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Female exclusion and epistemic justice: a critical analysis of the normative foundations of biomedical research

Exclusión femenina y justicia epistémica: análisis crítico de los fundamentos normativos de la investigación biomédica

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Abstract

The historical exclusion of women of childbearing age from clinical trials has created a structural knowledge gap that distorts the validity of biomedical evidence and perpetuates health inequalities. This deficit,

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based on assumptions of scientific neutrality and paternalistic discourses of protection, reveals a form of epistemic injustice that compromises both women's moral autonomy and the distributive justice of medical knowledge. This study critically analyzes the ethical, epistemological, and normative foundations that have legitimized this exclusion, proposing a framework for responsible inclusion based on the principles of distributive justice, relational autonomy, and scientific validity. The findings show that protection turned into exclusion consolidates gender inequalities and weakens the reliability of biomedical science. In a broader sense, it concludes that epistemic equity is not only a moral requirement but also an essential condition for the legitimacy and universality of scientific knowledge in democratic and pluralistic societies.

Keywords: distributive justice, relational autonomy, epistemic injustice, female exclusion, clinical trials, feminist bioethics.

1. Introduction

The structural exclusion of women of childbearing age from clinical trials represents one of the most persistent ethical and scientific dilemmas in contemporary biomedicine. Despite regulatory advances that promote equity in research, the effects of this exclusion are still evident in the unequal generation of knowledge, the formulation of health policies, and everyday clinical practice. The invisibility of female bodies in medical evidence has led to less safe treatments, delayed diagnoses, and therapeutic decisions based on male models. Far from being a technical problem, this exclusion reveals a profound conflict between justice, autonomy, and scientific rationality. In a context where medicine aspires to precision and personalization, the systematic omission of sexual difference highlights a paradox that compromises both the ethics and epistemic validity of biomedical knowledge.

On a theoretical level, contributions from political philosophy and bioethics offer conceptual tools for understanding the moral nature of this inequality. The theory of justice allows us to interpret

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biomedical knowledge as a primary social good whose unequal distribution affects health equity(1,2). Similarly, the notion of epistemic injustice illuminates the ways in which the cognitive exclusion of women produces moral and structural damage in science (3), while the theory of capabilities (4) and relational autonomy emphasize the link between individual agency and distributive justice (5).

However, a knowledge gap persists that prevents the coherent integration of the ethical, epistemic, and normative dimensions of the problem. Existing literature has documented the empirical effects of female underrepresentation but has often treated them in a fragmented manner or from the perspective of biological vulnerability. There is a lack of analysis that articulates the principles of distributive justice with the requirement of epistemic validity and explores how exclusion, presented as a protection strategy, has reproduced gender hierarchies within scientific knowledge. This theoretical omission has hindered the formulation of a normative paradigm of responsible inclusion that overcomes both medical paternalism and methodological reductionism.

The proposed research is justified by the need to critically examine the ethical and epistemic foundations that have legitimized female exclusion, to propose a model of equitable participation consistent with the principles of justice and autonomy. The absence of women in clinical trials is not an accidental error, but the result of historical decisions that reflect institutionalized gender biases. Therefore, rethinking the research framework from the perspective of epistemic equity implies not only correcting empirical biases, but also redefining the moral conditions of legitimacy in the production of biomedical knowledge.

In practical terms, the findings of this analysis have direct implications for scientific policy-making, the methodological design of clinical trials, and the review of international regulatory frameworks. Recognizing sex as a biologically and socially relevant variable would improve drug safety, diagnostic accuracy, and therapeutic efficacy. Similarly, the incorporation of proportional inclusion criteria and

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contextualized informed consent would strengthen procedural justice in biomedical research and reduce the knowledge gaps that currently affect women's healthcare.

From a contemporary perspective, the problem is part of broader debates on the democratization of knowledge, the ethics of global health research, and the challenges of precision medicine. Growing awareness of gender bias in science, driven by international organizations and feminist movements, has generated a demand for structural transformation in knowledge governance. In this context, epistemic justice stands as an indispensable condition for achieving health equity and scientific credibility in pluralistic and technologically advanced societies.

In this context, the objective of this article is to critically analyze the ethical, epistemological, and normative foundations that have legitimized the structural exclusion of women of childbearing age from clinical trials, with the aim of proposing a framework for ethical inclusion that coherently articulates the principles of distributive justice, relational autonomy, and scientific validity. The main contribution lies in offering a theoretical and normative basis capable of guiding research policies and practices that recognize bodily and epistemic diversity as pillars of a more just, rigorous, and representative biomedicine.

