OXFORD JOURNAL
OF STUDENT
SCHOLARSHIP

Sex Bias in Clinical Trials: How the Historical Underrepresentation of Women Shapes Drug Safety and Treatment Outcomes

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ABSTRACT

Clinical trials are foundational for drug approval, dosing standards, and treatment guidelines. Yet, women were systematically excluded from these studies for much of the 20th century. To address this gap, this literature review examines how the historical exclusion of women from clinical trials has transformed drug safety and treatment outcomes for female patients. By synthesizing sources across regulatory history, trial design, clinical consequences, and reform strategies, the review shows how exclusion at one stage of research compounds into the next. Specifically, missing data from early trials produces dosing guidelines that are calibrated to male physiology, which then become the standard used in drug approval and prescription for female patients. Across the existing literature, researchers consistently find that male-centered data continues to shape clinical guidelines in ways that do not reflect female physiology. As a result of this male-centered evidence base, consequences include higher rates of adverse drug reactions, inaccurate dosing, and delayed diagnoses.

INTRODUCTION

Clinical trials are used to approve medications, determine dosing guidelines, and establish safety warnings. Yet for most of the history of drug development, women were excluded from these studies, often due to concerns about reproductive risks and assumptions about hormonal changes (Liu and DiPietro Mager). In response, policy reform like the NIH Revitalization Act of 1993 attempted to address this historical exclusion by mandating the inclusion of women in federally funded clinical trials (Bennett). Because clinical trials historically relied primarily on male participants, much of the medical evidence guiding contemporary treatment has revolved around male physiology even if women frequently experience different drug effects. As a result, medications are primarily tested and developed based on male physiology, including differences in body composition and hormone regulation, and often do not reflect how women respond to treatment. This gap in sex-specific clinical evidence can lead to higher rates of adverse drug reactions and delayed risk recognition for female patients.

This literature review analyzes how the historical underrepresentation of women in clinical trials has contributed to sex-specific differences in drug safety and treatment outcomes, while also examining proposed frameworks and reform strategies that aim at improving sex equity. Based on the literature, this paper argues that the systematic exclusion of women from clinical trials has produced male-centered medical data, which has led to gaps in safety and treatment effectiveness for female patients. First, this review examines the historical and regulatory decisions that established the male body as the scientific default in medical studies. Then, this paper analyzes how eligibility criteria continue to limit women's representation in clinical research. From there, the review also evaluates how these research practices have influenced pharmacokinetic data and dosing standards. After that, the paper will explore how evidence gaps translate into real-world complications and ineffective treatments for women. Finally, the review analyzes existing frameworks and proposed strategies aimed at improving representation and strengthening accountability in clinical research.

Although substantial scholarship has documented women's exclusion and documented sex-based differences in drug response, these issues are often treated separately rather than as connected. By integrating historical exclusion and trial design practices, this review argues that sex inequity in trials is not only a matter of representation but also an issue with direct consequences for patient care. When drug development relies mostly on male-physiological data, women may face higher risks of adverse reactions and delayed risk recognition. Understanding how these evidence gaps came to be is critical for determining the scientific reliability of drug development research. This review highlights the need for more systematic inclusion of women in early-phase trials and for future studies. The core argument of this review is that exclusion of women is not a single moment of bias but a compounding process in which each stage of research builds on the incomplete evidence produced by the step before it.

LITERATURE REVIEW

Origins of Female Exclusion in Drug Development

The origins of women's underrepresentation in clinical trials can be understood through three interconnected factors: regulatory exclusion, scientific assumptions about male physiology, and delayed policy reform. To begin, Liu & DiPietro Mager examine how the exclusion of women from early-phase clinical trials established a male-centered foundation for drug safety evidence. According to their findings, the origins of women's underrepresentation in clinical trials can be traced to regulatory decisions that excluded women of childbearing age, a pattern that established a male-centered foundation for clinical evidence (Liu and DiPietro Mager 3). In particular, concerns have been documented about fetal harm, and possible litigation led to widespread exclusion of women of childbearing age, especially from early-stage drug testing. Following concerns about fetal harm, the U.S. Food and Drug Administration issued a 1977 guideline that recommended that women of childbearing potential be excluded from early-phase clinical trials(Liu and DiPietro Mager 3). Though research oversight bodies framed this

restriction as precautionary, these restrictions effectively removed many women from early stages of drug development (Liu and DiPietro Mager 2). Consequently, because regulators excluded women from early-phase clinical trials, pharmaceutical developers and clinical researchers used data based primarily on male participants (Liu and DiPietro Mager 2). Over time, the exclusion of women from early-phase clinical trials created a significant evidence gap in drug development that persisted for decades. Because research used data primarily from male participants, the resulting medical evidence often failed to account for sex-based differences in drug metabolism and response-efficacy (Liu and DiPietro Mager 1). This reliance on male-centered data explains how women's underrepresentation in trials later contributed to foundational differences in drug safety and treatment outcomes.

