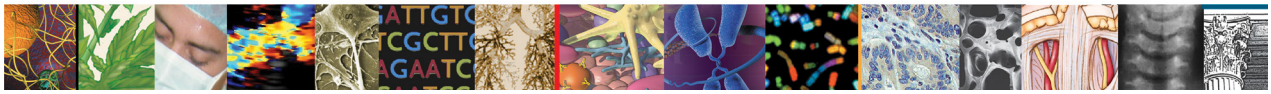

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Perspective

Fair Allocation of GLP-1 and Dual GLP-1–GIP Receptor Agonists

Ezekiel J. Emanuel, Ph.D., Johan L. Dellgren, B.A., Matthew S. McCoy, Ph.D., and Govind Persad, J.D., Ph.D.

The percentage of U.S. adults with overweight or obesity now exceeds 70%, and more than 10% of adults have type 2 diabetes. These people are at increased risk for heart disease, stroke, cancer, and premature death. Glucagon-like peptide-1 (GLP-1) receptor agonists, such as semaglutide, and dual GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptor agonists, such as tirzepatide, have been found to be effective for treating obesity and diabetes, significantly reducing weight and the risk or predicted risk of adverse cardiovascular events. There is a global shortage of these medications that could last several years and raises questions about how limited supplies should be allocated.

Belgium, Britain, and other countries have banned or discouraged use of GLP-1 receptor agonists for weight loss to prioritize use for diabetes. No U.S. state or federal agency has released similar guidance, although some health plans have restricted use for obesity, and Medicare doesn't cover these or other drugs for weight loss. Consequently, in the United States, allocation of these drugs has been largely on a first-come, first-served basis and has often depended on people's ability to pay, which has produced racial, ethnic, and socioeconomic inequities.[1]

We propose a fair-allocation framework that enables evaluation of the ethics of current practices and could guide governments, professional societies, and physicians in allocation decisions. This framework focuses on allocation within countries, although fair allocation among countries also requires ethical analysis.[2]

Fair allocation of scarce medical resources rests on four values: benefiting people and preventing or reducing harm, acting with equal moral concern, prioritizing disadvantaged people, and rewarding social contribution (see Table 1).[2] Benefiting people and limiting harm, including keeping more people alive and averting years of life lost, are essential objectives of any allocation framework.[2] Fair allocation also requires equal moral concern for all people, regardless of race, sex, or religion. To prioritize disadvantaged people, special consideration should be given to those who would be worst off without the intervention, particularly young people at risk for premature death.[2] Prioritizing people at risk for premature death aligns with the value of equal moral concern because time alive isn't an immutable or identity-defining characteristic. Time alive is a good to which all people have equal claim, and young patients have had less time alive than older people.[2] Because health and social disparities can lead to earlier onset of severe disease, a focus on preventing premature death may also miti-

Table 1. Fundamental Ethical Values Informing Fair Allocation of Scarce Medical Resources.*

Value	Explanation
Benefiting people and preventing or reducing harm	Maximizes the benefits of an intervention; measured in lives saved or in years of life saved
Equal moral concern	Recognizes equal moral importance of each person, irrespective of factors such as race, sex, religion, and income
Prioritizing disadvantaged people	Prioritizes people who would be worst off without the intervention, such as those who would otherwise be at risk for having a short life or for severe illness
Rewarding social contribution	Prioritizes specific people because they have promoted or will in the future promote other important values, such as maximizing health benefits, by means of their work or other efforts

* Adapted from Emanuel and Persad.[2]

gate other forms of disadvantage. Rewarding social contribution is most relevant in public health emergencies during which clinicians accept risks for other people's benefit — such as when allocating infectious disease countermeasures — and doesn't apply in this clinical context.

To maximize the benefits of scarce GLP-1 receptor agonists and dual GLP-1–GIP receptor agonists while prioritizing disadvantaged people, the primary aim should be to reduce potential years of life lost (PYLL) from obesity and type 2 diabetes. The PYLL metric incorporates a person's illness severity and age. Minimizing PYLL involves prioritizing younger people who are ill, who will have more potential years of life if their health improves. PYLL is calculated using a population-wide benchmark for life expectancy; it doesn't depend on an individual patient's life expectancy. Its use therefore aligns with the principle of equal moral concern because no person is penalized on the basis of race, income, or life-shortening disadvantages, such as other chronic illness.

