

# Incretinomimetics under a bioethical lens: between therapeutics, aesthetics and health justice

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## Abstract

GLP-1 receptor agonists and dual GIP/GLP-1 incretinomimetics have redefined the treatment of type 2 diabetes and obesity by combining glycemic control, weight loss, and cardiovascular benefits in selected settings. This systematized narrative review analyzed pharmacological foundations, efficacy, safety, and regulatory, economic, and distributive challenges of these therapies, articulating bioethical principlism with contemporary critical perspectives, including intervention bioethics, health justice, medicalization, and commodification of care. The review discusses tensions between therapeutic and aesthetic use, the risk of medicalizing weight loss, barriers to access, and impacts on health system sustainability. It concludes that the ethically defensible incorporation of incretinomimetics requires clinical prudence, informed consent, longitudinal follow-up, transparent prioritization criteria, and a commitment to equity, continuity of care, and protection against global inequalities in access to pharmacological innovations.

**Keywords:** Incretins. Obesity. Diabetes mellitus, type 2. Bioethics. Medicalization. Health equity.

## Resumo

### Incretinomiméticos sob olhar bioético: entre terapêutica, estética e justiça sanitária

Os incretinomiméticos agonistas do receptor de GLP-1 e agonistas duais GIP/GLP-1 redefiniram o tratamento do diabetes tipo 2 e da obesidade por associarem controle glicêmico, perda ponderal e benefícios cardiovasculares em contextos selecionados. Articulando o principlismo bioético a perspectivas críticas contemporâneas, incluindo bioética de intervenção, justiça sanitária, medicalização e mercantilização do cuidado, esta revisão narrativa sistematizada analisou fundamentos farmacológicos, eficácia, segurança e desafios regulatórios, econômicos e distributivos dessas terapias. Discutem-se as tensões entre uso terapêutico e estético, risco de medicalização do emagrecimento, barreiras de acesso e impactos sobre a sustentabilidade dos sistemas de saúde. Conclui-se que a incorporação eticamente defensável dos incretinomiméticos exige prudência clínica, consentimento esclarecido, acompanhamento longitudinal, critérios transparentes de priorização e compromisso com equidade, continuidade do cuidado e proteção contra desigualdades globais de acesso a inovações farmacológicas.

**Palavras-chave:** Incretinas. Obesidade. Diabetes mellitus tipo 2. Bioética. Medicalização. Equidade em saúde.

## Resumen

### Incretinomiméticos bajo mirada bioética: entre terapéutica, estética y justicia sanitaria

Los incretinomiméticos agonistas del receptor de GLP-1 y agonistas duales GIP/GLP-1 han redefinido el tratamiento de la diabetes tipo 2 y la obesidad, asociando control glucémico, pérdida de peso y beneficios cardiovasculares en contextos seleccionados. Esta revisión narrativa sistematizada analizó fundamentos farmacológicos, eficacia, seguridad y desafíos regulatorios, económicos y distributivos de estas terapias, articulando el principlismo bioético con perspectivas críticas contemporáneas, incluyendo bioética de intervención, justicia sanitaria, medicalización y mercantilización del cuidado. Se discuten las tensiones entre uso terapéutico y estético, el riesgo de medicalización del adelgazamiento, las barreras de acceso y los impactos sobre la sostenibilidad de los sistemas de salud. Se concluye que la incorporación éticamente defendible de los incretinomiméticos exige prudencia clínica, consentimiento informado, seguimiento longitudinal, criterios transparentes de priorización y compromiso con equidad, continuidad del cuidado y protección frente a desigualdades globales de acceso a innovaciones farmacológicas.

**Palabras clave:** Incretinas. Obesidad. Diabetes mellitus tipo 2. Bioética. Medicalización. Equidad en salud.

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The history of endocrinology therapeutics is marked by cycles of innovation that have radically transformed clinical practice. The discovery of insulin in 1921 ushered in the era of hormone replacement and made it possible for millions of people with diabetes to survive<sup>1</sup>. Decades later, sulfonylureas and metformin expanded the drug arsenal, offering greater flexibility and efficacy in blood glucose management<sup>2</sup>. Although the incretin effect was already known, incretin hormones, especially glucagon-like peptide-1 (GLP-1) and the glucose-dependent insulinotropic polypeptide, began to receive greater therapeutic attention at the end of the 20th century<sup>3,4</sup>.

Discovered in the 1980s, GLP-1 has been shown a potent modulator of glucose-dependent insulin secretion, reducing glucagon secretion, delaying gastric emptying, and promoting satiety<sup>3,4</sup>. These properties aroused immediate interest, but the short half-life of this peptide limited its clinical application. This obstacle was overcome with the development of GLP-1 receptor agonists with greater stability and resistance to enzymatic degradation, establishing a class that currently includes drugs such as liraglutide, semaglutide, and dulaglutide<sup>4</sup>.

