International coverage of GLP-1 receptor agonists: a review and ethical analysis of discordant approaches

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Introduction

Obesity can substantially diminish people's lifespan and quality of life. Severe obesity can shorten younger adults' lifespan by around 10 years compared with those with healthy weight.[1] Even moderate obesity is associated with truncated life expectancy. Moreover, health-related quality of life decreases as BMI increases.[2] Beyond these health effects, by 2035, the global financial burden associated with obesity is expected to exceed US$4·3 trillion annually.[3]

Glucagon-like peptide-1 (GLP-1) receptor agonists such as semaglutide and dual GLP-1 and glucose-dependent insulinotropic polypeptide receptor agonists such as tirzepatide could curb both the health and economic effects of obesity. In clinical trials, these receptor agonists reduce average bodyweight by approximately 15%—two to three times more than alternative medications.[4] GLP-1 receptor agonists have also been shown to be cardioprotective, reducing the risk of major adverse cardiovascular events by 20% compared with placebo for people with overweight or obesity.[5]

Because of the high unit price and total expense of these medications, countries are now deliberating on whether and how to cover them as treatments for obesity. We critically analyse GLP-1 receptor agonist coverage policies in 13 high-income countries on four continents and evaluate their justifications to draw practical, policy-relevant lessons to inform policy development.

Comparing policies on the coverage and pricing of GLP-1 receptor agonist drugs

We reviewed policies in high-income countries, because they are the most likely to cover these costly drugs through public health insurance systems. In selecting among high-income countries, we had four criteria. First, we tried to have geographical breadth, including countries in North America, Europe, Asia, and Oceania. Second, we strove to include different types of health systems, such as national health-care systems, competing payers or sickness funds, and free market systems. Third, we looked for diverse drug coverage and evaluation systems, with different countries incorporating cost-effectiveness analysis, comparative effectiveness evaluation, government price negotiations, and private pharmacy benefit management. Finally, we only included countries with publicly available data that we considered reliable.

National policies regarding coverage and price of GLP-1 receptor agonists are delineated in the appendix (pp 2–5). All 13 countries analysed (Australia, Belgium, Canada, Denmark, Finland, France, Germany, Iceland, Italy, Israel, Japan, the UK, and the USA) reimburse semaglutide (eg, Ozempic, Novo Nordisk) or another similar GLP-1 receptor agonist for at least some individuals with type 2 diabetes. Nine of the 13 countries fully deny reimbursement of GLP-1 receptor agonists for weight management, including Australia, Belgium, Denmark, Finland, Germany, Italy, and Israel. Canada and the USA do not have nationwide coverage of GLP-1 receptor agonists on public plans, although regional plans in these countries vary. For example, nine US state Medicaid plans cover GLP-1 receptor agonists for weight management in some capacity.[6]

Four of the 13 surveyed countries provide qualified national coverage for GLP-1 receptor agonists for weight management: France, Iceland, Japan, and the UK. Each of these countries has different conditions for coverage, restricting the eligible population (appendix p 2). The USA, the UK, and the European Medicines Agency have also allowed a new indication for Wegovy (Novo Nordisk) to treat patients with cardiovascular disease This indication creates new avenues for coverage in the USA and Europe, but does not yet constitute reimbursement expansion. Even if coverage is expanded under Wegovy's new cardiovascular indication, access would remain restricted, as recent analyses[7] have found that the vast majority of US patients on Medicare with overweight or obesity would remain ineligible.

Reported prices for Wegovy, the weight management formulation of semaglutide, can vary nearly 5-fold, from approximately $283 in Japan to $1349 in the USA for a 4-week supply (appendix p 5). Marginal manufacturing costs have been reported as being under $5.[8]

