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Invisible Variables: How the Underrepresentation of Women in Clinical Trials Skews Modern Medicine

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Abstract

Background: *Clinical research has predominantly enrolled male participants throughout the history, often at an expense of women's representation. Such gender disparity has raised concerns about the generalization of research findings and the safety of pharmacological interventions. This denotes a fundamental flaw in medical research, giving rise to our limited understanding of sex-based medicine.*

Objective*: This review examines the causes, extent and consequences of the underrepresentation of women in clinical trials, and also highlights recent advancements made towards gender inclusion.*

Methods: *A narrative review of peer-reviewed literature, regulatory documents, and international policy frameworks was conducted, drawing on evidence from the diverse aspects of medicine, ethics, society and health policy. Thematic analysis of the content was made according to the scope of the review.*

Result and Conclusions: *Gender disparity in clinical trials has led to significant challenges in drug and vaccine safety, disease diagnosis and management and bias in modern technologies. Equitable representation of women in clinical research is both a scientific, imperative and an ethical obligation. Coordinated regulatory, methodological, and institutional reforms are required to address the underrepresentation and its downstream consequences.*

Keywords: *Adverse Drug Reactions; Artificial Intelligence; Clinical Trial; Gender Bias; Health Equity; Pharmacokinetics.*

INTRODUCTION

Gender equity is a core ethical principle in healthcare, critical not only for the wellbeing of society, but also for determinants of individual health (WHO).[1] The systematic exclusion of women possesses significant real-world effects, generating inaccurate diagnoses, ineffective treatments, and unintended harms.

Clinical trials, which are research studies conducted on human participants for the evaluation of medical interventions, rely on methodologies such as randomization and inclusion of different population groups to ensure validity.[2,3] The scientific value of these studies, however, is compromised without proportional representation of different cross-sectional groups of people. The inclusion of diverse genders is a necessity for generating results that are generalizable.[4] The exclusion of women compromises essential information from medical literature, such as drug metabolism, optimal dosage, and overall effectiveness; and thereby jeopardizes the safety of medical interventions for half of humankind.

Inclusivity in clinical trial design is crucial for producing accurate, reliable, and translatable knowledge. Such designs ensure that healthcare systems produce interventions that are not only effective but also safe for every population. This brings the concept of Sex as a biological variable (SABV), which refers to the fundamental influence of biological sex on health and disease processes, necessitating its consideration in research design, data analysis, and reporting to ensure accurate, generalizable, and sex-specific medical knowledge.

Throughout the history of medicine, there have been significant fluctuations regarding the ethical considerations

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of clinical trials. These historical lessons teach us the pressing need to address gender bias in clinical research. Awareness of these ethical issues, which directly impacts our health and that of the broader population, is imperative for moving towards equitable healthcare. Addressing gender bias is not merely a matter of fairness; it is fundamentally a public health issue that necessitates collective action from researchers, policymakers, and healthcare providers.

Objectives: This review aims to explore the historical causes and extent of women's underrepresentation in clinical trials, assessing its impact on health outcomes and treatment efficacy. It also highlights recent advancements towards gender inclusion in clinical research, provides recommendations for stakeholders to promote more inclusive future research.

MATERIALS AND METHODS

This narrative review was prepared by gathering facts and events from a variety of sources, including peer-reviewed articles, government reports, and credible online documents. The collected articles were qualitatively analyzed, focusing on the themes of historical context, causes, and consequences of the underrepresentation of women in clinical trials. Specific attention was given to real-life examples and patient safety, as well as recent advancements toward achieving gender equity in these trials. The information was then integrated into a coherent narrative aligned with the review's objectives. The findings were discussed in the context of their real-life implications for various stakeholders, considering ethical and social factors, as well as potential policy implications.

RESULTS AND DISCUSSION

Tracing the Origins of Sex Disparity in Medical Trials

Comprehending the current gender disparity in clinical trials requires understanding of its origins. Historical events and regulatory decisions routinely excluded women, which had a long-lasting impact on medical research and care.

