Semaglutide and the future of obesity care in the UK

Fallows, Ellen; Ells, Louisa; Anand, Varun

The future of obesity care in the UK will partly be shaped by the National Institute for Health and Care Excellence (NICE) endorsement of semaglutide (Wegovy) to treat obesity in March, 2023.[1] Semaglutide joins another glucagon-like peptide 1 (GLP-1) receptor agonist liraglutide as an obesity treatment, together with behavioural interventions and bariatric surgery. Although semaglutide as an obesity treatment has been hailed as a game-changer,[2] the implications of this pharmaceutical focus in obesity management will unfold in UK general practice over the coming months. Lessons can be learnt from the USA, where semaglutide was licensed in 2021 and demand shortly outstripped supply and led to reduced availability of GLP-1 agents licensed for type 2 diabetes.[3] Wegovy also became a popular social media topic involving celebrities, leading Novo Nordisk to respond to criticism about inequitable access and unlicensed use of semaglutide.[4] An investigation by *The Guardian* highlighted similar risky prescribing in the UK, for example, to people with a healthy weight or with previous eating disorders.[5] There are major challenges for the effective, equitable, safe and sustainable use of these newer obesity medications in the UK.

The provision of weight management services in the UK is currently inadequate. Although NICE recommend that semaglutide is prescribed within tier 3 or tier 4 services (clinically commissioned multidisciplinary team approach), in 2015, only 13% of the 152 local authorities that were audited provided any tier 3 weight management services[6] and where provided the quality of these services varied considerably.[7] Even when services might exist, one study found that only half of primary care clinician respondents in a mock consultation would identify obesity, with under a quarter then offering referral for a weight management programme.[8] The COVID-19 pandemic resulted in cancellation of all bariatric surgery in the UK and 70% of weight management centres had reduced clinics.[9] As services continue to face pressures resulting from the impacts of the COVID-19 pandemic and despite accelerating rates of obesity,[10] UK weight management services have yet to be re-assessed. NHS England's National Obesity Audit,[11] commissioned in 2022 therefore comes at a crucial time.

Another challenge lies in recognising that inequities already exist in weight management for men, younger adults, minority ethnic groups and those living in socioeconomic deprivation.[12,13] The evidence from the main trials of GLP-1 receptor agonists for the treatment of obesity was

limited by a preponderance of female, white participants assessed over a short timeframe of 2 years.[14] This limitation is a particular concern given the chronic relapsing nature of obesity and how risk and prevalence of obesity can vary across different populations.[15]

Without good quality weight management support, there are risks of harms, treatment failure and relapse. Good quality care requires careful initial assessment, deprescribing around comorbid conditions, provision of behaviour and psychological support, together with review of dose and side-effects of the obesity medication. In the UK, semaglutide is not currently available on the NHS due to supply shortages but is available through online private services, offering what appear to be light-touch assessments with minimal follow-up.[5] Such prescribing carries risks given the deprescribing required after significant weight loss, for example, for comorbidities such as type 2 diabetes and hypertension. Medication down-titration can be complex, including severe risks of hypoglycaemia and hypotension.[16] Following deprescribing, weight regain after treatment requires monitoring for the relapse of these conditions.

If prescribed without adequate nutritional support, GLP-1 receptor agonists could theoretically increase the chance of relapse and the risk of malnutrition—issues that have yet to be studied in real-world settings. Clinicians typically do not have adequate nutrition and weight management training and may not be aware that obesity and malnutrition can co-exist.[17] Reducing the quantity of poor-quality foods consumed is not likely to reverse the underlying pathophysiology of obesity, which is thought to be related to the dysregulation of appetite due to inflammation in the hypothalamus potentially caused by food and other factors.[18] Therefore, failure to improve nutrition during treatment could worsen the sarcopenia, micronutrient deficiencies and microbiome effects of obesity.[19]