Why many countries deny reimbursement

Reasons for rejecting coverage of GLP-1 drugs for obesity vary. For example, similarly to the US Medicare law, German law excludes weight management medications from publicly funded reimbursement. More commonly, countries deny coverage of GLP-1 drugs for reasons related to cost. Total cost, irrespective of effectiveness, has been both an explicit justification, as in the recommendation by the Canadian Agency for Drugs and Technologies in Health, and a tacit worry for policy makers. In 2023, German politicians refused to consider changing their laws to allow reimbursement. One lawmaker anonymously cited concerns about the cost for an already over-stretched health budget.[9] Similarly, in remarks made to Parliament, the Danish Health Ministry claimed that the cost of covering Wegovy for their population with obesity would exceed $4 billion annually.[10] Following that comment, the Danish Parliament again

See Online for appendix

refused coverage. Dutch health authorities have also rejected coverage for Wegovy for weight management, citing concerns about the total cost, $1·42 billion, of reimbursement for the eligible population.[11]

Cost-effectiveness analyses have often been cited as a reason to deny coverage for GLP-1 receptor agonists for weight management. For example, in 2023, Australia's Pharmaceutical Benefits Advisory Committee explained its decision not to cover Wegovy by referencing insufficient cost-effectiveness.[12] Similarly, in 2023, Danish health officials found Wegovy's price excessive given its therapeutic value.[13]

How some countries permit reimbursement

Countries permitting reimbursement have combined this permission with policies to limit eligibility. The first eligibility criterion is the potential for medical benefit, defined by BMI and medically relevant comorbidities. All four countries offering coverage use these metrics, making GLP-1 receptor agonists available to individuals with a BMI higher than a specified value and individuals with slightly lower BMIs who have related comorbidities (appendix p 2). For example, France provides coverage for some patients with a BMI greater than 35 kg/m², whereas Iceland covers patients with a BMI greater than 45 kg/m² or those with a BMI greater than 35 kg/m² and a severe comorbidity (eg, coronary artery disease or kidney disease).

The second criterion is combining drugs with supportive care, including counselling for diet and exercise. Regular coordinated care improves medication adherence. Adherence is especially important with GLP-1 receptor agonists, which appear to have high rates of attrition in comparison with other medications for chronic conditions.[14] National Health Service guidelines in the UK mandate diet and exercise counselling for any individual on anti-obesity medication. In accordance with these recommendations, only obesity specialists at weight management clinics—which are equipped to counsel patients—can prescribe GLP-1 receptor agonists. Although this multidisciplinary support might improve medication adherence, it also effectively limits access to prescriptions as space at specialty clinics is scarce.

The third criterion of eligibility is age. For instance, French health authorities allow coverage only for people younger than 65 years. This restriction preserves reimbursement funds for younger people with obesity, who are at risk of premature death without the intervention and probably have more years of life to gain from it.[15]

A final criterion of eligibility is established individual efficacy. Iceland requires that adults show at least a 5% reduction in bodyweight at 6 months of treatment, a 10% reduction at 12 months of treatment, and a 15% reduction at 18 months of treatment for continued coverage. This requirement prioritises reimbursement for people who are responding to the medication.

Four lessons to guide future policies for coverage of GLP-1 drugs

Use up-to-date cost-effectiveness analysis

Coverage decisions must reflect up-to-date cost-effectiveness analyses. Cost-effectiveness is an essential tool for designing drug formularies and responsibly stewarding scarce public funds. Many countries used out-of-date cost-effectiveness analyses in their decision making, however, which did not incorporate evolving data on the clinical benefits of GLP-1 receptor agonists. Many of the cost-effectiveness analyses that informed policy decisions were conducted in 2022, after Wegovy was initially approved in the USA and the UK but before new and relevant studies were completed. For drugs whose benefits are well understood and unlikely to change, analyses from 2022 would still be accurate, but substantial analysis-altering data on semaglutide have been published since then.

More recent analyses from 2023 and 2024 have shown greater cost-effectiveness than older analyses from 2022 (appendix p 6), probably due to new evidence of the cardiovascular and renal benefits of GLP-1 receptor agonists. For example, the SELECT trial,[5] which showed the cardioprotective benefit of semaglutide, was published in November, 2023, and resulted in new indications in several countries (appendix p 2) for reducing major adverse cardiovascular events in adults with overweight and obesity.[16] Cost-effectiveness analyses completed just 2 years ago were unable to include these data and their effects on expected quality-adjusted life-years.