More recently, pharmacology has advanced with the introduction of dual glucose-dependent insulinotropic polypeptide/GLP-1 agonists that can activate two incretin receptors<sup>5,6</sup>. This dual action brought clinically relevant results, especially body weight reduction and glycemic control<sup>5,6</sup>. Tirzepatide, the first drug of its kind to achieve broad clinical prominence, has quickly become one of the most discussed drugs by the scientific community and the media. From a bioethical perspective, acknowledging this innovation trajectory imposes on professionals the duty to offer the best treatment available without losing sight of fair resource distribution<sup>7</sup>.

Based on the perspective of bioethical principlism, this study aims to analyze the pharmacological principles, clinical efficacy, risks, and uncertainties of incretin mimetics and the regulatory, economic, and distributive challenges that mark their incorporation into health systems. It especially seeks to examine the tensions between therapeutic and aesthetic use, the risks of weight loss medicalization, and the barriers to access and aims to offer physicians bioethical

references for responsible decision-making in the use of these therapies.

## Method

This systematized narrative review of the literature has a theoretical-reflective approach in bioethics. The adoption of this format—instead of a systematic review in its strict sense—is justified by the reflective and interpretative nature of its object, which articulates pharmacological foundations, clinical evidence, regulatory context, and bioethical deliberation. Its methodological path was outlined to provide transparency to source selection, organization, and interpretation, with an explicit description of the searched databases, used descriptors, chosen eligibility criteria, and selection stages.

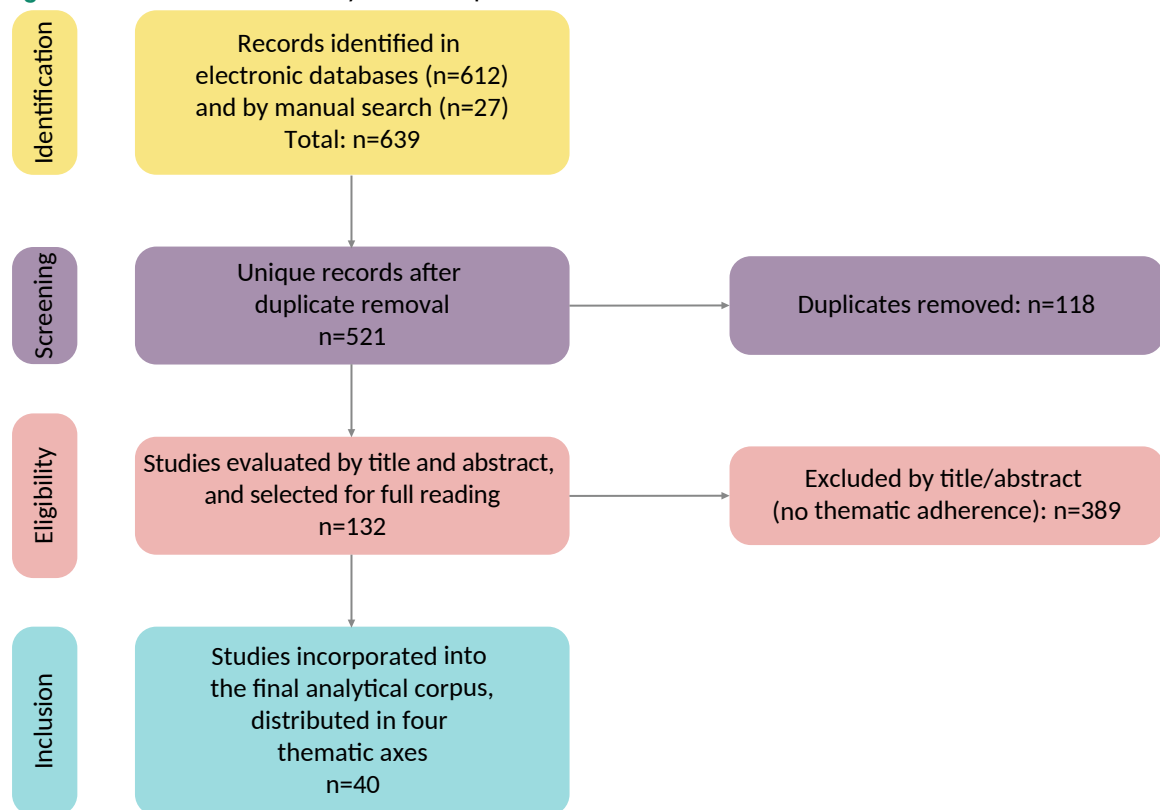
The search was conducted between January and March 2026 on the PubMed/MEDLINE, Scopus, Web of Science, Cochrane Library, LILACS, and SciELO databases, complemented by searching the Bioethics Research Library (Kennedy Institute of Ethics) and manually screening reference lists in research in journals specialized in bioethics (Hastings Center Report, Bioethics, and Bioethics Journal) and the official websites of regulatory agencies (Brazilian Health Regulatory Agency, the U.S. Food and Drug Administration, and European Medicines Agency) and international organizations (the World Health Organization and the Pan American Health Organization). Priority was given to pivotal clinical trials, cardiovascular outcome studies associated with incretin mimetics, and the most recent official regulatory documents. Controlled descriptors (MeSH/DeCS) and free terms combined by Boolean operators were used, including “GLP-1 receptor agonists,” “glucagon-like peptide-1,” “tirzepatide,” “semaglutide,” “obesity,” “type 2 diabetes,” “bioethics,” “principlism,” “medicalization,” “weight loss,” “health equity,” and “resource allocation” and their equivalents in Portuguese and Spanish.

