision surgery during the follow up; and e) incomplete records (missing qualitative or quantitative data of interest).

Initially, data extraction was carried out independently by two authors (**CS and PF**). In this way, pertinent studies were chosen through their titles and abstracts. After this step, 21

studies were selected for full-text reading. Subsequently, a comprehensive screening process was undertaken which resulted in 12 final studies to be included in the analysis- detailed characteristics of studies included in meta-analysis are shown in **Table 1.** Disagreements were solved by consensus. All the detail of the process is shown in Figure 1.

### 2.3) Data Extraction and Quality Assessment

Data extraction was performed independently by the same two authors and compare at the end of the process**.**

The following data was extracted: article identification (title, authors, date of publication, the study design, general description of the study); patients characteristics (number of patients, gender, age), weight primary surgery, maximum weight change after bariatric surgery, weight regain before additional GLP-1, weight change on GLP-1 therapy and body mass index (BMI) change on GLP-1 therapy.

To proceed with quality assessment of these studies, the Methodological Index for Non- Randomized Studies (MINORS) checklist, was used. MINORS is based on 12 items, when each study can obtain a maximum score of 24 points, and for each item detailed in the checklist, a score of 0 (nor reported), 1 (reported but insufficient) or 2 (reported and complete) is established. [7]

### 2.4) Statistical analysis

A meta-analysis of random effects (using the restricted likelihood method) was conducted, with the calculation of means and standard deviations (SD) of weight change, total percentage of weight loss (%TWL) and BMI change.

Heterogeneity was assessed based on the I-squared ($I^2$ ) measure and the p-value of Cochran's Q test. Typically, $I^2$ values >50% and p <0.10 are considered indicative of substantial heterogeneity. The analysis was performed using the R software (meta package).

## 3) Results

### 3.1) Search results and characteristics of the sample

As previously mentioned, an initial search of the PubMed, Scopus and Web of Science platforms resulted in 149, 83 and 1087 respectively, totalling 1319 potentially relevant articles. Then, 1298 were excluded due to the main reasons explained before, which resulted in 21 full-text articles assessed for eligibility. Furthermore, 9 more articles were excluded, resulting in a final number of 12 studies that met all the eligibility criteria for analysis. **Figure 1** presents a flowchart demonstrating the main reasons for excluding the remaining articles during this process.

The great majority (n=9) were retrospective cohort studies [9-17], one was a randomized placebo-controlled trial [18] and two prospectives cohort [19, 20]. Studies were performed between 2012 and 2023. In total, 975 patients were included undergoing metabolic surgery and postoperative treatment with GLP1 analogue. The performed surgeries included LRYGB, LSG, biliopancreatic diversion (BPD), vertical banded gastroplasty (VBG), and adjustable gastric banding (AGB). Due to partially incomplete information the actual exact numbers of each operation technique aren't clear. In all studies, the GLP-1 analogue Liraglutide or Semaglutide were used as complementary treatment.

A summary of some characteristics of the population, as well as relevant data about the weight evolution can be found on **Table 2.**

### Quality Assessment

Using the MINORS scale the median score was 19, with a range of 19-20, as detailed in **Table 3** (full-description available in the attachments). As the lowest score was 18, all the twelve included studies were accepted as suitable for inclusion in this quantitative analysis.

### 3.2) Weight change in patients undergoing bariatric surgery and GLP-1 analogue treatment

Four studies, involving a total 266 patients, reported the mean of the weight change expressed on kg. According to random effects model, there were a mean of weight change of 9.5972 kg [6.4176; 12.7769] with $p< 0.0001$ and $I^2$ of 93.5%. In this way, there were statistically significant differences in this parameter.

### 3.3) Total weight loss percentage in patients undergoing bariatric surgery and GLP-1 analogue treatment

This outcome (total weight loss percentage- TWL %) was reported in 4 studies, involving 229 patients. There were a mean weight loss percentage of -9.8806% [-13.4690; -6.2922] with p value <0.0001 and $I^2$ of 93.6%. According to these results there were statistically significant differences using GLP1 analogues.

### 3.4) BMI change in patients undergoing bariatric surgery and GLP-1 analogue treatment

A total of 197 patients from 3 studies were included in the analysis- Body Index Mass (BMI). There was a mean BMI change of -4.7792 $Kg/m^2$ [-5.1814; -4.3769]. The heterogeneity among the studies was quantified with an $I^2$ of 22.5%. The test of heterogeneity yields a p-value of 0.2753, suggesting that the observed heterogeneity is not statistically significant (Figure 2- BMI change).

**Discussion and conclusion**

Obesity is a persistent, recurring condition with multiple and complex causal factors.[21]

Surgical intervention for obesity marks a significant advancement, not only in treating excess weight but also in managing associated comorbidities. However, inadequate initial response or recurrence of obesity and its related conditions is increasingly common, often necessitating further nutritional counselling or revisional surgery in some situations.

In this systematic review and meta-analysis, we have comprehensively analysed the paper of GLP-1 analogues in promoting weight loss for patients who did not experience significant weight loss after metabolic surgery. This group of patients should undergo assessment by a multidisciplinary team, which should not only consider nutritional guidance and revisional surgery but also start considering novel pharmaceutical options as an effective alternative. [22]

Our results of weight change, total weight loss percentage represents important conclusions about GLP-1 analogues that could inform clinical practice and guide future research.