Pre-1900s – Male as the Default

Before the twentieth century, medical research was largely observational and ambiguous. Most clinical assumptions were based on observation of males, and female hormonal changes and diseases were not studied. Since males were responsible for the "normal" physiological parameters, even minor details and precision in assessing female health were handled nonchalantly, which led to misdiagnosis for a larger population of females seeking medical care.[5]

Mid-Twentieth Century (1940s–1970s)

Women remained underrepresented in clinical trials. Since all the women from their menarche to menopause were considered "potentially pregnant", the risk of fetal damage prevented researchers from including female subjects. The final knockout for female subjects came following the thalidomide tragedy in the late 1950s which resulted in devastating birth defects.[6] As a result, women were significantly discouraged from participating in clinical trials due to concerns about potential risks to reproductive health. Similar was the effect of the synthetic estrogen, diethylstilbestrol (DES), which was linked to health issues in their daughters. Consequently, in late 1970s, the US FDA adopted a policy of exclusion that basically prohibited all women from pharmaceutical research for fear of causing fetal harm. While this was supposed to refer only to Phase 1 trials (done either on healthy people or those at the terminal stages of some disease to determine toxic levels of a drug), it wasn't long before the rule was applied to pharmaceutical research.[7]

Late Twentieth Century – Protectionism to Inclusion

The 1985 report of the Public Health Service Task Force on Women's Health Issues recommended long-term research on how behavior, biology and social factors affect women's health. The following year, the US National Institute of Health (NIH) established a policy which then encouraged researchers to include women in clinical studies.

In July 1993, the Food and Drug Administration (FDA) changed its guideline that excluded adult women of childbearing potential from participating in early phase drug studies, which "may have led to a more general lack of participation of women in drug development studies, and thus to a paucity of information about the effects of drugs in women". The new guidance allowed, but did not require, representative inclusion of women in phase 1, 2 and 3 trials, and endorsed, but did not require, analysis of data on sex differences because the FDA did not "perceive a regulatory basis for requiring routinely that women in general … be included in particular trials." The agency did encourage consideration of the effects of the menstrual cycle and of exogenous hormone therapy on drug treatment outcomes, and the effect of drugs on oral contraceptives' efficacy, when feasible. As the FDA began to relax its exclusionary policies, researchers started to recognize the ethical and practical importance of including women in clinical trials .[7,8]

The Turn of the Century – Shifting the Balance

The scientific studies showed evidence of drugs working differently on men and women due to physiological and metabolic differences as well as hormone cycles. The Government Accountability Office report published in the year 2001 reviewed 10 prescription drugs withdrawn in the U.S. from 1997 to 2000 due to their toxicity (Table 1).[9] It is important to note that 8 of the 10 prescription drugs posed greater health risks for women than for men. Among those, four cases were due to higher prescription rates among women and four showed more adverse effects in women despite equal usage.

Table 1. Prescription Drugs Withdrawn from the United States market, Jan. 1, 1997 through Dec. 31, 2000 (as per United States General Accounting Office, 2001)[9]

Generic Name	Date Approved (M/D/Y)	Date Withdrawn (M/D/Y)	Greater Health Risk in Women
Fenfluramine hydrochloride	6/14/1973	9/15/1997	Valvular heart disease
Dexfenfluramine hydrochloride	4/29/1996	9/15/1997	Valvular heart disease
Terfenadine	5/8/1985	2/27/1998	Torsades de Pointes
Mibefradil dihydrochloride	6/20/1997	6/8/1998	Bradycardia in elderly women and interactions with 26 other drugs
Astemizole	12/19/1988	6/18/1999	Torsades de Pointes
Troglitazone	1/29/1997	3/21/2000	Liver failure
Cisapride monohydrate	7/29/1993	7/14/2000	Torsades de Pointes
Alosetron hydrochloride	2/9/2000	11/28/2000	Ischemic colitis

This report highlighted the foundational vulnerability of women in drug usage and put a spotlight on much-needed changes required to implement sex-stratified clinical trials.

Evolution of Clinical Trials in Nepal

The condition of clinical trials in Nepal has historically been limited, with most studies being community-based and Nepal acting mainly as a site rather than a leader.

