Sex- and Gender-Based Analysis Plus in Drug Development and Health Research: Representation Gaps and Current Challenges

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Drug development and health research were built on a narrow default. For much of the twentieth century, the standard research participant 'norm' was male, and findings from that participant were assumed to apply to everyone who would eventually take the drug (Liu & DiPietro Mager, 2016). Understanding this problem requires separating two terms that are often incorrectly used interchangeably. Sex refers to biological attributes such as chromosomes and physiology, whereas gender refers to sociocultural norms, roles, and identity (Delgado et al., 2025). While sex and gender are important characteristics to consider, Canada's Sex- and Gender-Based Analysis Plus (SGBA+) framework adds the "plus" for intersecting characteristics like ethnicity, race, age, and socioeconomic status, which shape how a person experiences a drug or a health system (Brabete et al., 2022).

Applying SGBA+ is not only an equity measure but a component of good science. Delgado and colleagues (2025) argue that integrating sex and gender "prevent[s] poor research outcomes and increase[s] their generalizability" across drugs, vaccines, devices, and procedures alike. The consequences of neglecting it are concrete: of the ten prescription drugs withdrawn from the U.S. market between 1997 and 2001, eight posed greater health risks to women than men, and four did so while being prescribed at comparable rates (Brabete et al., 2022). Sex differences in adverse drug reactions span classes as varied as anticancer agents, antipsychotics, and vaccines, and they do not run in one direction; women appear in more reports overall, while men face higher risk of serious reactions (Brabete et al., 2022).

Where sex-specific data are missing, differences in drug response go unmanaged. Women reported adverse reactions to metformin significantly more often than men at two and six weeks after initiation, while neuropsychiatric reactions to the antimalarial mefloquine were more common among men (Brabete et al., 2022). Cardiovascular medicine shows the same pattern at scale: women at high risk or with established disease are less likely than men to be prescribed aspirin, statins, and ACE inhibitors, and more likely to receive diuretics (Zhao et al., 2020). Without adequate enrolment, sex-disaggregated analysis, and sufficient statistical power, these gaps cannot close, because the evidence required to close them is never generated.

This paper examines how these disparities operate from biological differences to clinical consequences, and what major gaps continue to persist.

Biological Sex as a Fundamental Aspect of Health Research

Sex and gender are increasingly recognized as fundamental determinants of health, influencing disease, susceptibility, clinical presentation, treatment response, and long-term health outcomes (Ahmed et al., 2026). Biological factors such as genetics, hormones, immune function, and physiology interact with gendered social experiences to shape health across the lifespan (Mauvais-Jarvis et al., 2020; McClain et al., 2024). Despite decades of evidence demonstrating these complex interactions, healthcare systems continue to rely on a male-centric model (Bartz et al., 2020). As a result, many health policies, diagnostic tools, and therapeutic approaches have been developed from evidence that does not adequately represent the diversity of patient populations. While awareness of these populations has grown, significant conceptual, methodological, and structural barriers continue to limit the meaningful integration of Sex and Gender Based Analysis Plus (SGBA+) throughout the research process.

Chromosomal and Hormonal Differences

Many of these sex disparities originate at the molecular level. Sex chromosomes regulate gene expression long before birth and continue to influence health throughout the lifespan. For example, although females undergo X-chromosome inactivation to balance gene dosage, this process is incomplete, with approximately 15% to one-third of X-linked genes escaping silencing (Bartz et al., 2020). The resulting expression of genes from both X chromosomes enhances pathways involving immune regulation and tumour suppression (Bartz et al., 2020; Berardi et al., 2026). In contrast, the SRY gene on the Y chromosome in males extends its influence by regulating autosomal gene expression throughout the body, shaping male-specific disease susceptibility (Bartz, 2020).

Differences in hormonal physiology further contribute to sex-specific health trajectories throughout the life course. Sex hormones influence cardiovascular function, immune responses, metabolism, and aging, creating periods of both vulnerability and protection that differ between males and females. For example, endogenous estrogens generally promote vascular health and confer cardioprotective effects before menopause, whereas testosterone has been associated with adverse cardiac effects (Mauvais-Jarvis, 2020). These physiological differences help explain variations in disease onset, progression, and clinical presentation between the sexes. Emerging evidence also suggests that males experience a faster rate of biological aging than females, contributing to a greater lifetime risk of chronic diseases such as coronary artery disease and heart failure (Liu, 2025). These biological differences demonstrate that sex is not limited to reproductive function but instead represents a fundamental regulator of health across the whole body. Policies and research frameworks that overlook these mechanisms, risk generating evidence that cannot be generalized across populations.