Regarding weight and weight percentage, the meta-analysis by subgroups revealed that there was a statistically significant subgroup effect ($p < 0.0001$) although heterogeneity remains high within each subgroup ($I^2$ from 93.5 to 93.6%). Looking regarding BMI (Body Index Mass), the meta-analysis by subgroups revealed that, despite the heterogeneity being low ($I^2$ of 22.5%), there is no statistically significant subgroup effect ($p = 0.2753$).

In this way, according to our analysis it's clear that all the studies showed an additional weight loss, however high heterogeneity was detected, possibly due to

variations in how weight evolution was defined and reported in the included studies. In addition, this represents the reason why we only could represent one forest plot related to BMI change (Figure 2). Furthermore, the absence of a longer follow-up period in the studies limits the evaluation of the effect of GLP-1 analogues to a maximum of 2 years. The selection of surgical technique didn't affect the response to GLP-1 analogues, nevertheless, not all studies provided enough data on various procedures.

In summary, despite bariatric surgery proving to be effective for most of the patients, enduring challenges with sustained weight loss, unfavourable weight evolution and comorbidity relapse are commonplace in clinical practice. Integrating promising medical interventions like GLP-1 analogues may offer enhanced outcomes regarding weight reduction and comorbidity resolution for patients exhibiting inadequate response to surgery alone in the future.[23, 24]

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## Tables

| 1. | Name | Year | Type of study | Surgery | Medical Therapy | Administration interval | | Outcomes | Follow up (months) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Mean (months) | SD | | Mean | SD |
| | "Pajecki et al." | 2012 | Retrospective cohort | LRYBD | Liraglutide 1.2-3.0mg | 64 | 40 | Weight evolution. adverse effects | 8.6 | 7.3 |
| | | | | BPD | | | | | | |
| | | | | LSG | | | | | | |
| | | | | AGB | | | | | | |
| **2.** | "Mok" | 2021 | Randomized controlled trial | LRYBD | Liraglutide 3.0mg | 49.1 | 33.7 | Weight evolution | 6 | |
| | | | | LSG | | | | | | |
| **3.** | Wharton et al | 2019 | Retrospective cohort | LRYBD | Liraglutide 3.0mg | 93.6 | 68.4 | Weight evolution. adverse effects | 8 | 7.6 |
| | | | | AGB | | | | | | |
| **4.** | Rye et al. | 2018 | Retrospective cohort | LRYGB | Liraglutide 2.9 ± 0.2mg | 76.3 | 72.9 | Weight evolution. adverse effects | 4 | |
| | | | | VBG | | | | | 7 | |
| | | | | LSG | | | | | | |
| | | | | AGB | | | | | | |
| **5.** | Muratori | 2022 | Retrospective cohort | LRYBD | Liraglutide 0.6-3.0mg | 70.7 | 43.7 | Weight. adverse effects | 10.5 | 4.4 |
| | | | | LGB | | | | | | |
| | | | | LSG | | | | | | |
| **6.** | Lautenbach | 2023 | Retrospective cohort | LRYBD | Semaglutide 0.25-1.0 mg | 64.5 | 51.9 | Weight evolution | 12 | |
| | | | | LSG | | | | | | |
| **7.** | Lautenbach | 2022 | Retrospective cohort | LRYBD | Semaglutide 0.50 mg | 64.7 | 47.6 | Weight evolution | 3 | |
| | | | | LSG | | | | | 6 | |
| **8.** | Murvelashvili | 2022 | Retrospective cohort | LRYBD | Semaglutide 1.0mg | 96 | 77.28 | Weight evolution | 12 | |
| | | | | LSG | Liraglutide 3.0mg | | | | | |
| | | | | AGB | | | | | | |
| **9.** | Horber | 2020 | Prospective study | LRYBD | Liraglutide 3.0mg | 9 | 4 | Weight evolution | 24 | |
| **10.** | Elhag | 2021 | Retrospective cohort | LRYBD | Liraglutide 3.0mg | 59.1 | 31.75 | Weight evolution | 6 | |
| | | | | | | | | | 12 | |
| **11.** | Bonnet | 2023 | Retrospective cohort | LRYBD | Semaglutide 2.4mg | 100.8 | 52.8 | Weight evolution | 6 | |
| | | | | LSG | | | | | | |
| **12.** | Colbourne | 2022 | Prospective open cohort | LRYBD | Liraglutide 1.8-3.0mg | 15.5 | | Weight evolution | 12 | |
| | | | | LSG | | | | | | |
| | | | | AGB | | | | | | |

**Table 1:** Study characteristics. Administration interval- time interval between metabolic surgery and the first administration of the GLP-1 analogue; LRYGB laparoscopic Roux-en-Y gastric bypass, BPD biliopancreatic diversion, VBG vertical banded gastroplasty, LSG laparoscopic sleeve gastrectomy, AGB adjustable gastric banding.