The following inclusion criteria were adopted: 1) original publications, systematic reviews, meta-analyses, clinical guidelines, official regulatory documents, theoretical essays in bioethics, and conceptual reference books; 2) texts in Portuguese, English, or Spanish; 3) publication from 2015 to March 2026 for clinical, regulatory,

and epidemiological evidence (including classic works in bioethics, sociology of health, and political philosophy and foundational landmarks in the pharmacology of incretin mimetics and the history of endocrinology therapeutics published in prior to the established period when indispensable for historical, conceptual, or regulatory contextualization); and 4) thematic adherence to at least one of the four chosen analytical axes. Editorials without empirical or conceptual basis, letters to the editor, summaries of conference abstracts unavailable in full, and dissemination materials without peer review were excluded.

The selection process followed four sequential steps, represented in the flowchart in Figure 1: 1) initial identification of records in the electronic databases ( $n=612$ ) and by manual search ( $n=27$ ), totaling 639 records; 2) duplicate removal ( $n=118$ )—521 unique records remaining; 3) title and abstract screening, excluding 389 articles without thematic adherence, resulting in 132 studies; 4) full reading of the remaining 132 studies and selection of 40 works for analysis according to methodological quality, topicality, representativeness, and bioethical relevance criteria.

**Figure 1.** Flowchart of the study selection process



The included studies were then categorized into four thematic blocks corresponding to pre-defined analytical axes: 1) pharmacological foundations and magnitude of clinical benefits; 2) adverse events, safety, and limits of evidence; 3) therapeutic use, aesthetic use, medicalization, and autonomy; and 4) access, cost, regulation, and distributive justice. In the body of this study, these four axes

were developed in the sections “Mechanisms of action, efficacy, and limits” (axis 1), “Risks, safety, and uncertainties” (axis 2), “Bioethics of therapeutic and aesthetic use” (axis 3) and “Access, market, and distributive justice” (axis 4), complemented by the cross-sectional sections “Bioethical analysis: principles in tension” and “Practical implications of bioethics to the clinic,”

which articulate the four axes above via the bioethical interpretative key. This categorization systematically triangulated clinical evidence, regulatory evidence, and bioethical literature.

On the interpretative level, this analysis was guided by Beauchamp and Childress' principlism—beneficence, non-maleficence, autonomy, and justice—articulated with complementary frameworks of contemporary bioethics: intervention bioethics (Garrafa), protection bioethics (Schramm), health justice (Daniels), ethics of scarce resource allocation (Emanuel), medicalization critique (Conrad), health biopolitics (Rose), and care commodification analysis (Sandel). This triangulation aimed to overcome a strictly principled reading by articulating public health, sustainability, and equity concerns.

As a limitation, this study fails to fully comply with the PRISMA protocol checklists (intended for systematic reviews), having only adapted its selection flowchart to confer methodological transparency to this narrative-reflective review. As this is a review of scientific literature in the public domain, this study is exempt from consideration by a research ethics committee.

## Mechanisms of action, efficacy, and limits

Incretin therapy is based on two main mechanisms, functionally distinguishing the available subclasses. GLP-1 receptor agonists such as liraglutide, semaglutide, and dulaglutide mimic the action of the endogenous hormone, secreting insulin in a glucose-dependent manner, reducing glucagon secretion, delaying gastric emptying, and modulating appetite via central pathways<sup>4</sup>. Dual glucose-dependent insulinotropic polypeptide/GLP-1 agonists (represented by tirzepatide) broaden this spectrum by activating the receptor of the glucose-dependent insulinotropic polypeptide, an intestinal hormone that stimulates insulin secretion and exerts a synergistic effect with GLP-1 on adipocyte metabolism<sup>5,6</sup>. The simultaneous activation of two incretin receptors fails to represent a mere sum of effects: it configures a qualitative redefinition of the therapeutic potential with clinical, regulatory, and bioethical implications that this study proposes to examine.