Two landmark trials from the late 20th century are especially important. The hepatitis E vaccine trial was a randomized controlled trial conducted among Nepalese military personnel, involving thousands of healthy adult participants, with carefully controlled and relatively balanced male–female recruitment (though slightly male-predominant due to military sampling). It demonstrated high vaccine efficacy, making it a globally significant study.[10]

The vitamin A prophylaxis trial in children was one of the largest community trials in Nepal, involving over 28,000 children. Participants were nearly equally distributed between boys and girls, and the study showed a significant reduction in childhood mortality in both sexes, highlighting equitable recruitment and benefit.[11]

After COVID-19, clinical trials in Nepal have increased, particularly in infectious diseases, but the country still primarily serves as a recruitment site, and there is limited sex-disaggregated data in recent studies to assess gender bias.[12]

Reasons behind Sex-Based Bias in Clinical Trials

Sex-based bias stems from longstanding systemic, scientific, and cultural factors leading to development of clinical practices with little consideration for sex-specific differences. Understanding the roots of this bias is key to advancing gender-inclusive research.

Overcorrections from Past Incidents

Historical patterns of gender bias in clinical trials reflects broader social trends. Following the thalidomide and diethylstilbestrol tragedies[6], regulatory authorities recommended excluding women, especially those of childbearing potential from clinical studies. This institutional decision reinforced the notion of male physiology as the medical standard, and without legal requirements to include women, systematic exclusion continued.

Biological and Pharmacological Complexity

Besides the general trend, some biological variations favored women against being included in research. Female physiology shows significant differences compared to males, including hormonal fluctuations, genetic variations, and immune responses that can impact trial outcomes. Females generally have stronger immune responses than males.[13] This affects their disease susceptibility, vaccine responses, and immune-mediated reactions. Higher expression of Toll-Like Receptors (TLR7 and TLR9) in females leads to increased type I interferon production, while men show a weaker IFN-α response and higher interleukin-10 (IL-10) levels. Women also have a higher CD4:CD8 ratio, contributing to greater antibody production, but also a higher risk of autoimmune diseases like systemic lupus erythematosus (SLE). These differences may explain why women generally respond better to vaccinations, and also experience more severe side effects after immunization.[14,15]

These sex-based variations in immune physiology is attributed to factors such as estrogens, which boost immune activation by increasing the expression of TLRs, while testosterone suppresses immune activity by reducing T and B cell responses and lowering cytokine production. Females also have two X chromosomes; while one is randomly inactivated, some genes can escape this inactivation. X chromosome is also found to contain more immune-related genes.[16]

Women's bodies show larger variability in physiological functions due to hormone cycles, menstrual cycle, and use of contraceptive pills, pregnancy, and lactation phases, which can affect their immunity, therapeutic response, and adverse effects. For example, estrogen affects the pharmacokinetics of the drugs mainly via its effect on transporters and enzymes. Cytochrome P450 enzymes such as CYP3A4 are more active in women, thus producing sex-based variability in drug metabolism.[17]

Thus we can see, the failure to include sex as a co-variate in early-phase pharmacokinetic studies means that standard dosages are often derived from male-biased samples, making women vulnerable to inaccurate dosage or side effects.

Practical Challenges and Social Issues

The inclusion of women is often bound by societal constraints and practical limitations. Their social and familial responsibilities often leave them with limited flexibility with time, making long-term trial participation difficult. Additionally, the possibility of pregnancy during the trial introduces further complexity. Since it would be unethical to restrict reproductive choices, ensuring participant retention becomes a significant concern. Faced with these barriers, many researchers have defaulted to recruiting male participants, who are often perceived as more physiologically consistent and socially accessible.[5] Economic barriers, particularly for low-income or marginalized groups, further restrict access to research opportunities. Additionally, the concentration of large-scale projects in urban academic centers creates an accessibility gap. The lack of women in leadership roles within research and funding bodies results in male-centered priorities**.** This is compounded by a historical and persistent gender bias in healthcare, where women's symptoms are more likely to be dismissed as psychosomatic, leading to longer diagnostic delays and under-referral to specialist care and clinical trials.[18] Together, these factors perpetuate the underrepresentation of females in medical research and treatment development.

Preclinical Bias (Animal/Cell Studies):

Male animals and cell lines have predominantly been used in biomedical research, with the justification that female hormonal cycles create irrelevant variability. Even when particular diseases are more common in women, female animals tend to be underrepresented. These biased research designs preclude the detection of sex-specific biological pathways and mask important differences in disease presentation and treatment response. This preclinical exclusion propagates bias into clinical trials, compromising drug safety and efficacy for women.

Alzheimer's disease (AD) preclinical studies have historically biased towards male models, despite two-thirds of Alzheimer's patients being women. A systematic review of AD mouse models found that more than half models exclusively use male animals.[19,20] This means current treatment of AD has reduced efficacy and possibly misdirection of therapeutic targets in women.