| Author | Year | 1) | 2) | 3) | 4) | 5) | 6) | 7) | 8) | 9) | 10) | 11) | 12) | TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| "Pajecki et al." | 2012 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 0 | 2 | 2 | 1 | 2 | 20 |
| Wharton et al | 2019 | 2 | 2 | 1 | 2 | 1 | 2 | 2 | 0 | 2 | 2 | 1 | 2 | 19 |
| Rye et al. | 2018 | 2 | 2 | 1 | 2 | 1 | 2 | 2 | 0 | 2 | 2 | 1 | 2 | 19 |
| Muratori | 2022 | 2 | 2 | 1 | 2 | 1 | 2 | 2 | 0 | 2 | 2 | 1 | 2 | 19 |
| Lautenbach | 2023 | 2 | 2 | 2 | 1 | 1 | 2 | 2 | 0 | 2 | 2 | 1 | 2 | 19 |
| Lautenbach | 2022 | 2 | 2 | 2 | 1 | 1 | 2 | 2 | 0 | 2 | 2 | 1 | 2 | 19 |
| Murvelashvili | 2022 | 2 | 2 | 1 | 2 | 1 | 2 | 2 | 0 | 2 | 2 | 1 | 2 | 19 |
| Horber | 2020 | 2 | 2 | 1 | 2 | 1 | 2 | 2 | 0 | 2 | 2 | 1 | 2 | 19 |
| Elhag | 2021 | 2 | 2 | 1 | 2 | 1 | 2 | 2 | 0 | 2 | 2 | 1 | 2 | 19 |
| Bonnet | 2023 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 0 | 2 | 2 | 1 | 2 | 20 |
| Colbourne | 2022 | 2 | 2 | 1 | 2 | 1 | 2 | 2 | 0 | 2 | 2 | 1 | 2 | 19 |

**Table 2**- Minors scale. 0: not reported; 1: reported but inadequate; 2: reported and adequate. 1) a clearly stated aim; 2) inclusion of consecutive patients ;3) prospective collection of data; 4) end points appropriate to the aim of the study; 5) unbiased assessment of study end point; 6) follow-up period appropriate to the aim of the study; 7) loss of follow-up less than 5%; 8) prospective calculation of the study size; 9) an adequate control group; 10) contemporary groups; 11) baseline equivalence groups; 12) adequate statistical analyse

| Name | Size (n) | Sex. Male (%) | Age | | Weight primary surgery | | | | Maximum weight change post bariatric surgery | | | | Weight regain before additional GLP-1 | | | | Weight change on GLP-1 therapy | | | | BMI change on GLP-1 therapy | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Mean (years) | SD | Mean (Kg) | SD | BMI (Kg/ m2) | SD | Mean (Kg) | SD | BMI (Kg/m2) | SD | Mean (Kg) | SD | BMI (Kg/ m2) | SD | Mean (Kg) | SD | Mean (%) | SD | Mean (Kg/m2) | SD |
| "Pajecki et al." | 15 | 33.3 | 47.2 | 12.5 | 120.8 | 22.1 | 42.2 | 4.1 | 86.7 | 14.4 | NR | | 100.9 | 18.3 | NR | | 7.5 | 4.3 | NR | | NR | |
| "Mok" | 70 | 26 | 47.6 | 10.7 | 119.8 | 24.3 | 43 | 7.5 | NR | | NR | | | | NR | | 9.49 | 5.07 | NR | | NR | |
| Wharton et al | 117 | 12.8 | 51.2 | 9.4 | NR | | 49.7 | 12.1 | -40.7 | 25 | NR | | 21.2 | 19.6 | NR | | 6.3 | 7.7 | -5.5 | 6.2 | NR | |
| Rye et al. | 20 | 5 | 49.6 | 8.3 | 126.25 | NR | NR | | 92.45 | NR | NR | | 109.55 | NR | NR | | 10.15 | NR | NR | | -3.5 | NR |
| | | | | | | | | | | | | | | | | | 13.65 | NR | NR | | -4.7 | NR |
| Muratori | 62 | 3.33 | 43.6 | 9.9 | NR | | 45.4 | 5.5 | NR | | 29.5 | 4.9 | NR | | 34.2 | 4 8 | NR | | | | -5.1 | 2.5 |
| Lautenbach | 29 | 17.2 | 48.5 | 8.4 | 145.7 | 31.8 | 50.4 | 9.5 | 100.6 | 24.7 | 34.6 | 6.7 | 110.8 | 22.2 | 38.3 | 6.1 | NR | | -14.7 | 8.9 | NR | |
| Lautenbach | 44 | 27 | 46.4 | 8.8 | 145.7 | 33.5 | 49.4 | 8.9 | 102.9 | 25.6 | 34.7 | 6.5 | 113.5 | 25.2 | 38.3 | 6.4 | NR | | -6 | 4.3 | NR | |
| | | | | | | | | | | | | | | | | | | | -10.3 | 5.5 | NR | |
| Murvelashvili | 207 | 10.1 | 55.15 | 10.65 | 134.05 | 30.81 | 48.54 | 10.24 | 94.18 | 2.25 | NR | | 110.7 | 24.5 | NR | | NR | | -8.77 | | NR | |
| | | | | | 136.76 | 31.7 | 50.28 | 10.63 | 95.07 | 22.3 2 | NR | | 114.4 | 27.56 | NR | | NR | | -4.15 | | NR | |
| Horber | 95 | 12 | 54 | 12 | 122 | 18 | 45 | 6 | NR | | 25.7 | 3.8 | NR | | 30.4 | 5.1 | 13 | 8 | NR | | -4.8 | 2.9 |
| Elhag | 119 | 19 | 42.86 | 10.94 | 118.25 | 27.21 | 45.92 | 8.89 | 82.15 | 17.3 8 | 32.08 | 6.44 | NR | | NR | | NR | | -5.97 | NR | NR | |
| | | | | | | | | | | | | | | | | | | | -6.93 | NR | NR | |
| Bonnet | 129 | 15 | 53.6 | 10.8 | 125.2 | 23.6 | 45.7 | 7.8 | 96.1 | 23.8 | NR | | 29.2 | 17 | NR | | 11.6 | 6.3 | -9.8 | 5.7 | -4.3 | 2.4 |
| Colbourne | 68 | 16.2 | 40.5 | NR | 117.4 | NR | 44.8 | NR | 89.1 | NR | 34.6 | NR | 95.8 | NR | 35.2 | NR | 5.2 | NR | NR | | -1.85 | |