While Liu and DiPietro Mager trace the explicit removal of women from early-phase clinical trials, the Institute of Medicine shows that scientific assumptions reinforced male-centered evidence implicitly. Biomedical research has historically treated male physiology as the standard for human biology, researchers have been led to exclude female participants and treat women's hormonal cycles as confounding variables (Pankevich et al., ch. 2). This assumption shaped multiple stages of biomedical research, including animal studies that relied primarily on male specimens (Pankevich et al., ch. 2). The Institute of Medicine reports that this practice has created a research environment in which male-centered data is generalized to female patients without any testing on whether the treatments affected men and women differently (Pankevich et al., ch. 2). According to the Institute of Medicine, this pattern reinforced women's underrepresentation while also limiting scientists' ability to detect any existing sex-based differences (Pankevich et al., ch. 2). The report concludes that women's underrepresentation comes from an embedded bias that positioned the male body as the default (Pankevich et al., ch. 2). By treating female biology as a deviation from the norm, this framework led to researchers having incomplete clinical evidence for women (Pankevich et al., ch. 2). Taken together, Liu and DiPietro Mager and the Institute of Medicine describe two different mechanisms that produce the same outcome. Liu and DiPietro Mager found an explicit regulatory rule that removed women from trials, while the Institute of Medicine identifies an implicit scientific assumption that treated women's removal as appropriate. The pervasive assumption that male physiology is representative of the human norm has systemically excluded women from clinical knowledge, which creates evidence gaps that undermine the scientific validity of medical research for females.

In contrast to research on regulatory exclusion and scientific bias, Bennett documents how policy attempted to address these disparities but with limited immediate impact. Although the NIH Revitalization Act of 1993 formally acknowledged that earlier clinical trials created evidence that was not generalizable to female patients and required the inclusion of women in federally funded research, pharmaceutical companies and trial sponsors did not immediately comply (Bennett 1). However, these reforms did not immediately change clinical trials, particularly early-phase and industry-funded trials, which continued to disproportionately enroll male participants (Bennett 2). As Bennett explains, this lag between policy reform and actual research practice allowed underrepresentation to persist even after federal mandates were introduced (Bennett 2). This persistence explains why historical exclusion continued to shape evidence for drug safety decisions for women. As a result, the evidence base for drug

safety remained male-centered even after formal policy changes (Bennett 2). The pattern of exclusion Bennett identifies reveals that changing the rules that govern who must be included within clinical trials does not automatically change the research structures and norms that kept women out of trials in the first place. This gap between policy and practice meant women did not contribute to early-phase trials where foundational data is created, perpetuating incomplete evidence even after the introduction of reforms.

Trial Design Rules That Maintain Underrepresentation

Even after policy reforms aimed at increasing female participation, structural features of clinical trial design continue to limit women's participation. Duggal et al. show that restrictive eligibility criteria limit women's participation even after policy reforms. Duggal et al. find that eligibility criteria established by regulatory agencies and trial sponsors often restrict participation in ways that disproportionately exclude women (Duggal et al. 4). Requirements based on reproductive status and hormonal stability often make women ineligible for early-phase studies (Duggal et al. 2). These criteria are often framed and justified as safeguards against reproductive harm and trial-related risk but often unintentionally narrow participant pools and thus reduce the representation of clinical trial populations (Duggal et al. 1). Overly restrictive eligibility rules for trials generate evidence that does not reflect real-world patient populations (Duggal et al. 1). Because early-phase trials establish safety benchmarks and dosing guidelines, the continued exclusion of women means that drug safety does not fully reflect female physiology (Duggal et al. 2). As a result, restrictive criteria have contributed to the development of drug safety standards that may inadequately account for sex-based differences.