The understanding of these mechanisms has direct bioethical implications: as pharmacology advances from glycemic control to broad metabolic reconfiguration, drugs cease to be just a therapeutic instrument, becoming moral, economic, and cultural objects. The principle of beneficence requires that this power be accompanied by rigorous evaluations of real benefits, whereas residual uncertainty demands non-maleficence and clear communication for the exercise of truly informed autonomy<sup>7</sup>.

Pivotal studies have consolidated the clinical efficacy of these therapies in three measurable dimensions. Regarding glycemic control, GLP-1 receptor agonists reduce glycosylated hemoglobin by 1-1.5%, whereas dual agonists can achieve reductions close to 2%<sup>8</sup>. Semaglutide has shown weight loss reductions above 15% in individuals without diabetes in STEP 1, a result that surpassed that of any other anti-obesity pharmacotherapy. Tirzepatide has obtained even greater results; SURMOUNT-1 has shown average reductions above 20%, comparable to those of some surgical approaches<sup>5</sup>.

Regarding cardiovascular outcomes, LEADER has found a reduction in major events with liraglutide in high-risk diabetic patients<sup>9</sup>, SUSTAIN-6 has replicated this finding with semaglutide<sup>10</sup>, and SELECT extended the cardiovascular benefit of 2.4-mg semaglutide to adults with established cardiovascular disease and obesity without diabetes<sup>11</sup>. Regarding tirzepatide, SURPASS-CVOT has shown non-inferiority to dulaglutide regarding a set of outcomes (cardiovascular death, myocardial infarction, or stroke in patients with type 2 diabetes and established atherosclerosis)<sup>12</sup>.

However, these results should not be interpreted as absolute or generalizable to all clinical contexts. The frequent gastrointestinal adverse events—nausea, vomiting, diarrhea, and constipation—represent a major cause of discontinuation<sup>13</sup>. Part of the weight loss occurs at the expense of lean mass, with repercussions that are yet to be fully defined in the long term, such as sarcopenia, greater risk of falls, and frailty in older adults<sup>14,15</sup>. Benefit maintenance depends on therapeutic continuity: interruption of treatment is associated with weight regain and worsening cardiometabolic parameters<sup>16</sup>. The association with acute pancreatitis or

pancreatic neoplasm remains subject of debate, with no demonstration of a consistent increase in observational studies but with a recommendation for interpretative caution<sup>17,18</sup>.

The psychosocial dimension also produces relevant areas of uncertainty: there are reports of psychological dependence on such medication as a condition for maintaining self-esteem, which raises reflections on body image medicalization and medical responsibility to avoid reinforcing health standards centered exclusively on weight or appearance<sup>19-21</sup>.

Thus, the clinical efficacy of incretin mimetics is unequivocal, but it must be realistically and ethically interpreted as part of an integrated therapeutic arsenal rather than as an isolated panacea; as an instrument of health promotion, rather than as a promise of immediate aesthetic transformation<sup>7</sup>. Bioethics plays an essential role in integrating scientific enthusiasm with social responsibility. Moreover, all innovation must be accompanied by critical reflection on limits, risks, and possibilities of equitable access.

## Risks, safety, and uncertainties

No therapeutic advance is without risks, and incretin mimetics are no exception. The most frequently reported adverse events are gastrointestinal, such as nausea, vomiting, diarrhea, and constipation<sup>6,13</sup>. Although these symptoms are transient and manageable in most cases, they represent one of the main causes of treatment discontinuation in clinical studies and in everyday practice.

In addition to the predictable effects, uncertainties persist in areas of great clinical relevance. The association between GLP-1 receptor agonists and risk of acute pancreatitis or pancreatic neoplasia remains subject of debate. Observational studies and synthesis reviews have shown no consistent increase in these events, but the topic still recommends interpretive caution<sup>17,18</sup>.

Another emerging point concerns the impact on body composition. Part of the weight loss induced by incretin mimetics is not only due to fat reduction but also to loss of lean mass. The magnitude of this effect and its long-term

repercussions, such as sarcopenia, increased risk of falls, and frailty in older adults are yet to be fully defined<sup>14,15</sup>. This finding reinforces the need for multidisciplinary follow-up with strategies aimed at muscle preservation, including physical exercise and adequate protein intake.