2. Rawlsian justice and the epistemic distribution of biomedical knowledge

Rawls' theory of justice offers a normative framework of relevance for analyzing the distribution of benefits and burdens in the biomedical field. The difference principle, which allows inequalities only when they benefit the least advantaged, and the principle of equitable equality of opportunity, which requires that positions be open to all under fair conditions, allow scientific knowledge to be identified as a primary social good whose unequal distribution directly affects

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life opportunities (1). In this sense, biomedical research is configured as a space in which methodological decisions have profound ethical and political implications, since they determine who has access to the benefits derived from scientific knowledge.

From an extension of Rawlsian theory, health justice is understood as the protection of the normal range of opportunities that allows people to develop their life plans on equal terms(2) . Consequently, health is not an optional good, but a condition that enables effective participation in social cooperation. The exclusion of women from clinical trials violates this principle, as it generates incomplete knowledge that restricts the healthcare system's ability to offer adequate therapeutic responses to the entire population. The resulting epistemic inequality reproduces a structure of disadvantages that is perpetuated from research to clinical practice.

Furthermore, biomedical research creates tension between those who assume the risks and those who receive the benefits. Study subjects bear immediate burdens, while the fruits of knowledge are distributed diffusely and temporarily deferred. The principle of justice in research, formulated in international ethical frameworks, establishes that no group should bear disproportionate burdens or be excluded from potential benefits (6). The systematic exclusion of women of childbearing age violates this principle by denying them both access to therapeutic benefits and the guarantee that the results of research will be applicable to them. This double exclusion generates a compound distributive injustice, in which the initial inequality is reproduced across different social and temporal dimensions.

Added to this is the problematic treatment of female vulnerability. For decades, it has been argued that women of reproductive age require special protection because of the risk of fetal harm. However, this conception homogenizes the female experience and confuses vulnerability with moral or cognitive incapacity to give informed consent. Such an approach, in addition to being paternalistic, ignores differences in life plans, contraceptive use, or individual contexts (7). In contrast, a layered approach to vulnerability recognizes that any

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person may experience situational forms of vulnerability without this justifying their generalized exclusion. From this perspective, reproductive capacity is not an intrinsic condition of vulnerability, but rather a contextual circumstance that may require specific, non-prohibitive protection strategies.

Likewise, the selection of populations in clinical trials determines the validity and scope of the knowledge produced. The omission of women has created a structural bias that privileges male physiology, giving rise to an epistemic privilege that conditions medical practice and health policy (8). This bias is reflected in pharmacological doses calibrated for men, medical devices designed based on male models, and less robust clinical evidence on effects and efficacy in women. The World Health Organization maintains that avoidable, unjust, and remediable inequalities are at the core of health inequity (9). The exclusion of women meets these three conditions, allowing us to affirm that it constitutes a structural form of health injustice.

On the other hand, the principle of reciprocity complements distributive justice by requiring that those who benefit from knowledge contribute reasonably to its generation (10). The exclusion of women contradicts this principle, as it prevents their equal participation in both the risks and benefits of research. This violates the moral reciprocity between members of the scientific community and society. Furthermore, paternalistic justifications that appeal to the principle of difference to exclude women are invalid, as they perpetuate the very inequalities they seek to correct. Protection through exclusion produces deferred costs in terms of health and autonomy, undermining the goal of equity that the Rawlsian principle seeks to guarantee (11).

From the perspective of capabilities theory, the exclusion of women limits the full development of fundamental dimensions of social justice. The absence of specific biomedical knowledge affects bodily health, physical integrity, control over the environment, and practical reason by restricting the information necessary for informed therapeutic decision-making (4). The epistemic inequality

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derived from biased research thus compromises the material and symbolic conditions that sustain female agency.

Likewise, the intersectional perspective allows us to observe how inequalities are intensified when gender is articulated with other social categories. Racialized or low-income women face cumulative exclusions that reduce their participation in research and their access to the benefits of knowledge (12). The hegemonic model of the experimental subject as a white, middle-class male has generated an epistemic structure that systematically marginalizes those who deviate from this prototype (13).

