Literature Review: Trends in Obesity and the Effectiveness of GLP-1 Agonists

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Introduction

Obesity is a critical public health issue characterised by an excessive accumulation of body fat, which increases the risk of serious health conditions such as type 2 diabetes, cardiovascular diseases, and certain cancers. The World Health Organization (WHO) identifies obesity as a global epidemic, with prevalence rates tripling since 1975 and continuing to rise unabated (WHO, 2021). Currently, more than 1.9 billion adults are classified as overweight, of whom over 650 million are obese. This alarming trend extends beyond adults; childhood obesity has become a pressing concern, with 39 million children under the age of five classified as overweight or obese in 2020 (WHO, 2021).

In Europe, the situation is similarly dire, with nearly 60% of adults categorised as overweight or obese. Rates of childhood obesity have also shown a steady upward trajectory, particularly in southern and eastern European countries, where dietary patterns and economic transitions have contributed to worsening public health outcomes (Eurostat, 2023). A combination of sedentary lifestyles, high-calorie diets, and increasing urbanisation drives this epidemic. Furthermore, socioeconomic disparities exacerbate obesity rates, as lower-income populations often have limited access to healthy food options and physical activity opportunities (OECD, 2019).

Globally, the economic and healthcare implications of rising obesity are immense. Obesity-related health complications account for a significant proportion of healthcare expenditures, costing the global economy an estimated $2 trillion annually, or 2.8% of the world's GDP (McKinsey Global Institute, 2014). Projections indicate that without effective interventions, over 1 billion people will be living with obesity by 2030, with Europe and North America contributing significantly to this burden (World Obesity Federation, 2022).

This review will global and European trends in obesity prevalence, emphasising the socio-economic and healthcare implications of the epidemic. It will also evaluate the effectiveness of glucagon-like peptide-1 (GLP-1) receptor agonists as a promising pharmacological intervention and discuss future health outcomes and projections based on existing literature.

Global and European Trends in Obesity

Globally, the prevalence of obesity has escalated in both developed and developing regions. In 2016, over 1.9 billion adults were classified as overweight, of whom 650 million were obese (WHO, 2021).

The rise in obesity is not confined to adults; childhood obesity has emerged as a pressing concern, with 340 million children and adolescents categorized as overweight or obese.

In Europe, obesity affects approximately 23% of women and 20% of men, with the United Kingdom, Malta, and Hungary reporting some of the highest rates (Eurostat, 2023). Socioeconomic factors play a crucial role in this disparity. Lower-income groups often lack access to healthy food options and opportunities for physical activity (European Public Health Alliance, 2022). Additionally, cultural shifts towards sedentary behaviours and high-calorie diets exacerbate the problem.

Comparison of Obesity Trends: Europe vs. USA

The prevalence of obesity in Europe, though high, is notably lower than that in the United States. In the USA, adult obesity rates exceed 40%, with certain states reporting rates above 50% (CDC, 2023). This contrasts sharply with Europe, where adult obesity affects approximately 23% of women and 20% of men on average (Eurostat, 2023). The disparity can be attributed to differences in dietary habits, healthcare systems, urban planning, and socio-cultural attitudes towards physical activity. For example, the Mediterranean diet, prevalent in Southern Europe, is associated with lower obesity rates compared to the high consumption of ultra-processed foods in the USA (Rodríguez-Rejón et al., 2020). Moreover, European cities are often more walkable and bicycle-friendly, encouraging physical activity, whereas many urban areas in the USA are designed around car dependency. Despite these differences, obesity rates in Europe are rising rapidly, narrowing the gap with the USA, particularly in countries like the United Kingdom and Hungary, where rates approach American levels (OECD, 2019). Addressing this trend requires Europe to adopt proactive measures to prevent a further escalation of American obesity levels.

Health Implications of Obesity

Obesity is a major risk factor for non-communicable diseases (NCDs) such as cardiovascular diseases, type 2 diabetes, and certain cancers (Ng et al., 2014). The financial burden on healthcare systems is significant; for instance, the EU spends an estimated €70 billion annually on obesity-related healthcare and productivity losses (OECD, 2019). Beyond physical health, obesity also impacts mental well-being, contributing to stigma, low self-esteem, and depression.

Current Interventions for Obesity Management

Management of obesity involves a multifaceted approach that targets the underlying behavioural, physiological, and environmental factors contributing to excessive weight gain. Traditional methods such as dietary modifications and increased physical activity remain the cornerstone of obesity

management. These interventions emphasise calorie reduction, portion control, and the adoption of balanced, nutrient-rich diets, along with regular physical exercise tailored to the individual's needs and capabilities (WHO, 2021). However, long-term adherence to these strategies can be challenging, and many individuals experience weight regain after initial success.

For those who struggle to achieve or sustain weight loss through lifestyle changes alone, pharmacological interventions have become an increasingly important option. Medications approved for obesity treatment include orlistat, which reduces fat absorption in the intestine, and newer agents like glucagon-like peptide-1 (GLP-1) receptor agonists, which act on appetite regulation pathways in the brain (Astrup et al., 2014). These pharmacological therapies are particularly beneficial for individuals with obesity-related comorbidities such as type 2 diabetes or hypertension, offering both weight reduction and metabolic health improvements.