**Table 3**-Weight evolution

Figures

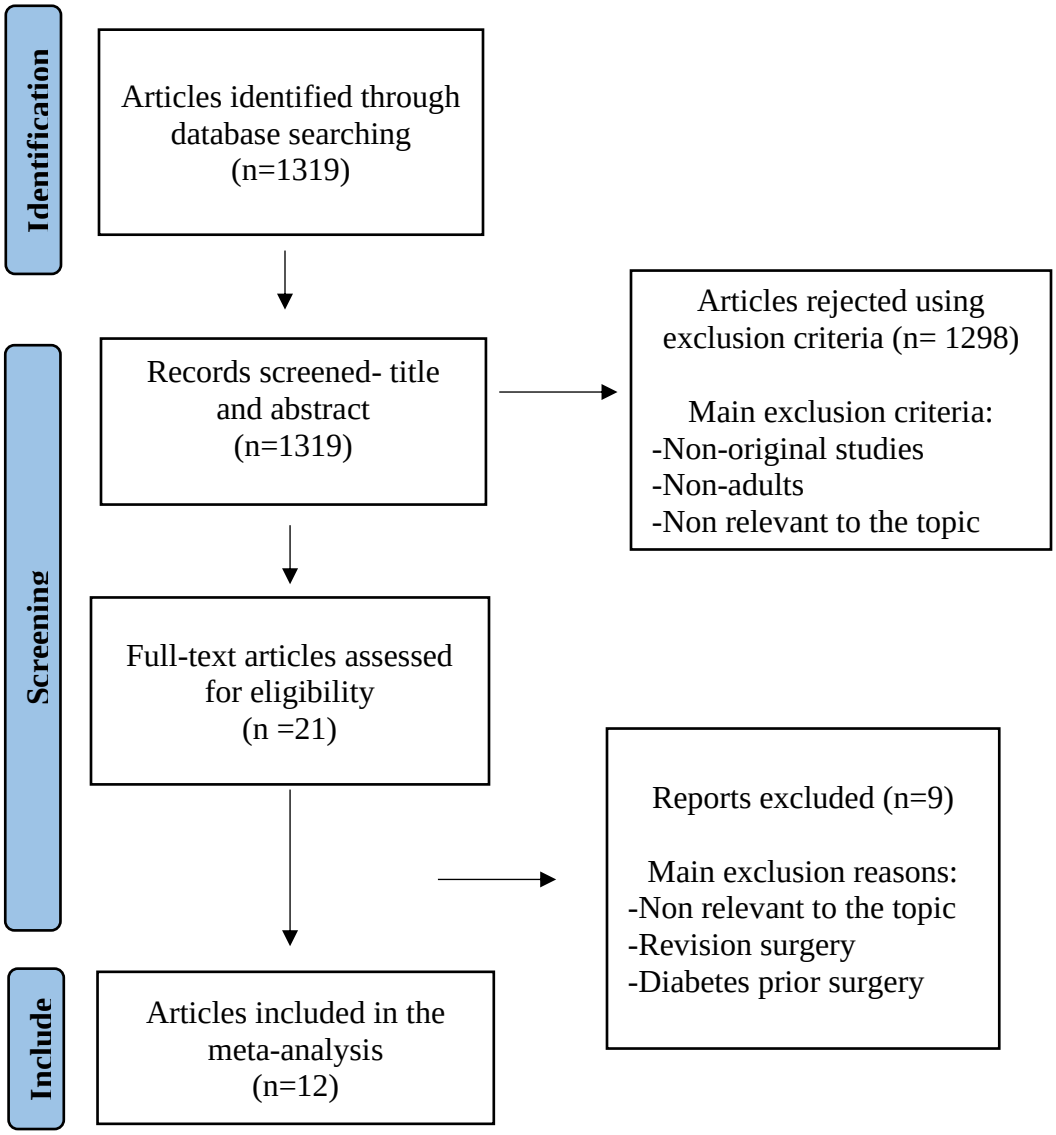


**Figure 1**- Prisma Flowchart.[6]

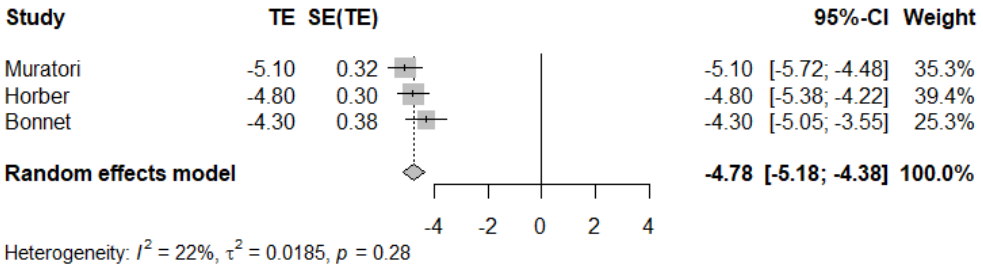


**Figure 2:** BMI change

## Appendix

1. Reporting Guidelines – The PRISMA Group (2020). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement.

2. Submission Guidelines – Obesity Surgery

## Reporting Guidelines The PRISMA Group (2020). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PRISMA 2020 Checklist