Women are also inadequately included in cardiovascular drug and device trials. Cardiovascular disease is the number one killer of both sexes worldwide. In analyzing cardiovascular animal studies, it was reported that female animals represented 34% of study subjects, limiting understanding of female-specific pathophysiology and drug responses. Symptoms such as fatigue, nausea, and back pain (common in women) are often arbitrarily excluded from established criteria for diagnosis, which have historically been male-centric (ex. chest pain; see below for more description).[21,22] The result is delay in diagnosis, under-treatment and poor outcomes for women.

A review of cancer biology articles published 2012-2017, found that among the cell line or animal models, only 22% used both sexes, with 59% exclusively male and 19% exclusively female. Similar trend can be seen in preclinical studies of colorectal and lung cancer.[23] Inadequate attention to sex-based differences varies widely in the chemotherapeutic dosing and toxicity profiles could mean women might get an inadequate dosing or higher adverse effects than males.

Mistrust and Historical Exploitation

There is distrust among people due to historical exploitation and medical racism, particularly in the minority or indigenous communities. The following past incidents have further degraded the trust factor.

The Tuskegee Syphilis Study remains a pivotal case in ethics failure within biomedical research, prompting modern institutional review processes and public scrutiny of consent practices.[24] Similarly, the coercive sterilization of indigenous women in North America demonstrates a pattern of reproductive injustice based on unscientific eugenic ideologies and structural discrimination.[25] The World Health Organization explicitly denounces any sterilization practice lacking free and informed consent, but our history and lack of cultural sensitivity continues to erode trust.

Consequences of Exclusion and Gender Disparity

Having established the historical roots and perpetuating factors of women's underrepresentation, let's examine its ramification in clinics, research and society, with examples.

Drug Safety and Dosing Issues

Females tend to report a greater number of adverse drug responses (ADR) to certain medications than males (Table 2). Women report 52% more ADRs than men, largely because dosages are already calibrated to male physiology.[23] These adverse drug effects only come into light during the post marketing surveillance. Yet, it is women who ultimately bear the consequences of this oversight. Even medications that are commonly used have more side effects in women, something that usually goes unnoticed not just by the general population but even by medical professionals.[26,27]

The Case of Zolpidem: A Sex Difference Fact

The 2013 decision by the U.S. Food and Drug Administration (FDA) to change the recommended dosing of zolpidem, a sedative drug, for women is a key example of how sex differences influence medical policies. The FDA cited pharmacokinetic studies that showed much higher blood

levels of the drug in women, which led it to recommend lowering the initial dose for female users.[28,29] Zolpidem is notably one of the few FDA-approved medications with officially recommended sex-specific dosing guidelines.

Although this example has been criticized for being a simplified view of sex-based medicine, and newer research has also demonstrated the reduced dose of zolpidem may be inadequate, this still marks an important shift in biomedical research and regulation. It raised awareness in research and clinical communities about the need to consider sex and gender as essential factors in drug development, safety evaluation, and prescribing practices.

Table 2. Examples of sex-based variation in adverse effect profiles of selected drugs [Compiled from 26-29]

Drug	ADR	Sex-related issue
Zolpidem	Higher blood levels in women	Next-day drowsiness, more common in women
Digoxin	Hormonal interaction affects drug action	Higher mortality in women
Aspirin (low dose)	Poorer response in stroke prevention	Less effective in women
Selective Serotonin Reuptake Inhibitors	Slower metabolism in women	Higher plasma levels and more adverse effects in women

COVID-19 Vaccine Sex-Differentiated Responses

A recent example is the COVID-19 vaccine trials, where male participants were predominantly considered. As a result, women experienced more intense and frequent side effects compared to men.

During the early stages of COVID-19 vaccine distribution in the United States, an analysis of the first 13.8 million doses demonstrated a stark difference: while women comprised 61% of vaccine recipients, they represented a disproportionate 79% of reported side effects.[30] This trend held true worldwide. For example, a retrospective study of hospital workers in China, a group of 1,107 women and 290 men, demonstrated that almost every category of adverse reaction, including pain, muscle ache, fatigue, and headaches or dizziness, was significantly more prevalent in women, irrespective of vaccine dose.[31] In support of this trend, one study from Japan in healthcare workers indicated that women reported a median of three side effects following the first dose versus two in men, and five following the second dose versus 2.5 in men.[32] Furthermore, women also recovered more slowly from these effects. In the Netherlands, nationwide data further supported the fact that women had almost double the likelihood of experiencing adverse reactions following both vector-based and mRNA vaccines, ranging from local reactions at the injection site to systemic symptoms.[33] These findings, which held true across populations, highlight a significant and unmistakable sex-based discrepancy in vaccine response that deserves increased focus in research and clinical practice.