Consequences

One of the clearest examples of the consequences of neglecting biological sex is observed in pharmacology. Biological sex significantly influences pharmacokinetics, the absorption, distribution, and elimination of medications, as well as the pharmacodynamic response to therapy (Berardi, 2026). The analysis conducted by Berardi and colleagues (2026) found that women generally exhibit slower gastric emptying, greater body fat composition, differences in hepatic enzyme activity, and reduced renal clearance compared to men. These physiological differences alter drug responses, their efficacy, and toxicity profiles. Drug development has historically relied on evidence generated primarily from male participants, resulting in dosing recommendations that fail to account for female physiology. Consequently, women experience severe adverse drug reactions at substantially higher rates than men and are hospitalized more frequently because of medication-related complications (Berardi, 2026). These disparities illustrate how the absence of sex-specific evidence can directly compromise patient safety.

The persistence of these inequities reflects the broader “male-normative” model. Even when women are included in clinical studies, biological sex is often treated only as a demographic characteristic or statistical covariate rather than as a dynamic variable (Miller, 2014; Sarri & Hoiseth, 2026). As a result, clinically meaningful sex-specific differences remain undetected, limiting the ability of healthcare providers to deliver personalized care.

Underrepresentation of Women in Health Research

Historical Underrepresentation

Exclusion was once a formal policy. After the thalidomide tragedy, the U.S. Food and Drug Administration (FDA) issued guidance in 1977 excluding women of “childbearing potential” from Phase I and early Phase II trials except in life-threatening conditions, a category defined broadly enough to capture any woman capable of becoming pregnant (Liu & DiPietro Mager, 2016). The FDA lifted that guidance in 1993, Congress mandated the inclusion of women and minorities in NIH-sponsored research the same year, and a 1998 rule required new drug applications to present safety and efficacy data by sex (Liu & DiPietro Mager, 2016). In Canada, the Canadian Institutes of Health Research (CIHR) made SGBA mandatory in grant applications in 2010 and, in 2018, required peer reviewers to rate sex and gender integration in each application (Chen et al., 2016).

Current State of Representation

Currently, the shortfall appears at two stages: who is included in research, and whether the data is analyzed effectively. Across all FDA-regulated studies from 2015 to 2019, women made up 49% of 292,766 participants, yet only about one-third of participants in cardiovascular trials (Carland et al., 2022). These gaps are not confined to cardiology. Across 20,020 US clinical trials enrolling roughly 5.11 million participants between 2000 and 2020, female representation fell short of the corresponding burden of disease in oncology, neurology, immunology, and nephrology, while cardiology and pediatrics showed the strongest negative association with female enrolment of any field (Steinberg et al., 2021). Raw percentages understate the problem because they ignore disease prevalence between the sexes. The participation-to-prevalence ratio (PPR) corrects for this by dividing the proportion of women in a trial by the proportion of women in the disease population, where 0.8 to 1.2 indicates adequate representation (Burgess et al., 2025). This disparity matters because it indicates that enrolment gaps track research cultures and trial design rather than any fixed property of a disease. Most trials are not powered to detect sex-specific outcomes, so findings are generated post hoc through underpowered subgroup analyses (Carland et al., 2022).

Barriers to Representation

Barriers operate at all levels of the research process. Women report a greater perceived risk of harm from participation, with decisions shaped by financial stability, education, and social environment (Tobb et al., 2022). Distrust rooted in the historical exploitation of women and minority groups further depresses enrolment among underrepresented minority women, who experience the highest cardiovascular mortality (Burgess et al., 2025; Tobb et al., 2022). Burgess et al. (2025) also conclude that under-representation of women as trial investigators is independently associated with under-recruitment of women as participants.

Funding and oversight are large factors in representation as well. A preprint analysis by Chen and colleagues (2026) found that only 11.33% of CIHR cardiovascular grant records from 2000 to 2024 were women-related projects, and that application-level SGBA requirements had limited influence on investment patterns, whereas the 2018 reviewer-level guidance aligned with a subsequent acceleration in funding. This suggests that requirements tied to the evaluation stage may shift behaviour more effectively than self-reported compliance, which ties directly into federal strategy design. Research ethics committees, meanwhile, lack tools to assess how sex, gender, and intersectional dimensions should be integrated, so brief mentions of sex in a protocol are often accepted as sufficient (Delgado et al., 2025).