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review. | Page 1, paragraph 1: "GLP-1 analogues in post-operative bariatric surgery patients: a systematic review and meta-analysis |
| **ABSTRACT** | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. (Recomendações da revista) | Page 2 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | Page 3, paragraph 2/3 "Glucagon-like peptide-1 receptor agonists (GLP1-RAs) are the currently most efficacious weight lowering drugs, which make them promising agents for the treatment of obese individuals (….) the combination of these drugs after bariatric surgery could be a strategy to prevent the weight regain" |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | Page 3, paragraph 4 "aim of this systematic review and meta-analysis is to study the possible beneficial effects of using GLP-1 analogues as an addition in adult patients after bariatric surgery." |
| **METHODS** | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Page 4, paragraph 4-5 "The inclusion criteria were defined: a) original studies published until October 2023; b) conducted in adults aged 18 or older which had bariatric/metabolic surgery; c) at least one group /subgroup had to have treatment with GLP-1 analogue after previous bariatric/metabolic surgery; and d) studies relevant to the topic, presenting original data: at least include follow up information of the weight evolution. We excluded a) non original studies; b) studies performed in children or adolescents; c) patients with type 2 diabetes using GLP-1 analogues prior /after surgery; d) patients who underwent revision surgery during the follow up; and e) incomplete records (missing qualitative or quantitative data of interest)." |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Page 4, paragraph 2"three different databases: PubMed, Scopus, and Web of Science". |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Page 4, paragraph 3"three different databases: PubMed, Scopus, and Web of Science until October 2023. The following query was used: bariatric surgery AND GLP-1 AND (weight regain OR insufficient loss); (metabolic surgery OR bariatric surgery) AND (GLP-1 OR semaglutide) AND (weight regain OR insufficient loss); [(metabolic AND surgery) OR (bariatric AND surgery)] AND (GLP-1 OR semaglutide) AND [(weight AND regain) OR (insufficient AND loss)]." |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Page 4, paragraph 2 "A systematic review of literature was performed by two authors independently". Paragraph 6 "In this way, pertinent studies were chosen through their titles and abstracts. After this step, 21 studies were selected for full-text reading. Subsequently, a comprehensive screening process was undertaken which resulted in 12 final studies to be included in the analysis-" |

| | | | |
|---|---|---|---|
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Page 5, paragraph 1 "Initially, data extraction was carried out independently by two authors (CS and PF) (...) Disagreements were solved by consensus." |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Page 5 paragraph 3 "The following data was extracted: article identification (title, authors, date of publication, the study design, general description of the study); patients characteristics (number of patients, gender, age), weight primary surgery, maximum weight change after bariatric surgery, weight regain before additional GLP-1, weight change on GLP-1 therapy and body mass index (BMI) change on GLP-1 therapy." |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | Page 4, paragraph 4 "To proceed with quality assessment of these studies, the Methodological Index for Non- Randomized Studies (MINORS) checklist, was used" |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | Page 6, paragraph 1 "A meta-analysis of random effects (using the restricted likelihood method) was conducted, with the calculation of means and standard deviations (SD) of weight change, total percentage of weight loss (%TWL) and BMI change. " |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | |
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | Page 6, paragraph 1 "Heterogeneity was assessed based on the I-squared ($I^2$ ) measure and the p-value of Cochran's Q test. Typically, $I^2$ values >50% and p <0.10 are considered indicative of substantial heterogeneity. The analysis was performed using the R software (meta package)."" |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | |

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| **RESULTS** | | | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Page 16, Figure 1- PRISMA Flowchart |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | Page 16, Figure 1- PRISMA Flowchart<br>Page 7, Paragraphs 1-2 |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Page 7, Paragraph 2 "The great majority (n=9) were retrospective cohort studies [9-17] , one was a randomized placebo-controlled trial [18] and two prospectives cohort [19, 20] . Studies were performed between 2012 and 2023. In total, 975 patients were included undergoing metabolic surgery and postoperative treatment with GLP1 analogue. The performed surgeries included LRYGB, LSG, biliopancreatic diversion (BPD), vertical banded gastroplasty (VBG), and adjustable gastric banding (AGB). Due to partially incomplete information the actual exact numbers of each operation technique aren't clear. In all studies, the GLP-1 analogue Liraglutide or Semaglutide were used as complementary treatment. A summary of some characteristics of the population, as well as relevant data about the weight evolution can be found on Table 2." |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | Page 14, Table 2- MINORS |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Page 13, 15, Figure 2 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | Page 8 |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Page 8, Figure 2 |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | Page 10, paragraph 2 |