Secondary consideration should be given to preventing harm associated with medical complications of obesity and diabetes. Tertiary consideration should be given to improving quality of life for people with more moderate disease. People using medications for primarily cosmetic reasons should receive no priority.

Tier 1 in the proposed framework includes patients with class III obesity (body-mass index [BMI; the weight in kilograms divided by the square of the height in meters], ≥40.0) and those with severe, uncontrolled type 2 diabetes (glycated hemoglobin level, >8%) whose disease hasn't responded to alternative drugs, such as sodium–glucose cotransporter 2 (SGLT2) inhibitors (see Table 2). Tier 2 includes patients with class II obesity (BMI, 35.0 to 39.9), followed by those with severe, uncontrolled diabetes who haven't tried SGLT2 inhibitors or similar drugs. Tier 3 comprises patients with class I obesity (BMI, 30.0 to 34.9), followed by those with diabetes (glycated hemoglobin level, >7%) who have tried alternative diabetes-management drugs. Finally, tier 4 includes people with overweight and other people with diabetes. Within each severity tier, younger patients are prioritized because of the distinctive risk of premature death they face.[3]

BMI is an imperfect measure of obesity's metabolic consequences. Nevertheless, no preferable population-level measure of body fat has been identified. BMI classifications are routinely used in public health and clinical practice and remain an important tool for initial diagnosis of obesity and prediction of the development of other medical complications, including prediction of premature death. Assessment should, however, recognize that some people have a higher risk of diabetes at a lower BMI than others because of increased visceral fat, as reflected in clinical guidelines. Similarly, glycated hemoglobin levels are used to diagnose and monitor treatment of type 2 diabetes. Disease-management recommendations inform cutoffs for prioritizing access to treatment.

Although both obesity and diabetes increase the risk of premature death, the higher priority, outside tier 1, should be to treat patients with severe obesity with GLP-1 or dual GLP-1–GIP receptor agonists, for two reasons. First, avoiding the initial development of type 2 diabetes can prevent its long-term, life-shortening effect.[3] A primary factor driving increas-

Table 2. Fair-Allocation Framework for GLP-1 and Dual GLP-1–GIP Receptor Agonists.*

Tier	Objective	Distribution Criteria
1	Minimize potential years of life lost by preventing excess and premature death	People with class III obesity (BMI, ≥40) and people with severe type 2 diabetes (glycated hemoglobin level, >8%) whose disease hasn't responded to alternative treatment Phase 1: younger patients (e.g., <50 yr of age) Phase 2: older patients
2	Prevent imminent medical complications, such as cardiovascular events	People with class II obesity (BMI, 35.0–39.9), followed by people with severe type 2 diabetes (glycated hemoglobin level, >8%) Phase 1: younger patients Phase 2: older patients
3	Prevent future medical complications, such as cardiovascular events	People with class I obesity (BMI, 30.0–34.9), followed by people with type 2 diabetes (glycated hemoglobin level, >7%) whose disease hasn't responded to alternative treatment Phase 1: younger patients Phase 2: older patients
4	Improve quality of life and social and emotional health	People with overweight (BMI, 25.0–29.9) or type 2 diabetes (glycated hemoglobin level, >7%) who aren't eligible under another tier Phase 1: younger patients Phase 2: older patients

* The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters. GIP denotes glucose-dependent insulinotropic polypeptide, and GLP-1 glucagon-like peptide 1.

es in diabetes, especially among younger people, is rising obesity prevalence.[3] Treating patients with obesity can mitigate the harms associated with long-term obesity while also preventing or delaying the onset of diabetes.

Second, prioritizing obesity is justified because other diabetes treatments may be as effective as GLP-1 or dual GLP-1–GIP receptor agonists — or more effective — depending on the outcome being assessed. SGLT2 inhibitors are three times as effective as GLP-1 receptor agonists in reducing hospitalizations for heart failure in people with diabetes.[4] The argument for using SGLT2 inhibitors before GLP-1 receptor agonists doesn't apply to tier 1 of the proposed framework, which includes patients whose disease didn't respond to SGLT2 inhibitors. Both GLP-1 receptor agonists and SGLT2 inhibitors are associated with clinically significant weight loss.[5] Approved pharmacologic alternatives for obesity, meanwhile, produce substantially smaller weight reductions than GLP-1 and dual GLP-1–GIP receptor agonists.