Beyond formal eligibility and trial design, Holdcroft documents persistent gender bias in how participants are recruited along with how trial data is interpreted. Gender bias affects multiple stages of the scientific process, including participant recruitment, data analysis, and reporting practices (Holdcroft 1). Women are frequently excluded because of concern for reproductive risk and contraceptive requirements (Holdcroft 1). Even then, studies that do include women may fail to analyze outcomes separately by sex (Holdcroft 2). As a result, findings derived primarily from male participants are often generalized to female populations without sufficient evidence that the same results apply to women (Holdcroft 1). The gender bias in recruitment and data interpretation contributes to women's underrepresentation even in studies that formally include female participants (Holdcroft 2). By failing to disaggregate outcomes by sex, researchers effectively treat male responses as the clinical standard and obscure sex-specific differences in drug safety and efficacy.

Finally, even when women are included in clinical trials, Merone et al. find that the lack of sex-disaggregated data prevents researchers from identifying differing treatment outcomes between male and female participants. Many studies fail to report and analyze outcomes by sex, even when there are differences between male and female participants (Merone et al. 4). Reporting inconsistencies across medical disciplines often hides sex-based differences within aggregated datasets (Merone et al. 4–5). Without sex-disaggregated data, researchers cannot determine whether treatments produce different levels of effectiveness or risk for women (Merone et al. 10). This lack of transparent, sex-specific efficacy data

limits the relevance of research to women's health. Trial design, recruitment practices, and reporting conventions continue to restrict women's representation in clinical trials and prevent researchers from finding important sex-based differences. Without analyzing outcomes by sex, researchers are unable to determine whether medications are equally safe and effective for female patients, which allows male-centered evidence to persist even when women are formally included.

Drug Safety Evidence Shaped by Male-Centered Trials

Male-centered clinical trial evidence shapes drug safety through differences in drug metabolism, dosing standards derived from male participants, and minimal sex-specific analysis. Zucker and Prendergast demonstrate that sex-based biological differences in drug metabolism highlight the limitations of clinical evidence. Evidence from pharmacokinetic studies and other clinical research demonstrates that women's underrepresentation in clinical trials has shaped the gaps in drug safety evidence and dosing (Zucker and Prendergast 2). Pharmacokinetic studies show that biological differences between men and women can significantly affect how drugs are absorbed, distributed, metabolized, and eliminated (Zucker and Prendergast 3). Women often experience higher systemic drug exposure because of differences that come down to enzyme and hormonal activity (Zucker and Prendergast 3). When pharmacokinetic studies rely primarily on male participants, these variants may go unrecognized during early stages of drug development (Zucker and Prendergast 12). Medications may appear safe during testing but produce stronger effects during clinical practice in female patients (Zucker and Prendergast 2). Failing to incorporate sex-specific analysis can lead to inaccurate assumptions about dosing and safety thresholds (Zucker and Prendergast 1). This pattern shows how male-centered trial data produces dosing guidelines that do not reflect female physiology, which is the central issue identified in this review.

While Zucker and Prendergast establish that sex-based differences in drug metabolism go undetected in male-dominated trials, Mandal shows how these undetected differences directly produce unsafe dosing standards in cardiovascular drug research. Given that women often experience higher drug exposure due to differences in metabolism and enzyme activity, Mandal shows that gaps in female representation contribute directly to unsafe dosing standards in cardiovascular drug research (Mandal 3). Because early-stage trials often enroll fewer women, dosing guidelines for drug approval are frequently calibrated to male physiological responses (Mandal 2). When clinical trials establish dosing standards using predominantly male participants, female patients may experience higher drug exposure and more adverse reactions once the medication is used in practice (Mandal 3). Mandal links underrepresentation in early-stage trials and downstream prescribing practices to argue that dosing guidelines which are developed from predominantly male data can increase the risk of inaccurate dosing and adverse drug reactions in female patients (Mandal 3–4). Mandal's findings show that underrepresentation in early-stage trials goes beyond the research process. Flawed dosing data from early-stage trials carries into dosing guidelines and prescribing practices that are ultimately experienced by female patients at the point of treatment.