| | | | |
|---|---|---|---|
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | |
| **DISCUSSION** | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | Page 11, paragraph 2 "Integrating promising medical interventions like GLP-1 analogues may offer enhanced outcomes regarding weight reduction and comorbidity resolution for patients exhibiting inadequate response to surgery alone in the future." |
| | 23b | Discuss any limitations of the evidence included in the review. | Page 11, paragraph 1 " however high heterogeneity was detected, possibly due to<br>variations in how weight evolution was defined and reported in the included studies. In addition, this represents the reason why we only could represent one forest plot related to BMI change (Figure 2). Furthermore, the absence of a longer follow-up period in the studies limits the evaluation of the effect of GLP-1 analogues to a maximum of 2 years. The selection of surgical technique didn't affect the response to GLP-1 analogues, nevertheless, not all studies provided enough data on various procedures." |
| | 23c | Discuss any limitations of the review processes used. | |
| | 23d | Discuss implications of the results for practice, policy, and future research. | Page 10, paragraph 4 "Our results of weight change, total weight loss percentage represents important conclusions about GLP-1 analogues that could inform clinical practice and guide future research."<br><br>Page 11, Paragrph 2 "In summary, despite bariatric surgery proving to be effective for most of the patients, enduring challenges with sustained weight loss, unfavourable weight evolution and comorbidity relapse are commonplace in clinical practice. Integrating promising medical interventions like GLP-1 analogues may offer enhanced outcomes regarding weight reduction and comorbidity resolution for patients exhibiting inadequate response to surgery alone in the future" |

| | | | |
|---|---|---|---|
| **OTHER INFORMATION** | | | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | Page 1 " None to declare". |
| Competing interests | 26 | Declare any competing interests of review authors. | Page 1 "None to declare". |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | Page 5, paragraph 1 "detailed characteristics of studies included in meta-analysis are shown in Table 1." |

*From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

**Submission Guidelines**

# OBESITY SURGERY - INSTRUCTIONS FOR AUTHORS

## Contents

## 1. ABOUT OBSU

Obesity Surgery is published by Springer Nature and is the official journal of the International Federation for the Surgery of Obesity and metabolic disorders (IFSO). Requirements are in accordance with the "Uniform Requirements for Manuscripts submitted to Biomedical Journals," www.icmje.org .

All manuscripts submitted to OBSU are blind-reviewed and decisioned through Editorial Manager (EM) http://www.editorialmanager.com/obsu . Letters to the Editor and Invited Letter Replies do not need to be blinded. Articles accepted for publication are done so with the understanding that they or their substantive contents have not been and will not be submitted to any other publication.

*Obesity Surgery* is a specialty journal, and the readership is well versed in the world statistics about the prevalence of obesity and metabolic/bariatric surgery, as well as other broad interdisciplinary topics. The Editorial Board, therefore, asks that submissions for publication adhere to what is new to be told. Focus the introduction and discussion of an article on the specific knowledge gap. Aim current studies toward sharpening reader attention to any new information provided. Brevity will also favor acceptance of a submission.

## 2. FILE SUBMISSION CHECKLIST

Before you begin your submission, make sure to have ready for upload all the file items described in the submission checklist below. Please use American English spelling. If any of the required file items listed below are missing, not correctly blinded, or otherwise incorrect, and/or if the English grammar is insufficient, your manuscript will be returned to you for correction.

For File Item descriptions, see section 4c., MANUSCRIPT SECTIONS AND FILE ITEM TYPES.

☑ **Title Page** (Word, RTF, TXT) **–** The complete title page is separate from the rest of the manuscript text. Any Keywords and non-blinded details should be placed in the Title Page.

If you are submitting a…

☑ **Text-based Manuscript** (Word, RTF, TXT), **include, as applicable:**

- Textual Abstract and 3 to 4 Key Points (different from Keywords, in bullet-point format)
- The complete manuscript text (must be blinded for review purposes – no author/affiliation details)
- Blinded statements for Conflict of Interest, Ethical/Board approval, and Informed Consent (as applicable)
- References in PubMed® style
- Optional: Embedded tables, schemes, figures, and captions
- Dynamic (supplementary) Video, if present, is not to exceed three (3) minutes in length; must be blinded and clearly narrated in English
- If present, video must be in either .MP4 or .MOV format.

If you are submitting a…

☑ **Video-based Manuscript** (Multimedia Article in MP4 or MOV)**, include:**

- Blinded Video Abstract and Key Points, as well as Ethical, COI, and Human/Animal Rights statements, and references
- Video not to exceed ten (10) minutes in length (blinded for review purposes)
- Narrated in English
- Video HD-ready in either .MP4 or .MOV file format, not to exceed 500 MB (website limit).

☑ **Figures/Images/Media** (JPG, EPS, TIFF)

- No identifying information about patients or logos unless permission specifically provided.
- Patient and/or publisher permissions (e.g., for images or logos, etc.), as applicable.

FOR REVISIONS ONLY:

☑ Revised/blinded text, tables, figures

- One clean copy (Word, RTF, TXT)

- One annotated copy

☑ A blinded, Point-by-Point Reply to Reviewer Comments (Word, RTF, TXT)

☑ Only required for Original Contributions and New Concepts: A blinded Graphical Abstract (Word, PPT, JPG, EPS, TIFF). This should be primarily graphic and consist of icons (not just text). You may use the Graphical Abstract template provided here and see example here. *(Note re: terminology - "Graphical Abstract" = "Visual Abstract")*

## 3. IMPORTANT SUBMISSION INFORMATION

### 3a. SYSTEM REQUIREMENTS

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### 3b. YOUR AUTHOR ACCOUNT

If you have previously accessed the system at http://www.edmgr.com/obsu/ *always use your existing account* for ALL subsequent submissions. If you have forgotten your Username or Password, use the “Send Login Details” link at the Login Page. Authors entering the journal's EM site for the first time can create a new account by clicking “Register Now.”