Alongside provision of adequate deprescribing and nutrition support, monitoring is required to assess for rare but serious potential adverse effects of semaglutide. Uncertainty remains over whether there is an increased risk of pancreatitis and pancreatic and thyroid cancers that have been reported with other GLP-1 agents.[20] Other safety issues include rapid glucose lowering which can precipitate retinopathy and an increased risk of biliary and renal disease.[19] Furthermore, the absence of long-term safety data for semaglutide requires vigilance in relation to these adverse effects and all-cause mortality, particularly given that people treated with GLP-1 receptor agonists have been found to have increased pulse rate, which has been independently associated with increased mortality. There are concerns around the gut microbiome effects of emulsifiers such as those used within the oral preparation of

semaglutide.[21] The gaps in provision of good quality care, including insufficient NHS weight management services and light-touch private prescribing, are likely to create additional caseload in already overwhelmed primary care, whose teams face skill and workforce challenges.

Many of the concerns around the need for equity in access to comprehensive weight management services and the safety and quality of care could be addressed if weight management centres were properly funded within community settings and led by experts in complex and longitudinal care, such as those in primary care. However, the feasibility of this approach will be hampered unless the declining GP workforce, increased workload and inadequate training in obesity management are addressed. There is some hope, with growing interest among clinicians to obtain additional qualifications in nutrition, weight management and behaviour change, with work by the Royal College of General Practitioners and the British Society of Lifestyle Medicine, among others, providing conferences and education on these topics. In the short term, at a minimum, training in obesity management and particularly nutrition needs to be provided for all primary care clinicians alongside assessments to monitor equity in access and care and use of weight management services across all populations in need. In the long-term, the clinical treatment of obesity as one of the root causes of many primary care presentations could reduce caseload.

Crucially, appetite suppressant medication must be considered as part of a whole systems approach.[22] Deprivation, poor quality ultra-processed foods, inadequate sleep, physical inactivity, stress, environmental pollutants and social isolation are all associated with brain inflammation disrupting our appetite regulation and driving the continuation of hunger signals despite abundance of food intake.[18] To maximise the long-term benefit of any obesity medication, it is imperative that the root causes and comorbidities of obesity are simultaneously addressed; this requires policy, public health and individual clinical work. The Novo Nordisk weight academy, provided to clinicians by semaglutide's manufacturers, highlights the roles of genes and the need for life-long medication in weight management.[23] However, this focus on medication at the expense of public health, risks an unsustainable and costly escalation of strategies between the food industry, profiting from foods that override our appetite regulation, and the pharmaceutical industry, profiting from drugs to help us regain weight control, a symbiosis that needs to be addressed under the commercial determinants of health lens. The arrival of these new medications must not distract us from the whole systems

response. Person-centred weight management interventions for patients need to be supported by policies that reduce the obesogenic factors in our environment to facilitate lifelong healthy weight and wellbeing.

EF provides paid consultancy work to Momenta LCD programme, a commercial company that provides evidence-based behaviour change as part of the NHS Type-2 Diabetes Remission Pilots, is Vice President of the British Society of Lifestyle Medicine, is a clinical adviser on obesity to the Royal College of General Practitioners and has attended meetings of the Obesity Management Collaborative in an advisory capacity without honoraria. LE reports funding from the NIHR, MRC, Leeds City Council, and Office of Health Improvement and Disparities, honoraria for PhD examinations and peer review from the Ministry of Health in Singapore, is an author on the ACTIONteens project and teaches at the EASO summer school but does not receive any funding for these roles. VA reports an NHSE PCN bursary for a Type 2 Diabetes remission project, was a health assessments GP for BUPA, has a GP Fellowship with the Hull Public Health Team working on a weight management project and is a Physical Activity Clinical Champion for Yorkshire and Humber.

**Ellen Fallows, Louisa Ells, Varun Anand*

ellenfallows@nhs.net

Brackley Medical Centre, Brackley NN13 6QZ, UK (EF); The British Society of Lifestyle Medicine, Haddington, East Lothian, UK (EF); Obesity Institute, School of Health, Leeds Beckett University, Leeds, UK (LE); Diadem Medical Practice and Hull Public Health Team, Hull, UK (VA)

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