Finally, under conditions of scarcity, a patient's preferences for oral over injectable formulations should not influence which drug a patient receives. Severe shortages of life-saving drugs mean that patients should receive whatever formulation is available.

Whether to prioritize current users of GLP-1 and dual GLP-1–GIP receptor agonists is an important question. Policies in Belgium and other countries don't prioritize current recipients of GLP-1 receptor agonists, who may be taken off the drugs. Because distribution of these medications has been unfair, reallocation may seem ethical, but there are strong reasons to reallocate the drugs sparingly.

First, many people stop taking these medications after only a short period of use. People who tolerate them for more than 12 months may continue to use them and benefit, although long-term data aren't available. Second, clinically significant weight loss generally occurs only after 2 to 3 months of use. This wait for new patients to benefit would waste a drug in critical shortage. Finally, taking people off these medications may harm them. People tend to regain weight after medication cessation. Although the effects of weight fluctuation after discontinuation of such medications are unknown, weight fluctuations in general are associated with increased cardiovascular and all-cause mortality. Consequently, during a temporary shortage, a fair-allocation framework supports a presumption that current users should maintain access. This presumption, however, can be rebutted. People without obesity or diabetes who are using these medications for primarily cosmetic purposes probably won't receive life-extending or cardioprotective benefits, which makes it appro-

priate to allocate the doses they would have used to other patients.

Policymakers in Germany, Australia, Canada, and other countries have been considering regulations for addressing dwindling supplies of these medications. Adopting this fair-allocation framework could reduce rates of premature and preventable death, prevent shortened lives for younger patients, and reduce treatment disparities.

Conversely, the fragmented nature of the U.S. health care system would make implementing a fair-allocation framework in the United States challenging. Although we believe Congress should reverse the current prohibition on Medicare covering drugs for weight loss, which would support fair allocation, there is no similarly straightforward mechanism for ordering nonfederal insurers, such as employers, private plans, or state Medicaid programs, to cover these medications. Yet ensuring access to weight-loss drugs for eligible patients who are too young to enroll in Medicare could remediate their life-shortening disadvantage.

Absent state or federal allocation frameworks, the actions of U.S. physicians could still support fair allocation of these medications. This framework could guide physicians and professional societies aspiring to ethical prescribing of GLP-1 receptor agonists and dual GLP-1–GIP receptor agonists.

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From the Department of Medical Ethics and Health Policy, Perelman School of Medicine, University of Pennsylvania, Philadelphia (E.J.E., J.L.D., M.S.M.); the Bergen Center for Ethics and Priority Setting, University of Bergen, Bergen, Norway (E.J.E., J.L.D., M.S.M., G.P.); and the Sturm College of Law, University of Denver, Denver (G.P.).

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1. Eberly LA, Yang L, Essien UR, et al. Racial, ethnic, and socioeconomic inequities in glucagon-like peptide-1 receptor agonist use among patients with diabetes in the US. JAMA Health Forum 2021;2(12):e214182.
2. Emanuel EJ, Persad G. The shared ethical framework to allocate scarce medical resources: a lesson from COVID-19. Lancet 2023;401:1892-902.
3. Emerging Risk Factors Collaboration. Life expectancy associated with different ages at diagnosis of type 2 diabetes in high-income countries: 23 million person-years of observation. Lancet Diabetes Endocrinol 2023;11:731-42.
4. Giugliano D, Scappaticcio L, Longo M, Bellastella G, Esposito K. GLP-1 receptor agonists vs. SGLT-2 inhibitors: the gap seems to be leveling off. Cardiovasc Diabetol 2021;20:205.
5. Ma H, Lin Y-H, Dai L-Z, Lin C-S, Huang Y, Liu S-Y. Efficacy and safety of GLP-1 receptor agonists versus SGLT-2 inhibitors in overweight/obese patients with or without diabetes mellitus: a systematic review and network meta-analysis. BMJ Open 2023;13(3):e061807.

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