Interpreting the evidence on cardiovascular outcomes requires greater precision. For some GLP-1 receptor agonists, the data show benefits in major cardiovascular outcomes, as in LEADER, SUSTAIN-6, and SELECT<sup>9-11</sup>. Regarding dual agonists, the scenario is no longer just speculative: SURPASS-CVOT has shown tirzepatide to be non-inferior to dulaglutide regarding a set of outcomes (cardiovascular death, myocardial infarction, or stroke in patients with type 2 diabetes and atherosclerotic cardiovascular disease)<sup>12</sup>. Even so, the comparative interpretation of the magnitude of this effect and its generalization to several clinical contexts require caution.

Finally, the psychosocial dimension of the use of incretin mimetics also produces zones of uncertainty. There are reports of psychological dependence on medication as a condition for maintaining self-esteem and reinforcing exclusionary body patterns, which raises reflections on body image medicalization<sup>19-21</sup>. Although this phenomenon is less tangible from a pharmacological point of view, it is central to bioethics since it refers to the medical responsibility of avoiding to reinforce health standards centered exclusively on weight or appearance.

## Access, market, and distributive justice

The impact of incretin mimetics is unable to be evaluated only from a biomedical perspective. GLP-1 receptor agonists and, above all, dual agonists, are high-cost drugs produced by a few global companies—a reality that concentrates bargaining power in the pharmaceutical industry and reduces the margin of autonomy of States in defining prices, coverage, and technological incorporation. Recent corporate reports show that products based on semaglutide and tirzepatide already move multibillion-dollar figures driven by the prevalence of type 2 diabetes and obesity and by the cultural phenomenon by

which these drugs have become symbols of therapeutic modernity<sup>22,23</sup>.

Although it has increased awareness of obesity as a chronic disease rather than as individual failure, the popularization of such medication risks treatment commodification: treating medication as aspirational consumer products shifts the focus from health to aesthetics, distorting the original purpose of such scientific innovation<sup>20,21</sup>.

This tension between innovation and access is expressed in health policies. On December 1, 2025, the World Health Organization published its first global guideline on the use of GLP-1 therapies to treat obesity. It recognized its therapeutic relevance but emphasized that these drugs must include comprehensive care and that accessibility remains an important global obstacle<sup>24</sup>. The recent regulatory trajectory in Brazil clearly illustrates this dilemma. In June 2025, the Brazilian Health Regulatory Agency approved a new therapeutic indication for tirzepatide for chronic weight control in adults with obesity or overweight associated with comorbidities<sup>25</sup> and, in February 2026, a new indication for semaglutide aimed at reducing the risk of major cardiovascular events in adults with established cardiovascular disease and obesity or overweight<sup>26</sup>. However, regulatory approval is only the first step: population access also depends on price regulation, public financing capacity, and decisions to incorporate into the Brazilian Unified Health System (SUS) and supplementary health.

The results have been restrictive in this plan. Semaglutide and liraglutide were evaluated by the SUS National Committee for Technology Incorporation, yet to incorporate it into SUS for obesity in the scenarios analyzed by the commission<sup>27,28</sup>. Moreover, these drugs remain out of reach for most Brazilian patients who depend on the public health system. In supplementary health, the Brazilian National Supplementary Health Agency faces a similar dilemma: whether or not to include drugs with high financial impact in its mandatory list. The absence of coverage encourages legal disputes and individualized access without solving the structural issue of equity<sup>29,30</sup>, producing what can be characterized, based on the discussion of Chieffi and Barata<sup>30</sup>, as a form of “equity by litigation.”

High-income countries tend to more rapidly adopt incretin mimetics into their systems, albeit

with restrictive eligibility criteria. In low- and middle-income countries such as Brazil, high costs, technological dependence, and budgetary constraints create significant barriers<sup>22,23,27</sup>. This disparity configures a form of global injustice from a bioethical perspective.

Thus, the principle of distributive justice must actively guide public policies. It is insufficient to recognize the effectiveness of incretin mimetics: it is necessary to confront those who benefit the most, equitably distribute scarce resources, and sustain care over time. This requires transparency in incorporation criteria, informed social dialogue, periodic reassessment of evidence, and the strengthening of post-incorporation monitoring.

The incorporation of these therapies should avoid replacing population-based strategies aimed at healthy eating, the encouragement of physical activity, and the addressal of the obesogenic environment<sup>31</sup>. Without such integration, obesity is medicalized without addressing its root causes, reproducing a cycle of drug dependence with a high social cost<sup>20,31</sup>. In turn, the response to the problem of market concentration requires articulating multilateral organizations, governments, and industry toward flexible pricing models, greater business transparency, and local productive strengthening.