Diagnostic Errors and Mismanagement

Apart from drug therapy, the symptomatic diagnostic criteria and imaging findings are also male-centered, leading to symptoms in women who tend to present "atypically" being misinterpreted or ignored. This bias translates into major delays; in particular, women are seven times more likely to be misdiagnosed and sent home during a heart attack than men. In contrast to men, who usually have chest pain when having a heart attack, women can have more subtle or atypical symptoms, including nausea, fatigue, shortness of breath, pain in the back or jaw, and even flu-like symptoms.[34,35]

This diagnostic deficit is not cardiology-specific. In stroke trials, women make up just above a third of trial participants, despite equal or greater disease prevalence. In stroke, women can present with confusion, fainting, or overall weakness deviating once more from the classic male presentation of slurred speech or facial drooping. These non-classical symptoms postpone recognition and treatment, resulting in poorer clinical outcomes.

Moreover, in autoimmune disorders that disproportionately impact women, patients may present with generalized symptoms such as chronic pain, fatigue, or mood disturbances. Yet these are oftentimes misconstrued as anxiety, depression, or hormonal changes, postponing diagnosis and proper care. Chronic conditions such as fibromyalgia, lupus, and endometriosis – all more common in women, often suffer delayed diagnosis, largely due to under-funding and lack of rigorous representation in trials.[18] This androcentric view of "standard" physiology extends into everyday practice, where women's pain and differing symptoms are often minimized or misattributed to psychological causes.

Historical experiences of misdiagnosis and misrepresentation in healthcare create apprehension towards seeking medical care, leading to prolonged avoidance of medical attention. This causes worsening of medical conditions or untreated illnesses, potentially increasing mortality rates. Such apprehension may also manifest as *iatrophobia*, an irrational fear of healthcare.

A gross level of disparity is described where attractive females are perceived as having less pain than unattractive ones. Many female symptoms have also been observed to be minimized or mocked, leading to silence around their issues. In the medical community, women are seen as needing to prove their illness severity compared to male patients, which is referred to as "Yentl Syndrome".

AI and Modern Technology Bias

Artificial Intelligence (AI) is being increasingly used in medical research, diagnostics and treatment.[36] However, only 22% women in phase I drug trials and 34% in cardiovascular trials, for example, has created longstanding medical knowledge gaps that are at risk of being carried forward by AI-powered diagnostic technologies of the future.[37] When AI models learn from these biased datasets, they naturally adopt and exaggerate pre-existing gender bias.

One striking example is in medical imaging: a 2019 study by Larrazabal et al. showed that AI classifiers trained on chest X-rays did considerably worse for female patients when female representation in the data fell below 25%, with up to 20% less diagnostic accuracy.[38] Another big-scale study published in Nature Medicine (2021) showed that an AI system for identifying pneumonia from chest radiographs consistently underdiagnosed women and black patients because of data imbalance, with underdiagnoses rates up to 17% greater in women than in men.[39] Such disparities are not merely technical; they incur actual clinical repercussions, resulting in misdiagnosis, postponed care, and systemic exclusion from novel digital health solutions.

Recommendations for the Future

Creating a more equitable healthcare environment requires proactive steps. Given the considerable impact of bias on women's health, it is necessary to implement thoughtful strategies at multiple levels. The following recommendations offer concrete actions to remove barriers, foster equity, and improve the clinical research environment for everyone.