Clinical Consequences of Sex Disparities

With the persistent male-normative model, women continue to face detrimental clinical outcomes (Mauvais-Jarvis et al., 2020). Compared to men, women spend 25% more years in poor health (Warren et al., 2025). Sex specific conditions such as menopause account for only 5% of women's health burden, whereas 56% arises from diseases that disproportionately affect women, as they present differently in women and there is insufficient sex-specific data to inform clinical practices (Warren et al., 2025). In a scoping review, researchers found significant scarcity of gender- and sex-disaggregated data across five different conditions, revealing that a concerning lack of data makes it challenging to address disparities in diagnostic accuracy and develop evidence-based solutions (Upadhyay et al., 2025). The lack of inclusion of women in clinical trials and medical research subsequently results in interventions and protocols that do not adequately address their needs (Warren et al., 2025). Crucially, diagnostic disparities are inextricably linked to risks in drug development when diseases are misidentified or missed, creating a flawed epidemiological foundation for pharmacological research that does not prioritize the female population.

Sex Differences in Clinical Presentation

Biological sex, driven by genetic heterogeneity and hormonal regulation, together with gender as a social construct, influences how diseases manifest and are experienced differently in women (Mauvais-Jarvis et al., 2020). Sun et al. (2023) conducted a comprehensive systematic analysis of sex differences in disease diagnosis across 208 million patients with over a hundred acute and chronic diseases. The researchers found that women were consistently older than men when first diagnosed, potentially due to differential disease presentation (Sun et al., 2023). Westergaard et al. (2019) conducted a similar study, analyzing health records for almost 7 million men and women from the Danish population and found substantive sex differences in disease incidence, age at diagnosis, and disease trajectory between men and women.

In cardiovascular health, women are less likely than men to receive a pre-hospital diagnosis of myocardial infarction, as they do not present with classic symptoms. Women commonly experience pain between the shoulder blades, nausea or vomiting, and shortness of breath rather than typical chest pain (Mauvais-Jarvis et al., 2020; Sun et al., 2023). Additionally, men commonly have larger visible blockages in coronary arteries than women, and premenopausal women's hearts develop less fibrosis than men's (Al Hamid et al., 2024; Mauvais-Jarvis et al., 2020). Despite these differences, as clinicians are trained to diagnose based on male-presenting symptoms, they often fail to recognize heart attacks in women, leading to a higher mortality rate in women related to heart diseases (Sun et al., 2023). Similarly, in respiratory illness, women with chronic obstructive pulmonary disease are often misdiagnosed despite the female lung being more susceptible than the male lung (Mauvais-Jarvis et al., 2020). From a neurological perspective, women have a worse clinical course and outcomes in Alzheimer's disease and related dementias, migraines, and stroke (Warren et al., 2025). However, the role of sex differences affecting the physiological course of neurodegenerative diseases is still an emerging field (Warren et al., 2025). Evidently, sex differences exist in disease presentation, yet the translation of this evidence into a sex-specific diagnostic framework and treatment is limited, highlighting the importance of integrating SGBA+ in medical research.

Gender and Sex Bias in Diagnosis and Treatment

Women receive fewer disease diagnoses than men after diagnostic evaluation, even when presenting with common somatic symptoms (Ballering et al., 2022). In primary care, women are

also less likely to undergo physical examinations, diagnostic imaging, and referrals (Ballering et al., 2022). In most diseases, diagnostic criteria remain incomplete because they are informed by pathophysiology based on men, giving rise to the "*Yentl Syndrome*" where a women must exhibit male-presenting symptoms to receive an accurate diagnosis (Mauvais-Jarvis et al., 2020; Alcalde-Rubio et al., 2020). These limitations lead to a diagnostic delay, where women experience longer intervals between symptom onset and diagnosis (Sun et al., 2023).

Diagnostic inequities have downstream consequences that influence treatment decisions, medication safety, and overall health outcomes for women. For example, although more women are diagnosed with chronic pain syndromes, their concerns and symptoms are taken less seriously, minimizing their pain as 'non-existent' or as a psychic issue (Samulowitz et al., 2018). Gender bias creates immediate consequences for pharmaceutical intervention, causing women to receive less pain medication and more antidepressants rather than somatic pain relief provided to their male counterparts (Samulowitz et al., 2018). Misdiagnosis exposes women to side effects of medications for conditions they may not have, while leaving underlying pathologies untreated. This representation gap and gender bias is further compounded in clinical trials, where evidence informing drug dosing, efficacy, and safety has largely been derived from the male population (Carey et al., 2017). Treating women based on male-centric norms has been catastrophic, evidenced by the drug safety history between the years of 1977 and 2000, where eight out of the ten prescription drugs withdrawn from the market posed a significantly greater risk to women (Carey et al., 2017). Ultimately, diagnostic inequities and research disparities create a harmful medical continuum where women not only wait longer for a diagnosis but are also treated with interventions and medications that have not been adequately validated for their physiology.