The updated cost-effectiveness of GLP-1 receptor agonists is better than for many other drugs on formularies in the countries that do not currently cover GLP-1 receptor agonist drugs.[17] Moreover, because obesity is a chronic condition with long-term health effects, life-preserving and life-extending benefits from long-term use appear probable and would alter the results of cost-effectiveness analysis. But long-term health benefits cannot yet be proven in clinical trials for this young class of drugs. Australia's coverage decision recognised this limitation, stating that "only short-term weight loss benefits were modelled".[12]

Given the rapidly emerging data about the increased benefits of GLP-1 receptor agonists (such as for neurological conditions),[18] geographical and temporal variability in cost, and the dearth of long-term use data, cost-effectiveness information must be regularly re-evaluated. Eligibility criteria should incorporate current cost-effectiveness analysis and be appropriately revised in light of new results.

Lower prices while preserving long-term innovation incentives

Cost-effectiveness also depends on drug prices, which are the result of country–company negotiations. The low marginal production costs and substantial benefits of GLP-1 receptor agonists compared with older weight

management drugs means that both drug manufacturers and national health plans will be better off if patients receive GLP-1 receptor agonists at a discounted price rather than resorting to older drugs. The price of GLP-1 receptor agonists for weight management varies widely across countries (appendix p 5), which indicates that costs are negotiable.

Negotiations, however, must not only consider current prices but long-term incentives for drug development. Some commentators argue for paying little more than the marginal cost of production for GLP-1 receptor agonists—for instance, by allowing immediate generic competition.[8] But adopting price reduction efforts for GLP-1 receptor agonists that do not consider incentive effects, while preserving the status quo patent and pricing regime for most other drugs, creates perverse and counterproductive incentives. Manufacturers would be financially better compensated for drugs with poorer cost-effectiveness but lower total costs than for more effective therapies such as GLP-1 receptor agonists with better cost-effectiveness but high total costs. Identifying the price that best balances lowering short-term costs against creating desirable and sustainable long-term incentives remains a challenging task. Countries will be tempted to set reimbursements at levels that free-ride on the incentives that other buyers generate, whereas manufacturers will be tempted to exaggerate the long-term harms of lower prices.

The low marginal production cost makes access to GLP-1 receptor agonists an appealing context in which to negotiate subscription or other alternative payment models, such as price–volume agreements or expenditure caps,[19] rather than paying per dose. A subscription model provides large payments to companies in exchange for a nearly unlimited supply of drugs to treat an entire eligible population. Negotiation of a subscription price between countries and drugmakers incentivises both sides to arrive at a price that covers more people with obesity at a reasonable total cost, meeting countries' needs, while providing sufficient profits for companies to incentivise future research.

Although their use is best known with cures such as hepatitis C antivirals, subscription models have also been proposed for chronic disease management. One research team observes that treatments "that could benefit from subscription agreements must be part of a recurring treatment regimen and have a low marginal cost of production", and identifies diabetes medications as strong candidates.[20] Other teams propose subscription agreements for HIV pre-exposure prophylaxis, which must be taken indefinitely.[21] The UK tried a subscription-type model for the cardiovascular disease management drug inclisiran[22] but faced prescriber discomfort, an issue unlikely to arise for GLP-1 receptor agonists because they are already widely prescribed.

Set priorities rather than issuing blanket denials

In high-income countries, blanket denial of coverage for these life-saving drugs is the wrong approach. Rather, individuals who could benefit the most from restricted coverage should be prioritised for coverage.[23] Even after negotiations, the total cost might remain too high to reimburse an expensive drug for a country's whole population. But the inability to cover all patients is no reason to categorically deny coverage to every person with obesity. Instead, governments should identify groups of people with the strongest claims to coverage, such as younger people or those most acutely affected by obesity.[23] Some countries have already adopted frameworks based on individuals' severity of obesity (appendix p 2). Total cost constraints ought to be considered as an issue of fair allocation. Policy makers must decide which people to prioritise when budget constraints preclude covering everyone who might stand to benefit.

