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EDITORIAL

A False Dichotomy: Rethinking the Debate Around Pharmacotherapy vs Bariatric Metabolic Surgery in Obesity Treatment

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Dear Editor,

A common question posed nowadays is whether pharmacotherapy will supplant bariatric metabolic surgery. However, we contend that framing the issue as a dichotomy is not constructive, and we argue that this perspective is inconsistent with clinical practice in other medical domains. In this correspondence, we will discuss the reasons why the current debate should be reframed.

Firstly, bariatric metabolic surgery (BMS) has been performed for several decades, with a robust body of evidence supporting its long-term efficacy and durability in the management of obesity and associated comorbidities, extending over 50 years. Furthermore, the cost-effectiveness of bariatric surgery has been consistently demonstrated across multiple studies and validated in large-scale models and comprehensive meta-analyses [1, 2]. In contrast, pharmacotherapy is still in its early stages and has yet to withstand the test of time. The longest relevant study on pharmacotherapy spans only 160 weeks, and data beyond 5 years remain scarce. Therefore, it is premature and unhelpful to ask if pharmacotherapy will replace surgery.

Secondly, it is well-established that bariatric surgery exerts its effects through multiple mechanisms [3, 4]. Replacing all of these diverse mechanisms through cheap, well-tolerated pharmacological means will present a significant challenge. To use the peptic ulcer disease analogy, we are probably in the stages of the invention of early antacid treatment currently and a long way off the development of a proton pump inhibitor.

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In recent years, we have observed the widespread use of approved and commercially available glucagon-like peptide-1 receptor agonists (GLP-1 RAs), such as liraglutide and semaglutide, as well as the dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 RA tirzepatide, for the treatment of obesity and its metabolic sequelae. These agents have demonstrated weight loss ranging from 5 to 15%, along with significant reductions in cardiometabolic risks. The efficacy of these pharmacotherapies is supported by contemporary evidence derived from numerous studies, including the SCALE trial for liraglutide; STEP, SUSTAIN, and PIONEER for semaglutide; and SURMOUNT and SURPASS for tirzepatide [5].

While these new pharmacological treatments represent a significant advance in obesity management and are likely to remain integral in this field, it is crucial not to overlook their potential limitations. Current evidence suggests that patients using GLP-1 RAs should complete at least 12 weeks of continuous therapy to achieve clinically meaningful weight loss with corresponding health benefits [6]. However, real-world data indicate significant issues with short- and long-term medication adherence. One study reported that less than half of patients on GLP-1 therapies completed the recommended 12-week regimen [7], while another found that only one-third of patients prescribed GLP-1 remained on treatment 1 year after initiation [8]. Factors contributing to poor adherence include cost, insurance coverage, supply–demand discrepancies, and side effects. More to the point, the discontinuation of pharmacotherapy, as shown in the STEP 1 trial extension, was associated with the regain of two-thirds of the weight loss and the elimination of cardiometabolic benefits within 1 year [9]. Additionally, pharmacotherapy can induce side effects, some of which, though rare, may result in significant patient harm. There are also unresolved questions regarding the long-term safety of continuous GLP-1 receptor stimulation induced by pharmacotherapy, in contrast to the intermittent postprandial activation seen with bariatric surgery. Lastly, the long-term cost-effectiveness and the broader

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impact of these treatments on healthcare systems remain undetermined.

It is widely agreed that obesity is a chronic, multifactorial, and multistage disease. Accordingly, it necessitates a multifaceted approach for effective management, much like the paradigms used in cancer treatment. The significant improvements in the treatment and prognosis of cancers such as rectal, gastroesophageal, and breast cancers over the past two decades have not solely been the result of new drug discoveries that have replaced surgery but rather the synergistic application of multiple treatment modalities, including surgery, chemotherapy, radiation therapy, immunotherapy, and the personalization of treatment based on cancer stage and patient characteristics, all under the guidance of a specialized multidisciplinary team [10]. There is no reason why a similar approach should not be employed in the treatment of obesity. The history of medical science teaches us that our patients benefit most when we combine treatments for their synergistic benefits rather than pit one against the other.

We believe that new pharmacotherapies should be regarded as a valuable addition to the range of obesity treatment options, with new medications and bariatric surgery functioning synergistically rather than in competition. This integrated approach will enhance the therapeutic arsenal in the management of obesity and provide patients with a broader array of treatment options. Additionally, it may help to address some current challenges in BMS practice. For example, pharmacotherapy could be employed as a neoadjuvant treatment to induce weight loss and facilitate safer surgery in patients with high BMI, or as an adjuvant therapy in patients who do not achieve sufficient weight loss or experience weight regain, as shown in the systematic review by Schneider et al. [11]. Similarly, surgery could serve as an alternative option for patients who experience significant side effects from medications and those with poor compliance.

We advocate for shifting the current debate on pharmacotherapy and BMS from an either/or framework to one focused on how to best integrate both modalities to optimize outcomes for individuals living with obesity. Existing guidelines should be updated to incorporate both options into treatment algorithms.

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Data Availability No datasets were generated or analyzed during the current study.

Declarations

Competing Interests The authors declare no competing interests.

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