The exclusion of women from biomedical research not only violates Rawlsian principles of fairness and reciprocity but also creates cognitive inequality that distorts the very production of knowledge. The epistemic dimension of injustice, when women are simultaneously the object and victims of the knowledge deficit, requires a more in-depth examination from the perspective of epistemic injustice theory, which allows us to understand how the bias of exclusion is rooted in the interpretive and normative frameworks of biomedical science.

3. Epistemic injustice as the basis for female exclusion in biomedicine

The theory of epistemic injustice provides a particularly fertile analytical framework for examining the cognitive and moral implications of the exclusion of women in biomedical research. This theory distinguishes between testimonial injustice, understood as the devaluation of a person's testimony due to identity-based prejudices, and hermeneutic injustice, which manifests itself when collective interpretive resources are insufficient to make sense of certain social experiences due to the systematic marginalization of certain groups (3). The exclusion of women from medical research reproduces both forms of injustice, as it discredits women's ability to assess risks

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and, at the same time, creates a deficit in the conceptual frameworks necessary to understand their clinical experiences.

Indeed, testimonial injustice becomes visible when ethics committees or researchers assume that women lack the necessary competence to consent to participate in studies involving potential reproductive risks. This assumption reduces the epistemic value of women's testimony regarding their understanding of risks, their reproductive decisions, or their willingness to rationally assume them. In contrast, male participation in studies involving infertility or mutagenicity risks is authorized without further questioning. Therefore, mistrust of women's judgment translates into preventive exclusion, nullifying the principle of autonomy and the moral recognition of women as rational agents (14).

For its part, hermeneutic injustice has more persistent structural consequences. The omission of women from clinical trials has created a systematic gap in the interpretive frameworks of biomedicine, affecting the understanding and diagnosis of female pathologies. The evidence on differences in the manifestation of myocardial infarction exemplifies this in a paradigmatic way. For decades, cardiological knowledge was built on exclusively male samples, establishing oppressive chest pain as a universal sign. However, women often present different symptoms such as fatigue, nausea, or epigastric pain, which has led to diagnostic delays and higher mortality (15). This interpretive deficit is not a scientific accident, but the direct result of an entrenched structure of epistemic exclusion.

Likewise, the concept of epistemic violence broadens our understanding of the problem by emphasizing that ignorance about female bodies is not a passive absence of knowledge, but rather an institutionally generated product. Regulatory and methodological practices that systematically exclude women from research produce a form of collective cognitive harm, as they consolidate patterns of structural ignorance (16). In this way, epistemic violence is reproduced both in the formulation of scientific priorities and in the criteria of methodological validity that legitimize the production of biomedical knowledge.

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From another critical perspective, the notion of white ignorance, developed to explain the cognitive mechanisms of racial domination, can be reinterpreted in terms of gender to reveal the existence of androcentric ignorance in science (17). This form of structured ignorance does not respond to an accidental cognitive deficit, but rather to an epistemic configuration that serves to preserve gender hierarchies. The naturalization of the male body as a universal norm turns the female body into a particular deviation, legitimizing its marginalization within medical research. Consequently, female exclusion perpetuates a patriarchal epistemic order that permeates both scientific practices and their conceptual foundations.

Furthermore, analyses from feminist philosophy of science have shown that the supposed neutrality of research is a methodological fiction. Gender biases infiltrate all stages of the scientific process, from the formulation of questions to the interpretation of results. Methodological choices that privilege male samples reflect a set of cultural assumptions about biological normality and sexual difference that are rarely questioned (18). Consequently, female hormonal variability, rather than being treated as an essential component of human physiology, becomes a methodological obstacle that justifies exclusion.

On the other hand, the idea of contextualized objectivity holds that scientific knowledge achieves greater rigor when it incorporates a diversity of critical perspectives in its validation process (19). The exclusion of women from research compromises this objectivity, as it limits the spectrum of experiences and points of view that could subject findings to intersubjective scrutiny. Therefore, the inclusion of women is not only a requirement of justice, but also an epistemological condition for the reliability of biomedical knowledge. Methodological homogeneity does not guarantee neutrality, but rather bias; only empirical diversity allows to produce rigorous and universally valid science.

Correlatively, population representativeness is a requirement for the external validity of clinical trials. Extrapolating results obtained exclusively in men to the female population implies an unfounded

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inductive generalization. Pharmacokinetic and pharmacodynamic differences between the sexes in absorption, hepatic metabolism, distribution, and renal excretion can significantly alter the response to drugs (20). These physiological differences, which in some cases reach variations of fifty per cent in plasma concentrations, demonstrate that the exclusion of women undermines therapeutic safety.