An ethical axis permeating these challenges is continuity of care. As part of the effectiveness of these therapies depends on prolonged maintenance and multidisciplinary support, it is insufficient to ensure episodic entry into treatment; it is necessary to think about follow-up, adherence, adverse event monitoring, response review, and, when necessary, safe interruption. Ethically defensible prescriptions are not limited to the initial moment of indication—they presuppose a realistic evaluation of the concrete conditions for sustaining the treatment over time from the outset<sup>16</sup>.

## Bioethical analysis: principles in tension

### Beneficence and not maleficence

The principle of beneficence sustains the obligation to promote patients' welfare via provenly effective treatments. Incretin mimetics meet this criterion in that they reduce

complications associated with type 2 diabetes and obesity<sup>5,9</sup>. However, beneficence does not act in isolation: it must be continuously balanced with non-maleficence, that is, the duty to avoid or minimize harm. Known adverse events, remaining uncertainties regarding long-term risks, and the possibility of inappropriate or decontextualized use show that therapeutic benefit fails to eliminate the need for clinical prudence<sup>7</sup>.

## Autonomy

Patients' autonomy is often invoked in this debate, especially in view of the growing demand for incretin mimetics for the treatment of chronic diseases and for aesthetic purposes, often influenced by social pressure, body performance expectations, and the idealization of the thin body. In this context, respecting autonomy, rather than meaning automatically adhering to patients' demands, aims to ensure a free, informed, and ethically contextualized decision without connivance with practices that reinforce stigmas or excessively medicalize daily life<sup>7,20,21</sup>.

## Justice

Perhaps the most challenging principle in this context is that of justice. How to ensure equitable access to high-cost therapies in societies marked by deep inequalities? Bioethics requires considering benefits to individuals and the collective impact of therapeutic and regulatory choices. The broad incorporation of incretin mimetics may imply the displacement of resources from other equally priority areas of health, so that it imposes the need for transparent prioritization criteria<sup>27,29</sup>.

Thus, clinical and health deliberation must coherently integrate beneficence rather than maleficence, autonomy, and justice, guiding decisions that go beyond individual cases and consider professional responsibility, sustainability, and equity.

## Complementary bioethical critical perspectives

The principlist reading, although widely legitimized in the biomedical field, has been the object of fruitful criticism by contemporary currents of bioethics the mobilization of which is especially

fruitful to analyze the phenomenon of incretin mimetics. The bioethics of intervention, formulated by Garrafa and Porto<sup>32</sup> based on the Latin American health reality, argues that the emphasis on individual autonomy, when detached from social determinants and structural asymmetries, tends to reproduce inequalities that the principle of justice itself should address.

Applied to incretin mimetics, this criticism gains special relevance: the idea of the "autonomous" choice for high-cost drugs becomes problematic in a context of aesthetic pressure, socioeconomic vulnerability, and informational asymmetry in relation to pharmaceutical industry. Moreover, the bioethics of protection proposed by Schramm<sup>33</sup> shifted the axis of deliberation from morally autonomous subjects to the care of those most susceptible, proposing that the State and health systems have a positive moral duty to protect people under increased vulnerability. Regarding SUS and supplementary health, this perspective bases prioritization policies that protect groups at higher cardiometabolic risk before giving in to the pressure for the universal incorporation of high-cost drugs still under cost-effectiveness evaluation.

The sociology and philosophy of health offer equally indispensable analytical tools. The concept of medicalization developed by Conrad<sup>34</sup> describes the process by which conditions that are not strictly pathological come to be defined and treated in medical terms, with implications for identity, autonomy, and disorders of bodily experience. Incretin mimetics exemplify this movement (perhaps like no other recent pharmacological class): obesity is no longer just a risk factor or comorbidity, becoming a systematic object of continuous pharmacological interventions with ethical repercussions on corporeality, therapeutic dependence, and self-perception.

In a converging direction, Rose<sup>35</sup> analyzed how contemporary biomedicine transforms subjectivity into an intervention and optimization field by expanding the boundaries of the normal and the pathological and converting "self-care" into a permanent pharmacological demand. This reading requires critical vigilance in clinical practice in the face of the indefinite expansion of indications and the risk of medication occupying

the place of structural transformations in the obesogenic environment.

Regarding justice, Daniels<sup>36</sup> provides a robust foundation for the thesis that health is a special condition because it protects individuals' "normal range of opportunities," which implies a positive obligation on States to promote equitable access to effective interventions. Applied to incretin mimetics, this perspective reinforces that the absolute refusal of incorporation without structured alternatives can violate health justice for patients with established cardiovascular disease or severe obesity with well-characterized clinical indication.