Sex-Specific Treatment Outcomes in Clinical Practice

Beyond dosing, male-centered clinical evidence also shapes how diseases are understood and treated in female patients, leading to care that does not reflect how conditions actually manifest in women. Warren et al. describe how sex-specific differences in disease progression reveal broader disparities in women's health outcomes (Warren et al. 3). Across multiple disease categories, including neurological disorders, autoimmune conditions, and cardiovascular disease, women experience different patterns of disease progression and symptom presentation that can result in worse health outcomes (Warren et al. 4–5). Such differences often lead to longer periods of poor health and complicated treatment plans (Warren et al. 2–3). Clinical care often does not account for how symptoms present and disease mechanisms (Warren et al. 6). The disconnect between how biomedical research is conducted and how diseases actually manifest in female patients reveals that clinical evidence lacks sex-specific validity. As a result, limited sex-specific research can lead to clinical care patterns that do not adequately reflect how diseases manifest and progress in females, which has consequences for treatment effectiveness.

Where Warren et al. show that diseases present differently in women, Vitale et al. show what happens when treatment is designed without accounting for sex-based differences. Clinical studies on disease consequences show that male-centered evidence can contribute to differences in effectiveness and complication rates for female patients (Vitale et al. 18). Differences between men and women in coronary artery disease include how the disease is presented and treatment outcomes (Vitale et al. 21). Women often have different symptom patterns than men and often have more advanced disease at diagnosis (Vitale et al. 21). Smaller coronary vessel size can influence how quickly the disease progresses and then the effectiveness of any sort of intervention (Vitale et al. 21). Since many cardiovascular treatments were initially tested primarily in male populations, sex-specific physiological differences were not always considered in treatment design (Vitale et al. 19). As a result, the lack of sex-specific evidence has contributed to higher complication rates for female patients undergoing cardiovascular treatment (Vitale et al. 18). Ultimately, these findings demonstrate that when treatment protocols fail to account for sex-specific differences documented in research, female patients face higher risks of complications during treatment.

Measuring and Correcting Sex Inequity in Trials

Efforts to address sex inequity in clinical trials focus on measuring disparities, integrating sex-specific analysis into research design, and expanding the scope of women's health research. Spiering et al. develop a quantitative framework to measure women's representation in clinical trials and propose reforms that address the structural causes of the sex inequity. According to Spiering et al, the participation-to-prevalence ratio quantitatively evaluates whether women are represented in trials relative to the severity of disease in order to evaluate structural causes of sex inequity (Spiering et al. 2). The participation-to-prevalence ratio provides a benchmark for evaluating whether clinical trials reflect the population most likely to receive the results (Spiering et al. 2). Analyses of cardiovascular research show that women remain consistently underrepresented compared to the proportion of women affected by

cardiovascular conditions in the general population (Spiering et al. 4–5). Recruitment targets based on this ratio could help ensure that clinical evidence reflects female patients' disease burden and treatment response (Spiering et al. 1). By quantifying these disparities in women's representation across multiple disease categories, researchers can pinpoint where clinical evidence fails to reflect patient populations and create accountability standards that directly address the evidence gaps and male-centered biases that have been documented in this review.

While Spiering et al. focus on representation metrics, Gualtierotti emphasizes the importance of integrating sex differences directly into research design and standards. Many diagnostic guidelines and treatment protocols have historically been developed using male evidence (Gualtierotti 1). Sex must be treated as a core variable to be analyzed rather than a secondary demographic factor (Gualtierotti 3). Specifically, Gualtierotti's framework for integration includes designing trials that are powered to detect sex-based differences (Gualtierotti 5). Trials must ensure that pharmacokinetic data is evaluated separately by sex so that differences in drug metabolization in female patients are not hidden within male and female averages (Gualtierotti 5). In addition, clinical guidelines must be updated to reflect these differences. Researchers should incorporate sex-specific dose recommendations when appropriate (Gualtierotti 5). Each of these steps matters because without them, even trials that formally include women will continue to produce male-centered evidence. Incorporating sex-based differences in drug response and progression can improve the accuracy of women's health outcomes (Gualtierotti 7). By integrating sex-stratified analysis into clinical research design and dosing research, clinical research trials can produce evidence that accurately reflects differences between male and female patients.