Empirical evidence confirms the consequences of this exclusion. Analysis of reports of adverse drug reactions in the United States between 1997 and 2001 showed that 80 percent of drugs withdrawn from the market posed significantly greater risks to women, a risk that had not been identified during clinical development (21). Cases such as that of zolpidem show that the apparent protection derived from exclusion translates into uncontrolled and delayed exposure. Insufficient knowledge about sex differences shifts the risk from the laboratory to everyday medical practice.

Publication bias reinforces this dynamic of invisibility. Even when women are included in trials, the results are often presented without disaggregation by sex, omitting relevant differences and consolidating the false presumption of neutrality (22). Analytical omission perpetuates an epistemic hierarchy in which female experiences are considered secondary, and knowledge derived from mixed samples equally representative. Thus, the potential of data to illuminate sex differences remains latent but inaccessible, constituting a form of secondary hermeneutic injustice.

Based on this, the distinction between research on women, for women, and from women allows us to understand the persistence of structural biases in biomedicine. Only research developed from female perspectives can challenge the androcentric assumptions that structure the field (23). The mere numerical inclusion of women in studies is not enough; it is necessary to incorporate their experiences as sources of questions, criteria for interpretation, and frameworks for validation. The epistemic transformation of biomedical knowledge therefore requires a participatory epistemology that recognizes situated experiences as vectors of objectivity.

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From the epistemological point of view, knowledge produced from marginalized social positions has a unique critical potential, precisely because of its distance from dominant structures (24). Women affected by clinical decisions based on biased evidence accumulate knowledge about the limitations of the biomedical system that institutions tend to dismiss. The exclusion of these voices perpetuates testimonial injustice and deprives the scientific field of corrective perspectives that could improve the quality of knowledge.

Recognition of epistemic injustice in biomedicine necessarily leads to an analysis of the ethical mechanisms that perpetuate such exclusion. Among these, the tensions between protection and autonomy reveal how biomedical paternalism is legitimized under discourses of care and safety, nullifying women's deliberative capacity. Exploring this tension allows us to situate the problem not only in the realm of knowledge, but also in the moral and regulatory practices that sustain it.

4. Tensions between protection, autonomy, and medical paternalism

The principle of autonomy is one of the essential normative foundations of contemporary bioethics, establishing that every competent person has the right to decide about their own body and life without unjustified external interference. In conceptual terms, respect for autonomy implies recognizing the deliberative capacity of individuals, guaranteeing access to sufficient information for decision-making, and ensuring the absence of coercion or manipulation (25). From this perspective, the categorical exclusion of women of childbearing age from clinical trials directly violates the three dimensions that make up this principle, by simultaneously denying them the capacity to make decisions, the right to relevant information, and the possibility of free choice.

Women's decision-making capacity is eroded when they are excluded because of their reproductive potential without consideration of

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their individual circumstances, intentions, or decisions. Such a practice presupposes a generalized moral incompetence and disregards their rational judgment about the risks associated with participation in biomedical research. This logic is close to strong paternalism, understood as the substitution of the autonomous judgment of competent persons by the decision of others who claim to know better what is in their interests (26). The exclusion of women thus responds to a paternalistic rationality that disguises epistemic mistrust under the argument of protection, perpetuating the denial of moral agency.

On the other hand, the notion of relational autonomy formulated in feminist bioethics provides a more accurate understanding of the exercise of self-determination in contexts of structural inequality. From this perspective, autonomy is not an isolated individual property, but a socially configured capacity that depends on material conditions, interpersonal links, and institutional structures that can enhance or restrict it (5). Therefore, the ethical analysis of female exclusion must consider the relational dynamics and power asymmetries that shape decision-making, without this justifying universal exclusion criteria. Structural vulnerability does not eliminate autonomy, but rather requires strengthening the social conditions that enable it.

Likewise, informed consent is the practical expression of autonomy in clinical research. Its validity requires transparent communication of risks and benefits, as well as the opportunity to accept or refuse participation in conditions of understanding and freedom. Categorical exclusion nullifies this process by depriving women of access to information and the very possibility of deciding. Significantly, the practice contrasts with the treatment given to men, who are considered capable of giving informed consent even in the face of comparable reproductive risks. This asymmetry does not stem from an impossibility of communication, but from an unjustified presumption of female incompetence to assess risks (27).