Emanuel and collaborators<sup>37</sup>, systematizing ethical principles for the allocation of scarce resources have proposed criteria that combine benefit maximization, equitable treatment, prioritization of the most serious cases, and recognition of the instrumental and intrinsic value of people—criteria the transposition of which to high-cost therapies remains underexplored in the Brazilian literature (which may support future prioritization protocols at SUS).

Finally, Sandel's<sup>38</sup> criticism to the commodification of social goods offers a valuable lens to interpret the cultural phenomenon involving GLP-1 analogues. When medication with shown clinical benefit begins to circulate as aspirational consumer goods (promoted on social media associated with bodily ideals), there is a risk of corrupting the sense of care: medicine stops responding to needs and begins to feed socially manufactured desires, producing artificial demand that further access inequities.

To articulate these criticisms of classical principlism is not to suggest its replacement but to expand its analytical capacity to respond to the challenge of complex bioethics that is socially situated and attentive to the asymmetries of power that permeate contemporary pharmacological innovation.

## Bioethics of therapeutic and aesthetic use

The boundary between the therapeutic and aesthetic uses of incretin mimetics constitutes one

of the most sensitive points of the contemporary debate. From a regulatory and clinical point of view, the formal indications for weight control generally refer to adults with a body mass index equal to or above 30 kg/m<sup>2</sup> or equal to or above 27 kg/m<sup>2</sup> in the presence of weight-related comorbidities<sup>39</sup>. These conditions justify use since the expected benefits generally outweigh the risks as long as the prescription is included in adequate clinical follow-up and associated with non-pharmacological measures.

The bioethical problem arises when this therapeutic logic is distorted by demands that, rather than being based on well-characterized clinical needs, stem from expectations of rapid weight loss, aesthetic adequacy, or body improvement. In these cases, the medicalization of appearance tends to divert medication from its original purpose and convert it into an aspirational consumer good. Although relevant, patient autonomy fails to legitimize all prescription demands; they must be understood as critically situated, informed autonomy exercised in an environment free of market pressures, body stigmas, and unrealistic promises<sup>17,20,21</sup>.

The ethical repercussions of this expansion are manifold. First, there is an impact on availability. Drugs of high therapeutic value becoming widely demanded outside priority clinical contexts increases the risk of access scarcity and difficulty for patients who depend on them due to well-established indications. Secondly, there are economic repercussions: non-therapeutic use increases the pressure on the market, contributes to persistent high prices, and deepens the exclusion of socially more vulnerable groups<sup>22,23</sup>. Thirdly, the risk of body diversity pathologization is reinforced (as if bodies unlike the thin ideal should be pharmacologically corrected).

In this perspective, the problem is no longer just clinical. It involves distributive justice, medical practice integrity, and a criticism of care commodification. The aesthetic use of incretin mimetics is not merely a matter of individual autonomy, it includes a collective impact on distributive justice, availability, cost, and equity<sup>7,20</sup>.

The role of physicians is central in this scenario. Respecting autonomy, rather than meaning automatically adhering to patients' request, refers to deliberations based on evidence,

proportionality, and professional responsibility. The prescription of incretin mimetics is unable to be reduced to the market response to socially manufactured aesthetic demands. Use outside demonstrable clinical benefit increases the risk of therapeutic trivialization, undue exposure to adverse events, and compromised equity in access.

Thus, medical ethics recommends that indication remains linked to consistent clinical criteria to reconcile beneficence, non-maleficence, responsible autonomy, and distributive justice<sup>7,21</sup>.

### Practical implications of bioethics to the clinic

The bioethical discussion about incretin mimetics, rather than ending at the theoretical level, imposes concrete consequences on daily clinical practice. Physicians prescribing or evaluating these therapies should give special attention to four axes.

The first concerns nomination criteria. Ethically defensible prescriptions must be anchored in well-characterized clinical need, body mass indices within regulatory thresholds, presence of relevant comorbidities, or documented cardiovascular risk rather than in aesthetic demand, media pressure, or expectation of rapid weight loss without clinical substrate<sup>7,25,26</sup>. In lieu of meaning bureaucratic rigidity, this entails technical responsibility: physicians who expand indication beyond the available evidence compromises patient safety, equity in access, and the integrity of medical practice.

The second axis is the quality of communication with patients. Informed consent goes beyond the signing of a form in this context. It involves explaining in an accessible way the actual expected benefits, most frequent adverse events, need for continuity of therapy, and consequences of discontinuation, including weight regain and cardiometabolic worsening (as per the literature<sup>16</sup>). It also involves openly naming the uncertainties that still exist about long-term effects, such as loss of lean mass and its functional repercussions<sup>14,15</sup>. Well-informed patients stand in a better position to decide with real autonomy rather than under the influence of unrealistic promises amplified by social media.