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After you log into your account and enter your Author Center, EM will lead you through a step-by-step submission process. Note: Always keep original copies of your manuscript files. The system will not allow you to complete your submission if any required submission fields are incomplete. If you cannot finish your submission in one visit, you may save a draft and later re-enter the process at the same step by clicking on the “Incomplete Submissions” link in your Author Main Menu.

We recommend that you have all items listed in the File Submission Checklist complete and ready for upload before starting your online submission. After uploading the files, the system will convert the files to PDF. Thoroughly review the PDF of your submission before confirming your submission. Note: documents that are not viewable to reviewers (cover letter, title page, etc.) may not appear in your PDF proof; simply make sure that they have been successfully uploaded in your list of uploaded files. After confirming that your submission is complete, click “Submit.” All contributing authors will receive an emailed confirmation. If the submission is not complete, inaccurate, or not fully blinded when the editorial office receives it, it will be returned to your Author Center, with an e-mail notifying you of what needs to be corrected.

Once your manuscript is correctly submitted, it will be assigned to an editor, and the review process will begin.

### 3d. SUPPORT AND ASSISTANCE

If you have questions or need assistance at any point during the

submission and review process, contact our OBSU Managing Editor: Attn: Deana Rodriguez, Managing Editor, OBSU Editorial Office Phone: +001 (562) 961-9928 E-mail: obsu.rodriguez@gmail.com

## 4. MANUSCRIPT PREPARATION

- Authors must use person-first language: e.g., "patients with obesity" rather than "obese patients."
- Double-space the text and set page borders at one inch.
- Number all pages.
- Use a normal, plain font (e.g., 12-point Times Roman) for text.
- Express all scientific units in SI units.
- Abbreviations may be used but must be spelled out the first time the term is mentioned.

### 4a. MANUSCRIPT TYPES AND FORMAT

The manuscript types that Obesity Surgery accepts include Original Contribution, New Concept, Review Article, Brief Communication, Letter to the Editor, and Multimedia Article. You may submit your manuscript following the format requirements detailed in the MANUSCRIPT FORMATS table below.

Each manuscript type requires specific submission format and file types. When required by the nature of the report, manuscripts that do not follow these formats may be considered. Please note that the page, word, and figure limits in the table below are a guideline rather than a rule; the editors and reviewers make the final evaluations. Please remain succinct in your wording.

## MANUSCRIPT FORMATS

The double-spaced page and word counts below are a guideline rather than a rule. Title Page, references, figures, legends, and tables are not considered in the page/word counts below. See section 4c below, ***MANUSCRIPT SECTIONS AND FILE ITEM TYPES***, for descriptions of each file item.

| MANUSCRIPT | Description | Pp/Words | Blinded Manuscript Text Contents | Figures |
|---|---|---|---|---|
| **Original Contribution** | Paper involves clinical or basic science research | 8pp/2400words | • Title<br>• Structured textual Abstract, includes subheadings (250 words)<br>• 3 to 4 one-line, bulleted Key Points (different from Keywords)<br>• Graphical Abstract (required upon revision)<br>• Introduction/Purpose<br>• Materials/ Methods/ Results/ Conclusion<br>• Blinded COI/Ethics/ Consent Statements required<br>• References<br>• Figure Legends (if any)<br>• Tables (if any)<br>• Supplementary video (if any) | Up to 6 |
| **New Concept** | Innovative technologies, devices, procedures, ortreatment protocols; should include a detailed description of the procedure and the results. | | | |
| **Review Article** | A scholarly literature review of a current topic. Maybe solicited or unsolicited. | 10pp/ 3000 words | • Title<br>• One-Paragraph textual Abstract (125 words)<br>• 3 to 4 one-line Key Points<br>• Graphical Abstract (optional, upon revision)<br>• Format may vary based on topic<br>• Blinded COI/Ethics/ Consent Statements required<br>• References<br>• Figure Legends (if any) | Up to 6 |
| **Brief Communication** | A short report that presents research, an innovatedconcept, or a procedure. | 3pp / 800 words | • Title<br>• No Textual Abstract, but<br>• Yes 3 to 4 one-line Key Points at beginning of text<br>• Graphical Abstract (optional, upon revision)<br>• Methods /Results/ Conclusion<br>• Blinded COI/Ethics/ Consent Statements required<br>• Limit references to eight (8)<br>• Figure Legends (if any) | Up to 2 |
| **Letter to the Editor** | A short report, case series, or opinion, or an unstructured comment on a published paper. The editors reserve the right to accept, reject or excerptletters without changing the views expressed by theauthor(s). | 4pp/ 1200 words | • Title page and main text do <u>not</u> need to be blinded.<br>• No Textual Abstract, No Graphical Abstract<br>• Unstructured<br>• COI/Ethics/ Consent Statements required<br>• Limited number of references | Up to 3 |

| MANUSCRIPT | Description | Pp/Words | Blinded Manuscript Content | Figures |
|---|---|---|---|---|
| **Multimedia Article** | Manuscripts submitted as dedicated Multimedia Articles must be accompanied by a text Abstract that briefly describes the video. | 2pp / 500 words | • Title<br>• No Graphical Abstract<br>• Blinded Text Abstract including Title, Key Points, Introduction, Materials/ Methods/ Results/ Conclusion/ Blinded Statements required, References (if any)<br>• Blinded video(s) in .mp4 or .mov format only; not to exceed 10 minutes/500 MB, with narration required, in English. | N/A |