Medical paternalism reinforces this inequality by reproducing traditional hierarchies between experts and patients, in which tech-

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nical knowledge prevails over individual deliberation. Such paternalism not only denies autonomy, but also perpetuates historical power relations that infantilize women under the rhetoric of care (28). The restrictions that are presented today as scientific precautions have patriarchal roots that define women as subjects in need of institutional guardianship. Consequently, the exclusion of women from research cannot be understood as a simple rational response to biological risks, but rather as a practice inscribed in a genealogy of control over female agency.

At the same time, the notion of presumed consent that prevails in everyday clinical practice reveals a fundamental ethical contradiction. When drugs that have not been adequately evaluated in the female population are prescribed, it is implicitly assumed that women consent to the risks arising from this uncertainty without receiving sufficient information about the lack of evidence (29). In this way, the ethics of consent are reversed: the right to decide on informed participation in regulated research is denied, while tacit acceptance of risks in unregulated medical care is presumed. The inconsistency between the two contexts highlights the structural dimension of exclusion and its discriminatory nature.

Informed consent, understood as a continuous communicative process, requires not only initial understanding, but also ongoing opportunity for review and withdrawal (30). Institutional decisions that replace individual deliberation ignore the diversity of women's reproductive and biographical circumstances. The application of uniform criteria to those who use long-acting contraceptive methods, those who have already completed their childbearing, or those who face documented infertility demonstrates the moral rigidity of exclusion procedures. The homogenization of experiences under a supposed universal risk lacks ethical and scientific justification, as it ignores the heterogeneity of actual conditions of vulnerability.

Furthermore, the regulatory evolution of international bioethics has moved from models of exclusion to paradigms of protected inclusion. This change recognizes that systematic exclusion generates new forms of vulnerability by preventing access to therapeutic

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benefits and relevant knowledge. According to international guidelines, populations considered vulnerable should not be excluded without strict justification, and when their inclusion is necessary, specific safeguards should be implemented to ensure their effective protection (31). This approach is particularly relevant for women of childbearing age, whose inclusion can be managed through proportional risk monitoring and control strategies, without resorting to blanket prohibitions.

The unequal application of protection criteria between men and women clearly exposes the discriminatory nature of exclusion. Men regularly participate in research involving reproductive or genetic risks on the assumption that informed consent is sufficient to legitimize their participation. Women, on the other hand, are denied this possibility, reproducing the prejudice that they require special protection that they themselves cannot decide on. The double standard that tolerates risks for men and censors those for women reveals a structural bias that perpetuates stereotypes about fragility and dependence (32).

Likewise, the notion of autonomy as a social practice emphasizes that self-determination requires institutional recognition and equitable access to spaces for deliberation (33). The exclusion of women from clinical trials therefore implies a form of structural invisibility that deprives them of the right to participate in collective decisions about the production of biomedical knowledge. This is not only a denial of autonomy in particular cases, but also the consolidation of an epistemic regime that defines who can speak, decide, and contribute to the construction of medical knowledge.

The review of tensions between protection, autonomy, and paternalism highlights that ethical decisions in research have direct material repercussions. The denial of female autonomy is not a moral abstraction, but a structural cause of therapeutic inequality and clinical risk. It is therefore essential to examine how the underrepresentation of women in biomedical research translates into concrete consequences for medical practice and drug safety.

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6. Clinical and therapeutic consequences of female underrepresentation

The practical consequences of female exclusion in biomedical research are particularly serious in drug prescribing and clinical care. The production of knowledge based almost exclusively on male evidence has led to systematic dosing errors, a higher frequency of adverse effects, and lower therapeutic efficacy in the female population. Indeed, sex differences in pharmacokinetics generate significant variations in bioavailability, half-life, volume of distribution, and clearance, with direct implications for therapeutic response and toxicity (34). Therefore, research that omits female representation produces incomplete knowledge that compromises the safety and efficacy of treatments.

In physiological terms, body composition is a decisive source of pharmacokinetic variability. The higher proportion of fat and lower water content observed in women substantially modifies the volume of distribution of lipophilic and hydrophilic drugs, influencing the duration and intensity of their effects. Highly fat-soluble drugs, such as benzodiazepines or certain general anesthetics, have prolonged half-lives and longer-lasting effects in women. This difference cannot be corrected by simple adjustments for body weight, as the relevant compartments vary independently of total weight (35). Consequently, doses extrapolated from male studies may lead to either overdosage, with an increased risk of toxicity, or underdosage, with a loss of clinical efficacy.

