

A public health perspective on new weight loss medications

New agents are not the answer to obesity

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Since the 1980s, most countries have seen substantial rises in the prevalence of obesity. Effective, acceptable treatments are much needed and the GLP-1 agonists (semaglutide and tirzepatide) that work by suppressing appetite may appear at first glance to fulfil that need.[1,2] In one key trial, semaglutide plus a 'lifestyle' intervention for adults (74% female) with obesity (mean BMI 37.9 kg/m²) led to 12.7kg (95% CI: 11.7-13.7) more weight loss than the lifestyle intervention alone (15.3kg v 2.6kg; results by sex not reported). Whilst still insufficient to achieve a healthy weight for most study participants, this weight loss was substantially greater than that associated with other pharmaceutical and behavioural options.[2-4]

They appear to be increasingly popular despite a lack of long-term data on safety. Emerging reported serious adverse effects include pancreatitis, bowel obstruction, gastroparesis, pulmonary aspiration during anaesthesia, suicidal ideation and self-harm – but warrant further investigation (no differences in side effects are reported by sex, although use appears to be higher amongst women).[5] For many people living with obesity and a high risk of co-morbidities, the benefits will likely outweigh risks, at least in the short term. But will the new weightloss medications work from a public health perspective?

First, relatively few people are likely to benefit. In the UK, NICE recommends semaglutide for adults with a BMI \geq 35 kg/m² and co-morbidities (with a lower threshold for some ethnic groups) for a maximum of two years and only within specialist multi-disciplinary weight management services.[6] NICE has not appraised tirzepatide, although the MHRA has authorised its use for weight loss.[7] An estimated 4 million adults (around 30% of those with obesity) in the UK have a BMI \geq 35 kg/m² and may be eligible.[8,9] However, access to specialist multi-disciplinary weight management services is very limited, so the numbers able and willing to access treatment will be much less, particularly in the short-

term. New models of delivery, for example through primary care[10], and changing thresholds for prescription (subject to emerging understanding of risks and benefits), may increase access. Moreover, any benefits may be short-lived, stopping medication will result in weight re-gain (differences not reported by sex),[11] and it is unclear what services people will be offered after two years of treatment.

Second, where do these medications sit alongside other treatments and what are the resource implications? The new medications fill a gap, offering something more effective than widely available community (non specialist) weight management services, but less effective and invasive than bariatric surgery which is restricted to adults with severe obesity.

More challenging is the direct cost of these agents and the associated opportunity cost of diverting resources away from other options. Based on the current list price, the annual cost of treatment would be £2,275 per person (the actual cost paid by the NHS is confidential, protected by commercial agreements), plus additional costs for healthcare practitioner time, as well as diet and activity support.[6] Paying for large numbers of adults to use these drugs risks using a significant proportion of overall NHS resources.

Semaglutide also appears less cost-effective than other weight loss options. NICE estimates that semaglutide costs £16,400 per QALY,[6] compared to £10,126 per QALY for bariatric surgery and £557 per QALY for community weight management.[12] Other cheap and highly effective medications (statins, anti-hypertensives for example) are available that reduce the cardio-metabolic risk associated with obesity. There needs to be careful consideration of what proportion of scarce NHS funds and healthcare practitioner time should be used to support GLP-1 agonists.

Third, a public health perspective considers the impact on health inequalities. Healthcare interventions, particularly new and expensive interventions, tend to be accessed disproportionately by people with greater financial and social resources.[13] NICE guidance only applies to the NHS, but private sector prescribing of weight loss medications is growing and has contributed to shortages of semaglutide for the treatment of diabetes.[14,15] This is both harmful to patients and inefficient, failing to use scarce medications to help those with the greatest capacity for benefit, as well as widening health inequalities.

Supply constraints may be short-term. However, given the need for intensive follow-up as well as engagement with diet and physical activity programmes, it is likely that people with more resources

will always find it easier to navigate these systems and benefit from the new medications. Uptake of weight loss medications stratified by socio-economic status should be monitored and care systems designed to ensure equitable access.

Finally, the 'medical approach' to disease prevention – offering preventive medications to those above an arbitrary risk threshold – has major limitations.[16] Much of the health risk associated with excess weight at a population level accrues to the very large number of people living with overweight or class I obesity (BMI: 30-34.9kg/m²), who will largely remain ineligible for weightloss medications. A public health approach instead addresses underlying environmental causes of poor diet and sedentary behaviours. Unfortunately, the UK Government has repeatedly failed to control the sale and marketing of unhealthy food, including missing its own targets, ignoring high profile reports, and watering down its own policies.[17,18] National policy makers must do more, but the NHS, schools, and local authorities can also take action to tackle underlying causes of excess weight.[18]

The new weight loss medications, whilst an important addition to the armoury, must not be allowed to divert attention or resources from a broad holistic approach both to prevention and support for individuals. These agents will likely have an impact relatively quickly in a small subset of the population with obesity. The bigger question is at what cost – both in direct monetary terms and in opportunities forgone.

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