Mandating Sex- Inclusive Research Design

As Peters et al has recommended, sex-specific data should be reported from all clinical trials for meta-analysis and also to provide appropriate information to guide healthcare.[40] In this line, organizations and global policy increasingly recognize the need to address sex and gender imbalance as a scientific, ethical, and policy priority. The sex and gender equity in research (SAGER) guideline and ethics-committee mandates call for the design, analysis, and reporting of sex-disaggregated data.[41] National policies (e.g. in Australia) require mandatory inclusion, oversight, and enforcement extending beyond clinical research to include cell lines and animal models as well .[42]Lifecycle strategies focus on engaging and retaining participants at all research stages, from outreach and enrollment to intervention, outcomes assessment, analysis, and dissemination. WHO guidance (2024) further mandates the involvement of underrepresented groups, including pregnant women, from trial inception.[43] Together, these measures reflect a consensus on correcting sex disparities, and the Sex as a Biological Variable (SABV) policy is being applied across different research stages.

Enforcing Sex- Disaggregated Data Analysis

In order for women to be part of clinical trials, the data must be reported and analyzed separately by sex. Statistical methods must identify differences in efficacy and adverse effects as pharmacokinetics, pharmacodynamics, and immune responses are different between the sexes. Not only do sex-specific data reveal differential drug responses to treatment, but they also promote precision in medicine via the ability to tailor therapies to one's biological profile rather than a one-size-fits-all approach. Appreciation of these differences is essential to delivering truly personalized and equitable healthcare.

Removing the Barriers for Female Recruitment and Retention

In order to enhance women's participation in clinical trials, both socio-cultural and logistical barriers should be considered. Logistical barriers can be alleviated through the provision of childcare, travel assistance, and flexible scheduling. Sociocultural impediments such as mistrust and unfamiliarity needs to be addressed via community involvement, culturally appropriate education, and targeted communication. The presence of more female investigators and staff can also make the research environment more inclusive and welcoming.

Using Equitable Models in Pre-Clinical Trials

Eliminating gender bias in clinical trials starts with ensuring sex equity in preclinical research. This sex-balanced approach allows the detection of sex-specific biological effects at an early stage, enhancing the safety and effectiveness of treatments for both sexes. This should be followed by demands by funding agencies and universities for the justification of single-sex studies and encouragement of sex-balanced research designs as conditions for grants and publication policies. By including sex equity at the preclinical level, the stage is laid for more generalizable, consistent, and specific downstream clinical research.

Refinement of AI Tools

The input of the data in the AI tools must be handled in a sensitive manner and the issue of inclusivity with reference to sex, gender, ethnicity must be properly taken into consideration. This would allow for redesign in modern medicine where the previous data gaps can be refurbished thus leading to patients being assessed based on their own individuality. The diagnostic and treatment protocols thus derived would be less biased resulting in hopefully an equity-based medicine. New AI models need to emphasize transparency, ethical guidelines, and continuous monitoring of AI systems to prevent perpetuation of historical gender biases present in medical research and practice.[44]

Making and Implementation of Global Policies

The appeal for sex and gender inclusivity in medical research and practice needs to be reinforced at the global policy level. Organizations like the WHO, United Nations, and leading medical bodies have the authority to set standards that ensure

inclusivity in research, clinical trials, and healthcare systems. As artificial intelligence becomes increasingly integrated into diagnostics, treatment protocols, and decision-making tools for health, bridging previous gaps in clinical data especially women's exclusion is more crucial than ever. Without intervention, these biases risk being embedded and amplified in future medical technologies. Strong, mandated global policies are essential both to correct past inequities and to ensure fair, data-driven healthcare for all.

Besides the policy level actions, foundational shifts like sex- and gender-based medicine (SGBM) integration into the education is an important step in shifting the paradigm. It needs to be coupled with training to researchers, clinicians, and health policymakers. Medical curricula should be revised to include comprehensive education on sex differences in various dimensions of medical education.[45]

Limitation of the study: The narrative review structure of this study imposes subjectivity in selecting sources and themes. The review does not claim to be a comprehensive account of the topic given the nature of the review. Attempts have been made to include the diversity in perspectives of the account and the sources such as academic, clinical, ethical and social viewpoints to minimize the bias.

CONCLUSIONS

It is said that although women have not had a significant part in making of science, science has had a significant part in making of women. The price of ignoring women in research is quantifiable, damaging and avoidable. This review emphasizes the urgent need for inclusive science that represents all individuals. Equitable representation requires rigorous plans, mandating data analysis stratified by sex, ensuring inclusion criteria are adhered to in trial protocols, and investing in research that examines sex as a biological variable. This practice is expected to make evidence-based medicine more robust, outcomes better for women, and promote equity in research. The future of clinical science will be the one where sex and gender equity is a fundamental expectation, not an afterthought.

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