Furthermore, hepatic biotransformation regulated by the cytochrome P450 enzyme system reveals considerable sexual differences. In particular, the CYP3A4 isoenzyme, which metabolizes approximately half of all available drugs, exhibits 20% to 30% greater activity in women, resulting in accelerated elimination and lower plasma concentrations when equivalent doses are administered (36). In contrast, other isoenzymes such as CYP1A2 and CYP2E1 show reduced activity, resulting in slower metabolism. These opposing variations

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between isoenzymes confirm that there is no universal adjustment pattern and that each therapeutic agent requires differentiated pharmacokinetic characterization according to sex.

In addition, hormonal influence introduces an additional dimension of complexity. Cyclical fluctuations in estrogen and progesterone modulate the expression of metabolic enzymes, transporters, and receptors, altering pharmacodynamics and clinical response at different times of the menstrual cycle (37). Instead of being recognized as a relevant biological variable, this variability has historically been treated as a methodological obstacle that would justify the exclusion of women. However, homogenizing the sample through exclusion does not eliminate variability, but rather transfers it to the clinical context, where it manifests itself in an uncontrolled manner. The consequence is a medicine that ignores fundamental physiological differences and exposes women to predictable risks.

In the cardiovascular field, the underrepresentation of women has had critical repercussions. Most trials on acute myocardial infarction have included less than 30 percent women, despite the fact that cardiovascular disease is the leading cause of death in women (38). This bias has created three levels of inequality: diagnostic, therapeutic, and preventive. The definition of symptoms was based on male experience, leading to diagnostic delays when women present atypical symptoms; Therapeutic protocols have been optimized based on male responses, reducing their effectiveness and increasing risks. Cardiovascular risk factors have been characterized based on male populations, underestimating the influence of specifically female conditions such as obstetric complications or polycystic ovary syndrome.

In psychopharmacology, the exclusion of women has also had serious adverse effects. Although the prevalence of depression and anxiety in women is twice that observed in men, female participation in clinical trials of antidepressants and anxiolytics has historically been limited. Differences in the pharmacokinetics of selective serotonin reuptake inhibitors result in up to 50 percent higher plasma

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concentrations in women receiving identical doses, with a higher incidence of gastrointestinal side effects, sexual dysfunction, and bleeding (39). In addition, the efficacy of treatments varies throughout the menstrual cycle due to hormonal modulation, a phenomenon that has not been sufficiently characterized due to a lack of specific studies. This lack of knowledge results in inappropriate prescriptions that reduce therapeutic effectiveness and increase iatrogenic burden.

The effects of gender bias are evident in pain management. Women report greater frequency and intensity of chronic pain, yet most preclinical studies of analgesics are conducted exclusively in male animals (40). This omission has resulted in less effective analgesic strategies for the female population. In the case of opioids, women require higher doses to achieve equivalent analgesia, although they have a higher incidence of adverse effects such as nausea and sedation. This disparity reflects pharmacodynamic differences in opioid receptors that were only recognized after decades of clinical use, confirming that the initial exclusion created a knowledge gap with direct consequences on medical practice.

Similarly, anesthesiology clearly illustrates the cost of applying male dosing models to women. Experience with propofol shows that differences in distribution volume and clearance require significantly lower doses to achieve equivalent anesthetic levels. In fact, women require 30 to 40 percent lower doses than men to achieve the same effects (41). However, the absence of initial studies evaluating these differences led to millions of women receiving inappropriate doses for decades, with an avoidable increase in cardiovascular and respiratory depression. The late identification of these differences is empirical evidence of the cost of methodological homogenization.

In oncology, inequalities in representation also affect both therapeutic efficacy and safety. Women experience a higher frequency and intensity of adverse effects such as mucositis, nausea, alopecia, and myelosuppression, resulting from pharmacokinetic and pharmacodynamic differences that were not studied in early stages of

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development (42). At the same time, certain regimens show superior tumor responses in women, suggesting the possibility of gender-differentiated protocols that optimize efficacy and tolerability. However, the lack of systematic research on these differences limits the implementation of adapted therapeutic strategies, perpetuating an inefficient and epistemically biased treatment model.