Ravindran et al. argue that how women's health is framed narrowly within most modern research contributes to the disparities in clinical evidence that continue to undermine safety standards and treatment effectiveness. Women's health has historically been defined by reproductive issues which has limited attention to other major health concerns that affect female populations (Ravindran et al. 1). Noncommunicable diseases such as cardiovascular disease, mental health disorders, and chronic illness make up a large part of women's diseases yet these conditions receive less targeted attention (Ravindran et al. 2). Women's health research risks overlooking broader sex-specific differences when the research focuses on reproductive topics. This narrow framing creates a compounding problem because when women's health is defined primarily around reproduction, evidence gaps form in the conditions that Ravindran et al. identify as underprioritized. Ravindran et al. show that until women's health is defined broadly enough to include the conditions most likely to harm female patients, clinical guidelines will work in too narrow of a frame. Across all five areas examined in this review, the evidence points to the same pattern: when clinical research treats male physiology as the default, the resulting evidence fails female patients at every stage, from how drugs are tested and dosed to how diseases are understood and treated.

METHODS

This literature review examines how the historical underrepresentation of women in clinical trials has contributed to sex-specific differences in drug safety and treatment outcomes. A literature review approach is suited to address this question and synthesize findings across a variety of areas within medical research, including regulatory history, trial design practices, pharmacokinetics, and clinical outcomes. No single study could encompass all these domains. Journal articles were initially identified through searches of PubMed, Google Scholar, and the Crossref database using search terms including 'women in clinical trials,' 'sex differences in pharmacokinetics,' 'sex-disaggregated data,' and 'gender bias in drug development'. This process yielded 30 sources that were screened through an annotated bibliography, of which 13 were selected for inclusion based on relevance, and 17 were excluded for being outside the scope of clinical trial design and sex-based differences. Journal articles were prioritized because they represent the most current available evidence on clinical trial design, making them the most appropriate source for a review examining the validity of medical evidence. The articles were selected based on relevance to clinical trials, drug development, and discussion of sex-based differences.

The paper organizes the literature into five distinct sections: origins of exclusion, trial design practices, drug safety evidence, clinical outcomes, and reform strategies. Origins of exclusion establishes how regulatory and scientific decisions created male-centered evidence that persisted for decades even after reform efforts. Trial design practices demonstrate how structural barriers such as restrictive eligibility criteria, recruitment bias, and aggregated reporting continue to exclude women from research. Drug safety evidence shows the dosing consequences of male-dominated trials produce pharmacokinetic gaps that leave female patients exposed to medications not calibrated to their physiology. Clinical outcomes reveal how these evidence gaps translate into higher complication rates, delayed diagnoses, and less effective treatment for female patients. Finally, reform strategies identify existing frameworks and proposed solutions, including the participation-to-prevalence ratio, sex stratified analysis requirements, and an expanded definition of women's health that together address the structural causes of sex inequity within the research pipeline. This structure reflects a progression from historical roots of sex inequity, current mechanisms, and concrete consequences. By organizing evidence this way, the review answers how women's exclusion from clinical trials translates into compromised drug safety and treatment effectiveness for female patients.

Despite covering a large body of biomedical research, this review has limitations that future researchers should consider. The most significant is that the existing literature rarely establishes direct causal links between the underrepresentation of women in trials and specific adverse outcomes, which means that this review infers those connections by synthesizing evidence across multiple studies. Future research should prioritize studies that trace specific evidence gaps to individual harms in order to establish a causal chain. Additionally, this review draws primarily from cardiovascular research because that is where the most developed body of sex-specific evidence exists. This means that findings may not fully capture how underrepresentation operates across neurological, autoimmune, and mental health conditions where the literature is thinner. Future researchers should examine whether the patterns identified hold across a

broader range of disease categories. Finally, this review does not account for how intersecting factors such as race, socioeconomic status, and geography may compound the effects of sex-based exclusion in clinical trials. Not accounting for these factors may limit the generalizability of findings across different populations of female patients.

RESULTS

This literature review considers how the historical underrepresentation of women in clinical trials has produced a male-centered evidence base that has shaped drug safety and treatment outcomes for females. First, women's exclusion from early-phase trials stems from regulatory decisions and scientific assumptions that treated male physiology as the standard. Although policy reforms acknowledged this bias, they could not immediately transform research practice. Second, contemporary trial design accentuates women's underrepresentation through restrictive eligibility criteria, recruitment bias, and failure to analyze outcomes separated by sex. Third, because trials enroll primarily male participants, women's drug exposure is often undetected and results in dosing guidelines that are not calibrated to female needs. This review documents real-world consequences and how male-centered trial data produces higher complication rates for women. However, measurable solutions exist, such as the participation-to-prevalence ratio, sex-disaggregated analysis requirements, and expanded definitions of women's health. Taken together, these findings answer the research question by demonstrating that the systematic exclusion of women from clinical trials has not remained contained to the research stage but instead has compounded across trial design, dosing standards, and clinical practice. A body of medical evidence has been produced that fails to reflect female physiology at every stage. The consequence is that female patients receive treatment built on incomplete data.