## 4b. TERMINOLOGY

Please follow the mandatory manuscript terminology standards**.**

- Weight loss must be expressed as change in BMI or %total weight loss (%TWL)
- The term for the operative procedure that was previously labeled “Mini Gastric Bypass (MGB)” should no longer be used. Instead, use the accepted term “One Anastomosis GastricBypass (OAGB)”.
- Authors must use person-first language: e.g., "patients with obesity" or “patients with a BMIover 50 kg/m$^2$" rather than "obese patients.”
- We support uniform, defined reporting of the sex used for human, animal, tissue, and cellresearch in ALL manuscripts published in our journals. If only one sex is reported, authorsmust include a justification statement as to why only a single-sex study was conducted.
- Patient data extending beyond 30 days must include **“**lost to follow-up” information in the Abstract and Results section, including all tables and figures, with the denominator provided as to how many patients were available at **each time point** and the number of patients actuallyseen.
- Avoid using stigmatizing language (e.g., use the term "extreme" or "clinically severe" rather than “morbid”).

## 4c. MANUSCRIPT SECTIONS AND FILE ITEM TYPES

When you upload your manuscript documents to EM, the system will ask you to indicate each manuscript “File Item.” Your manuscript will be submitted in various parts. Your blinded “Manuscript” will be uploaded separately from the “Title Page.” Images may be submitted separately, as should any electronic supplementary material and videos (either as supplementarydynamic videos or a dedicated Multimedia Article file).

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In the "File Upload" step, submit your Title Page separately from the blinded text of the manuscript under the category, "Title Page." *Do not upload your Title Page as a PDF file.* This page will not be seen by reviewers and should include the following:

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b. Complete names, titles, departments, and institutional addresses of each contributingauthor (See ICMJE Guidelines for co-author qualifications), with an asterisk indicating the corresponding author.
c. "Correspondence to" followed by name and contact information for correspondingauthor. Only one author may be indicated as the corresponding author.
d. Equal Contribution: If any authors have contributed equally, you may include the following statement: “Authors (name) and (name) have contributed equally to thiswork.”
e. The main text Word Count (does not include references, figures/captions, or tables).
f. Any grant information and acknowledgment of grant support.

g. Acknowledgments*: Should only be included on this separate Title Page. List individualsother than authors who directly participated in the work. *Acknowledgment(s) require written permission from the person(s) being acknowledged. Any dedications should also be included here.
h. At least 3 Keywords.

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a. Include a note on the Title Page stating that the collaborators for the ‘’XYZ Group” are listed in the Acknowledgements.
b. Place your Acknowledgments paragraph, containing all authornames, at the bottom of the Title Page.
c. Affiliations are not mandatory for all collaborators, but affiliationsare preferred. If they are included, city/state/nation is required.
d. The Collaborator group must gather all author names &affiliations [if any].
e. Please double check all information to ensure names arecorrectly spelled.

II. File Item: Graphical Abstract (blinded, *required* at revision for Original Contributions andNew Concepts; *optional* for Reviews and Brief Communications)

*NOTE: The “Graphical Abstract” file will only be required if we request a revision of your manuscript.* It should be a selection of high-quality images or icons - a visual summary of theinformation provided in your textual Abstract. The use of color is encouraged. You may use the Graphical Abstract template provided here and view a completed example here. It must be submitted in Word, PPT, JPG, TIFF, or EPS format. *Do not upload your Graphical Abstract as a PDF file.* This Graphical Abstract may be used via IFSO/Obesity Surgery’s social media toprovide more visibility to your study, if it is accepted.

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III. File Item: Blinded Manuscript – Main Text (*required*; blinded for review)

The “Blinded Manuscript” file should include the Main Text, References, and FigureLegends (if any). Tables may also be included in this text document or submitted separately. *Do not upload your manuscript documents as PDF files.*

This “Blinded Manuscript” text document should be double-spaced and include thefollowing manuscript headings.

- Abstract* and Key Points**

a. *For Original Contributions and New Concepts:* Abstract must be structured in four paragraphs (Introduction/Methods/Results/Conclusion) and limited to 250 words. Three to four bulleted, one-sentence Key Points should be included at

the end of the Abstract text.

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- Blinded Conflict of Interest Disclosure Statement (see Section 5a. for details)
- Statements regarding ethics and consent. (see Section 5b. for details)
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***References***


1. Yoon DY, Mansukhani NA, Stubbs VC, Helenowski IB, Woodruff TK, Kibbe MR. Sex bias exists in basic science and translational surgical research. *Surgery.* 2014;156(3):508-516.
2. U.S. Government Accountability Office. National Institutes of Health: Better Oversight Needed to Help Ensure Continued Progress Including Women in Health Research. 2015
3. Mansukhani NA, Yoon DY, Teter KA, Stubbs VC, Helenowski IB, Woodruff TK, Kibbe MR. Determining If Sex Bias Exists in Human Surgical Clinical Research. JAMA Surg. 2016 Nov 1;151(11):1022-1030.
4. National Institutes of Health Office of Extramural Research. Consideration of Sex as a Biological Variable in NIH-funded Research.

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