Evidence on the clinical effects of female exclusion shows that the problem transcends ethical or epistemic dimensions and requires comprehensive regulatory reform. Only through principles that guarantee representativeness, distributive justice, and relational autonomy can confidence in the universal validity of biomedical knowledge be rebuilt. Consequently, the following section proposes a normative framework aimed at equitable inclusion and epistemic reparation for the historical damage caused by structural underrepresentation.

7. Normative principles for representative and fair biomedical research

Overcoming the inequalities resulting from the structural exclusion of women in biomedical research requires a profound transformation of the regulatory framework governing knowledge production in this field. This transformation must coherently integrate the principles of distributive justice, epistemic equity, and relational autonomy, so that the traditional protectionist approach is replaced by a model of responsible inclusion that fully recognizes women's moral and cognitive agency. The necessary normative reformulation rests on an articulated set of ethical pillars that redefine the obligations of researchers, institutions, and regulatory bodies.

The adoption of the presumption of inclusion as a basic ethical standard is an essential condition for ensuring representativeness and scientific validity. Under this principle, the participation of women of childbearing age should be understood as a moral and

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methodological requirement, unless there are clearly justified scientific or ethical reasons that legitimize their exclusion in specific circumstances. Such a reversal of the burden of argument implies recognizing that exclusion, rather than inclusion, requires explicit justification, since it reproduces structural inequalities and weakens the validity of results (43). In this way, inclusion ceases to be an exceptional concession and becomes the norm in a science that aspires to equity and universality.

Likewise, proportional risk management offers an ethically and methodologically sound alternative to categorical exclusion. This principle proposes that reproductive risks should be addressed through specific mitigation strategies that preserve the safety of participants and, where appropriate, that of potential embryos or fetuses, without restricting women's autonomy. Such strategies may include pregnancy tests prior to the start of interventions, the use of effective contraceptive methods during the exposure period, detailed counseling on risks and benefits, and clinical monitoring of reproductive outcomes (44). Proportionality requires calibrating the intensity of protective measures according to documented or reasonably foreseeable risk, avoiding the imposition of excessive restrictions that function as covert barriers to participation.

On the other hand, the systematic characterization of sex differences should be conceived as an essential component of scientific validity. This obligation implies including women in sufficient proportions to perform sex-stratified analyses, formulating specific hypotheses about possible differences, and reporting results in a disaggregated manner, even when the differences do not reach statistical significance (45). This requirement is not merely a matter of transparency, but an epistemic requirement that links scientific reliability with the distributive justice of knowledge. Incorporating sex as a fundamental biological variable in experimental design and statistical analysis strengthens the accuracy and applicability of medical evidence, while correcting decades of accumulated bias in biomedical research.

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Similarly, the notion of informed relational autonomy redefines consent in contexts of reproductive risk, avoiding both individualistic abstraction and institutional paternalism. This conception is based on the recognition that decisions to participate are mediated by social structures, cultural expectations, and power relations that can condition voluntariness without nullifying it(46) . Informed consent, therefore, must be structured as a reflective communicative process that provides complete information, considers contextual factors, and guarantees deliberative spaces free from economic or symbolic coercion. Relational autonomy does not weaken decision-making capacity, but rather places it in its real social context, providing it with the material and institutional conditions that make it possible.

In a complementary dimension, epistemic redress stands as an unavoidable principle for restoring cognitive equity lost after decades of systematic exclusion. This obligation involves prioritizing research aimed at reevaluating drugs and treatments already on the market for which evidence of safety and efficacy in women is insufficient, promoting studies on the effects of hormonal fluctuations on therapeutic response, and revising clinical guidelines in light of emerging findings (47). Epistemic justice requires not only correcting the present but also amending the past, as scientific equity demands the recovery of knowledge that structural omission denied to generations of women.

The effectiveness of this regulatory framework depends, however, on broad institutional transformations. Research ethics committees must develop analytical criteria that distinguish between risks that justify exclusion and risks that can be managed through appropriate measures, rejecting any exclusion based on generalized assumptions about vulnerability. In turn, regulatory agencies must establish that the characterization of sex differences is an indispensable requirement for the approval and marketing of therapeutic products, recognizing that the absence of data on the female population constitutes an unacceptable scientific gap. At the same time, academic institutions must reform their training programs to include

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sex-specific medicine as a cross-cutting dimension in medical and scientific education, overcoming the view that considers male physiology as the norm and female physiology as the exception (48).