While the sources mostly converge on analysis of the existence and scope of women's underrepresentation in clinical trials, some contradictions and limitations showed up across the literature. The primary limitation is that few sources establish a causal relationship to drug outcomes. Although many sources establish that women are consistently excluded and that sex-disaggregated data is rare, fewer studies draw a direct causal line between exclusion and specific adverse drug outcomes for individual patients. Additionally, policy-focused sources tend to treat the 1993 NIH Revitalization Act as a significant turning point, while empirical studies of trial enrollment show persistent underrepresentation well into the 2000s and 2010s. These contradictions suggest that the literature has not reached consensus on how effectively existing reforms have addressed the problem, which points to a need for future research that measures whether inclusion has produced clinical evidence that reflects female physiology and improves patient outcomes.

DISCUSSION

This literature review examines how the historical underrepresentation of women in clinical trials has shaped drug safety and treatment outcomes: the origins of regulatory exclusion, excluding structural

features of trial design, the dosing consequences of male-centered evidence, treatment outcomes in practice, and proposed frameworks for correcting sex inequity. Across all areas, the literature documents a pattern in which clinical evidence is built on male-representative populations yet applied universally to female patients. The NIH Revitalization Act of 1993 represents an important regulatory milestone but failed to close the gap in sex-specific drug safety. The gap persists because policy is unable to overcome structural issues in trial design, recruitment, and conventional data reporting.

The evidence across this review points to an issue of scientific validity in clinical research. The broader significance of these findings is that sex inequity in clinical trials is a structural flaw in how medical knowledge is produced and applied. When drug safety standards are built on male physiology and used to treat everyone, the scientific validity of that evidence is compromised for female patients. This matters because clinical standards have authority: when approved dosages and protocols do not reflect female physiology, the consequences show up as adverse drug reactions and misdiagnosed symptoms. Addressing this requires reconsidering what counts as sufficient evidence for a drug to be deemed safe and effective across all patient populations.

Despite the breadth of sources within this review, several limitations in the existing literature constrain the conclusions that can be drawn. The most pressing issue is that few studies establish a direct causal link between exclusion and patient harm. Future research should prioritize studies that measure adverse drug reactions stratified by sex and trace specific evidence gaps to documented harms. The scope of available literature also shapes this review's reach: cardiovascular disease receives the most developed body of sex specific research, which means conditions such as neurological disorders, autoimmune diseases, and mental health conditions are underrepresented in the field. Expanding research into these domains is necessary for a more complete picture of how male-centered evidence affects female patients across all conditions. Finally, the existing literature focuses almost entirely on binary sex differences between male and female participants. The existing literature largely fails to examine how underrepresentation in clinical trials affects people of marginalized gender identities whose physiological profiles may not align with the binary male and female categories that clinical research relies on.

Future studies should examine how clinical trial design can be made more inclusive across the full spectrum of gender identities and whether more diverse trial leadership could improve both representation and the quality of sex-specific evidence that is produced.

CONCLUSION

This review finds that the systematic exclusion of women from early-phase clinical trials has produced a male-centered evidence base that continues to shape drug safety standards, dosing guidelines, and treatment protocols in a way that does not reflect female physiology. The more important finding is that the exclusion of women at the trial level compounds down the research pipeline. This review contributes to existing literature by tracing the chain of sex-based exclusion explicitly starting from regulatory

exclusion through trial design barriers, pharmacokinetic gaps, and clinical complication rates. In doing so, it answers the central research question by demonstrating that underrepresentation has produced medical evidence that is structurally incomplete for female patients with consequences that extend from the research stage all the way to the point of care.

Looking ahead, future research should establish clearer causal links between the underrepresentation of women in trials and adverse outcomes specifically in female patients. Trial sponsors should be required to design studies that are powered to detect sex-based differences and accordingly publish sex-disaggregated outcomes. Beyond this, research should also prioritize treatment effectiveness in female populations across multiple domains such as cardiovascular, neurological, and autoimmune. Until the evidence base reflects the full range of patients it is meant to serve, drug safety standards will remain incomplete.

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