Together, the four criteria used in the countries that reimburse GLP-1 receptor agonists for obesity present an ethically compelling approach to setting priorities. Considering factors predictive of medical benefit, such as BMI and comorbidities, ensures that the drugs are provided to people who stand to gain the most from the treatment. The same is true for considering individual histories of efficacy. These metrics can be scaled for different countries and plans, allowing coverage to respond to population needs and financial capacities.

Considering age, meanwhile, prioritises people at risk of being supremely disadvantaged by early death.[23] This consideration is also likely to produce a greater benefit by averting potential years of life lost and preventing the development of comorbidities. By contrast, universally refusing reimbursement leads to people purchasing medicines privately, which creates an effective allocation system based on people's ability to pay.[23] Ability-to-pay allocation is appropriate for dubiously effective or discretionary medications, but inappropriate for a medication that treats a severe condition such as obesity, the effects of which track societal disparities. In the USA, which largely uses ability-to-pay allocation for GLP-1 receptor agonists, GLP-1 receptor agonist usage is currently concentrated not in the areas with the most obesity, but in neighbourhoods with the highest average income.[24] This allocation is not ethical.

Treat high-cost obesity drugs in the same way as high-cost drugs for other conditions

All 13 countries reviewed cover treatment with GLP-1 receptor agonists such as Ozempic for type 2 diabetes despite the high cost and the availability of very effective alternative treatments, such as SGLT2 inhibitors.[25] French health authorities judged that Ozempic had no added clinical value in comparison with existing drugs, but still chose to reimburse it for people with uncontrolled type 2 diabetes (appendix p 2). Despite the robust set of effective alternative drugs, scarce funds are being used to grant access to GLP-1 receptor agonists for people with

diabetes, albeit with management restrictions such as step therapy in some countries. Conversely, GLP-1 receptor agonists are clearly the superior, cost-effective drugs for treating obesity, yet coverage is prohibited or severely restricted.[23]

Three differences between the use of GLP-1 receptor agonists for diabetes and the use of the same drugs for obesity could explain these differences in coverage policies. The first difference is the time the drugs have been on the market. Ozempic and similar drugs used for obesity were released as a treatment for diabetes several years before the weight management formulations were developed and approved. The second difference is that these drugs were initially developed to treat diabetes rather than obesity. Perhaps latent bias against people with obesity is motivating the scarce coverage. People who consider obesity a consequence of personal choices might be unwilling to use public funds to reimburse a costly medication, even if costly medications are covered for other conditions that result from personal choices, including some cancers and cardiovascular conditions. The third difference is that many more people have obesity than diabetes, making the budgetary effect of anti-obesity drugs much higher than that of drugs for diabetes.

None of these differences, however, justifies categorically rejecting reimbursement for GLP-1 receptor agonists used to treat obesity while universally permitting their reimbursement for diabetes. Countries ought to adopt fair policies to address drug coverage and pricing, regardless of the drugs' novelty or the condition they treat. Excluding new medications simply for their novelty fails to maximise their potential benefit. Excluding new medications because they treat a so-called lifestyle disease fails to maintain a standard of equal moral concern.[23]

Conclusion

Countries with experience of navigating GLP-1 receptor agonist coverage decisions for people with obesity offer lessons for others now facing similar decisions or reconsidering their existing policies. Blanket refusals of coverage remain common both at national and subnational levels, which is unethical. Countries should treat cost limitations similarly to supply shortages:[23] they should deploy policies that carefully prioritise specific populations rather than totally deny coverage. Universal coverage denials fail to maximise the potential benefits of a life-saving drug, worsen inequality, and show unequal moral concern for potential beneficiaries who could gain greatly. By contrast, an ethical approach would draw on insights from the countries that have offered coverage to at least some patients. By setting priorities, health plans can marshal their resources to benefit the patients for whom treatment would make the biggest difference.

Contributors

JLD conducted the research and wrote the initial draft of this Viewpoint. GP and EJE reviewed and substantially edited the manuscript and tables in the appendix.

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