Similarly, research funding entities play a decisive role in consolidating the new paradigm. The policies of international organizations that recognize sex as a fundamental biological variable have set a precedent by requiring explicit justification for the inclusion or exclusion of women in preclinical and clinical studies, creating concrete incentives for more equitable science (45). The extension of such policies at the global level is essential to ensure sustained structural change. Public agencies, private foundations, and the pharmaceutical industry must assume shared responsibility for promoting research that reflects the biological and social diversity of humanity, recognizing that scientific equity is not an ethical luxury, but a condition of rigor and epistemic legitimacy.

The development of an inclusive regulatory framework allows us to glimpse a horizon of epistemic and scientific justice in biomedical research. However, the consolidation of this paradigm requires synthesizing the theoretical, ethical, and empirical arguments addressed, evaluating their scope and implications for contemporary science policy. The final conclusions return to this purpose, integrating the findings and outlining the transformations necessary for a genuinely equitable biomedicine.

8. Conclusions

The theoretical discussion developed here reaffirms that the exclusion of women of childbearing age from biomedical research cannot be understood as an accidental or merely technical phenomenon. Rather, it expresses a historical configuration of scientific rationality that has legitimized inequality through protectionist ethics and androcentric epistemology. Critical examination of the ethical, epistemological, and normative foundations reveals that protection turned

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into exclusion constitutes a form of structural injustice that affects both the distribution of risks and benefits and the production of reliable knowledge. The theoretical intervention therefore lies in dismantling the paternalistic and universalist assumptions that underpin the validity of a science that has operated on a partial sample of humanity.

The conceptual contribution proposed takes the form of a coherent articulation of three interdependent principles that reconfigure the horizon of contemporary biomedical research. Distributive justice redefines the moral responsibility of research systems by demanding equity in access to the benefits of knowledge and in the assumption of its risks. Relational autonomy proposes a notion of situated consent, capable of recognizing women's moral agency without ignoring the social conditions that condition it. Scientific validity, for its part, is no longer understood as methodological neutrality but rather as an epistemic practice that requires diversity of perspectives and representations. From their convergence emerges a notion of responsible inclusion that is not limited to numerical participation but demands the transformation of the ethical and cognitive criteria that have historically structured the biomedical field.

The practical implications of this approach are profound and extend to both regulatory processes and institutional policies. The incorporation of the presumption of inclusion as the default norm requires a review of ethical evaluation guidelines and clinical trial approval guidelines so that the absence of women is no longer considered an acceptable practice. Proportional risk management provides an operational framework that allows protection to be reconciled with equity through specific mitigation strategies rather than general exclusions. The obligation to characterize sex differences in experimental design translates into a technical and ethical requirement for validity, the omission of which should be considered a serious methodological flaw. Epistemic repair, for its part, implies a responsibility to reexamine existing evidence and correct knowledge gaps inherited from decades of invisibility.

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Future lines of research should focus on exploring the structural dimension of exclusion and its effects on global cognitive justice. Comparative analysis of inclusion policies in different geographical and economic contexts would make it possible to identify the most effective institutional mechanisms for ensuring epistemic equity. Similarly, it is relevant to explore the links between gender, race, and class in the production of biomedical knowledge, with a view to constructing regulatory frameworks that are sensitive to intersectionality. The integration of participatory methodologies and situated epistemology approaches can contribute to democratizing research by incorporating women's experiences as a legitimate source of scientific validation. The research agenda derived from this approach seeks not only to correct bias but also to reconstruct the epistemic architecture of science on principles of plurality, responsibility, and justice.

Contemporary biomedical ethics faces the challenge of redefining its notion of universality in light of feminist critiques and demands for global equity. The transformation toward a model of responsible inclusion is not limited to technical reform but involves a philosophical reorientation of the way science conceives its relationship with vulnerability, difference, and human agency. Justice, autonomy, and scientific validity thus converge in an ethics of knowledge that does not aspire to impossible neutrality, but rather to impartiality built through deliberation, reciprocity, and recognition. In this direction, biomedical research can recover its promise to serve all of humanity, not just a part of it, and move toward a truly fair, reflective, and universal scientific practice.

9. AI usage statement

An OpenAI GPT-5-type extensive language model tool was used exclusively for the detection and correction of writing and spelling errors. The text was then thoroughly reviewed to ensure that the tone and intent of the original draft were preserved.

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