The third axis is active resistance against aesthetic and market pressure. Physicians occupy a unique position in this field: they are simultaneously the guardian of clinical indication and the main filter between the social demand for weight loss and access to the medication. Consultations becoming a prescription counter per request without critical evaluation compromises individual ethics and the collective sustainability of access because non-therapeutic use contributes to scarcity, price increases, and exclusion of patients who most need these therapies<sup>20,21,23</sup>. Acknowledging and naming such pressure with patients (explaining them why a certain case fails to justify indication) constitutes a clinical and ethical act of equal relevance.

The fourth axis refers to planning the continuity of care even before starting treatment. Given the therapeutic dependence on these medications to result persistence, physicians must evaluate since their first consultation whether patients will be able to sustain treatment over time financially, logistically, and from the point of view of the necessary multidisciplinary support. Starting therapy without a realistic perspective of continuity can generate transitory benefits followed by abrupt weight regain, frustration, and psychosocial damage. Thus, responsible prescribing begins with honesty about the concrete conditions of each patient<sup>40</sup>.

These four axes, rather than exhausting the complexity of clinical practice with incretin mimetics, offer an operational reference so that beneficence, non-maleficence, autonomy, and justice cease to be just enunciated principles and start to guide real decisions in consultations in the health system and in the relationship with each patient.

### Final considerations

This study has limitations typical of a narrative review. Moreover, it intends to neither exhaust the available literature nor replace systematic evaluations on technological incorporation. It deals with a rapidly evolving field with continuously updated regulatory, clinical, and pharmacovigilance data. Still, its adopted approach has sufficiently delineated its central ethical dilemmas: weight loss medicalization,

tension between clinical need and aesthetic desire, risk of furthering inequities, and sustainability challenges in health systems.

Incretin mimetics are a relevant milestone in the treatment of type 2 diabetes and obesity. Its clinical impact (shown in large trials) goes beyond the reduction of blood glucose and body weight, achieving cardiovascular, metabolic, and psychosocial outcomes.

In the light of bioethics, incorporating these therapies requires prudent deliberation between beneficence, non-maleficence, autonomy, and justice. Beneficence recommends effective treatments to those who can benefit substantially from them. Non-maleficence requires recognizing adverse events, limits of evidence, need for longitudinal follow-up, and risks associated with use without adequate clinical indication. Autonomy requires clear information, shared decision-making, and critical resistance to aesthetic and market pressures that can distort freedom of choice. In turn, justice requires discussing financing, priority criteria, price regulation, and protection against inequalities in access, especially in countries such Brazil, in which health inequities remain deep.

The challenge of incorporating such medication into SUS and supplementary health is significant. Their high cost and the budgetary impact are real barriers, but the absolute denial of access is also ethically unsatisfactory. The strongest path seems to reside in progressive incorporation strategies that prioritize groups at higher risk with and greater potential for benefit, associated with price negotiation, strengthening of productive capacity, and maintenance of structural policies for prevention and health promotion.

On the other hand, indiscriminate aesthetic use, motivated by social or market pressures, must be

faced with ethical and regulatory clarity. In this context, the role of physicians is decisive: they must prescribe effective drugs, exercise professional responsibility, resist the commodification of health, and sustain technical and bioethical criteria in clinical practice.

In this scenario, continuity of care is an often underestimated cross-cutting ethical axis. The effectiveness of these therapies depends on prolonged maintenance: when treatment is interrupted, the benefits dissipate with documented speed<sup>16</sup>. This means that an ethically responsible prescription, rather than ending with the initial indication, presupposes a prior and honest evaluation of the real conditions for sustaining the treatment over time considering financial capacity, multiprofessional support, and institutional ties. Initiating therapy without a realistic perspective of continuity can generate transitory benefits followed by weight regain, frustration, and psychosocial damage, converting therapeutic innovation into a new source of inequality. Thus, physicians' responsibility fails to end with the prescription: it extends to longitudinal care planning and honesty about the limits of what the system and patients can actually sustain.

In summary, incretin mimetics express the power of contemporary biomedical science and reveal its limits and contradictions. They are, at the same time, a therapeutic promise and a source of new moral conflicts. By offering critical instruments to assess its impacts, bioethics plays an essential role: reminding us that medicine goes beyond technological innovation—still a human commitment to justice, responsibility, and care. This convergence can integrate innovation and equity without losing sight of the centrality of care and the integrity of health systems.

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