In severe cases, surgical interventions such as bariatric surgery provide a more definitive approach. Procedures like gastric bypass, sleeve gastrectomy, and adjustable gastric banding are highly effective in inducing significant and sustained weight loss, particularly for individuals with a body mass index (BMI) exceeding 40 or those with obesity-related complications (ASMBS, 2020). However, these surgeries are associated with risks, high costs, and the need for lifelong dietary adjustments and medical follow-up.

Emerging interventions, including digital health technologies like weight-loss apps, telehealth coaching, and wearable devices, are gaining traction in obesity management. These tools provide real-time feedback and personalized guidance, making it easier for individuals to monitor their progress and maintain motivation (Wharton et al., 2022). Despite advancements in treatment options, achieving widespread and equitable access to effective obesity interventions remains a significant challenge, particularly in lower-income populations or regions with limited healthcare infrastructure.

GLP-1 Agonists: Mechanism of Action

Glucagon-like peptide-1 (GLP-1) agonists, originally developed to manage type 2 diabetes, have become a promising pharmacological intervention for obesity treatment due to their ability to influence energy balance and weight regulation. These drugs mimic the action of the endogenous GLP-1 hormone, which is secreted by the intestines in response to food intake. GLP-1 receptors are present in several regions of the brain, including the hypothalamus, where they play a critical role in appetite regulation. By activating these receptors, GLP-1 agonists enhance feelings of satiety, reduce hunger, and suppress food cravings, ultimately leading to a reduction in caloric intake (Müller et al., 2018).

Additionally, they slow gastric emptying, prolonging the sensation of fullness and further aiding in appetite control.

The most commonly prescribed GLP-1 agonists for obesity include liraglutide (Saxenda) and semaglutide (Wegovy). Liraglutide, initially marketed as Victoza for diabetes, is administered through once-daily subcutaneous injections. Semaglutide, an advanced GLP-1 agonist, has a longer half-life, allowing for more convenient once-weekly subcutaneous injections. This improvement in delivery methods significantly enhances patient adherence compared to older agents requiring multiple daily doses (Wilding et al., 2021).

Effectiveness of GLP-1 Agonists

Recent clinical trials have demonstrated the efficacy of GLP-1 agonists in achieving substantial weight loss. For instance, the STEP trial showed that participants receiving semaglutide achieved an average weight reduction of 15% to 20% of their body weight over 68 weeks, far exceeding the results from traditional interventions such as diet and exercise alone (Wilding et al., 2021). Beyond weight loss, these medications offer additional metabolic benefits, including improvements in glycaemic control, reductions in blood pressure, and enhanced cardiovascular health, making them particularly effective for individuals with obesity-related comorbidities (Astrup et al., 2020).

Despite their proven efficacy, GLP-1 agonists are not without challenges. As they are typically administered via injection, this may deter some patients due to needle-related anxiety or discomfort. Researchers are exploring alternative drug delivery methods, such as oral formulations, to improve accessibility and adherence. Semaglutide, for example, is now available in an oral tablet form (Rybelsus) for diabetes management, and similar developments may soon be extended to obesity treatment (Lau et al., 2021). Such advancements could revolutionize the delivery of GLP-1 agonists, broadening their appeal and accessibility to a larger patient population.

Limitations and Challenges

Despite their proven efficacy in promoting significant weight loss and improving metabolic health, GLP-1 agonists face several challenges that may limit their widespread use. Cost and accessibility remain major barriers, with medications like semaglutide costing approximately €300 per month, making them prohibitively expensive for many individuals, particularly in lower-income populations (Pharmaceutical Journal, 2022). Additionally, side effects such as nausea, vomiting, and diarrhoea are common, potentially impacting patient adherence and satisfaction with treatment. Another significant

concern is long-term sustainability; while GLP-1 agonists are effective during active treatment, many patients experience weight regain after discontinuation, underscoring the need for long-term or adjunctive management strategies to maintain benefits (Rubino et al., 2022). Addressing these issues will be critical to maximizing the therapeutic potential of GLP-1 agonists in the fight against obesity.

Future Projections of Obesity Trends

If current trends persist, the global prevalence of obesity is expected to reach 1 billion people by 2030, with Europe contributing significantly to this burden (World Obesity Federation, 2022). However, increased adoption of pharmacological interventions, including GLP-1 agonists, could alter this trajectory. Projections suggest that widespread use of semaglutide could prevent up to 1.5 million cases of obesity-related diabetes in Europe over the next decade (Wharton et al., 2022).

Conclusion and Implications

The rise in obesity represents a complex interplay of biological, behavioural, and environmental factors. GLP-1 agonists offer a scientifically validated approach to weight management, particularly for individuals with obesity-related comorbidities. However, addressing obesity on a population level requires a multifaceted strategy that combines pharmacological treatments with policies promoting healthier lifestyles, improved food environments, and equitable access to healthcare.

Future research should focus on making GLP-1 agonists more accessible, minimising side effects, and understanding their long-term impact. Additionally, advancements in machine learning and data analytics could help identify high-risk populations and optimise treatment plans, ultimately mitigating the global burden of obesity.

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