Intersectional Analysis Beyond Sex and Gender

When current studies look to implement SGBA + policies, they tend to find success in the number of women enrolled to participate. In a study by Rotz and colleagues (2022), they interviewed researchers who implied that simply checking off the male and female criteria for their population was enough to consider gender and equity issues surrounding the underrepresentation of certain populations. Many consider inclusion as a binary of men and women, interpreting them as opposite ends of a spectrum, without considering the potential overlap between these categories. Not only this, but they underestimate the influence of intergroup variation (Ritz, 2025). For instance, Ruben and Stosic (2024) illustrated this by studying participants' perceptions of a patient's pain when the patient's gender and race were known. Overall, the pain felt by women and people of colour was underestimated more than men's and white people's, respectively. Yet, women of colour faced the most bias when estimating their pain. From this arises a need to consider more than just gender, but other factors than influences patient identity.

<u>Diversity in Drug Development</u>

Intersectionality is a framework to consider when addressing this problem. It often incorporates social structures alongside gender to understand the barriers experienced by people from different minority communities. Using this helps others acknowledge systemic privileges and oppression based on their overlapping identities. These identities could range from gender, race, age, disability, sexual orientation, socioeconomic status, or language (Health Canada,

2025). These factors can lead to within-group variation, and without this knowledge, only surface-level solutions are used that may not apply to entire target populations. Yet even when intersectionality is considered, further gaps arise through the underrepresentation of these groups. For example, Khadraoui and colleagues (2023) found that the odds of women of Asian, black and Hispanic descent enrolling in a gynecological cancer clinical trial were lower compared to white women. Moreover, white women were considered overrepresented within these trials.

When researchers, specifically in drug development, treat women as a simple homogeneous population, they do not account for the innate differences within this population. Simply adding more women as participants in trials does not solve the problem. As mentioned, Steinberg and colleagues (2021) found that between 2000 and 2020, sex reporting had improved, yet with this, women were still underrepresented in several disease areas. For example, in neurology, where women's disease burden is 56%, they only accounted for 53% of trial participants. Thus, barriers to accessing safe and efficient treatment based on race, age, and socioeconomic status are not recognized. Health Canada (2022) uses disaggregated data to test the safety and efficacy of health products. They wish to verify that diversity of clinical trial participants reflects those who will actually use the product. Researchers also argue that clinical trial exclusion criteria are based on anticipatory motherhood, even if healthy individuals are not pregnant and have no intention of becoming pregnant (Cottingham & Fisher, 2022), showing a need for representative and unbiased samples. Thus, an intersectional lens is needed to improve this issue.

Policy Gaps

A key challenge to implementing an intersectional approach, even with the SGBA framework, is to move beyond sex and gender and the collection of demographic attributes to more scientific evidence that would serve these underrepresented populations. Even with the increased awareness to have diversity within samples and increase women's participation within clinical trials, valuable demographic information is collected without sufficient analysis of results, as Aulakh and colleagues suggest (2007). In this study, they analyzed the results of 169 randomized controlled trials and found that only 53% performed a sex and gender subgroup analysis, with only 35% performing them accurately. If results of an intersectional demographic are under- or overinterpreted, they can directly influence the potential safety and efficacy of certain medication across populations. Yet with these accurate analyses come further challenges with the need for a larger sample size and additional resources to recruit diverse populations. This was seen in a review by Duma and colleagues (2018), which explained the decrease in recruitment of minorities for cancer clinical trials over 14 years. Generating evidence while understanding the constraints of a clinical trial illustrates the strain of implementing intersectionality within drug development.

Conclusions

Sex and gender-based disparities in healthcare are not isolated issues but interconnected challenges that emerge throughout the research process, from intersectional participant recruitment to diagnosis, treatment and clinical outcomes. As this paper demonstrates, the historical underrepresentation of women, the limited use of sex-disaggregated analyses, and the

continued reliance on male-centred models have contributed to evidence that does not fully reflect the populations it is intended to serve. Although Canada has made important progress through the implementation of Sex and Gender Based Analysis Plus (SGBA+), meaningful integration remains inconsistent.

Addressing these gaps requires more than increasing the number of women included in research. Sex, gender, and other intersecting factors must be considered as more than a characteristic but as a dynamic variable that influences health outcomes. Ultimately, SGBA+ policies are essential not only for advancing equity, but for improving the quality, reliability, and applicability of health research for everyone.

References

Ahmed, S. B., Becker, J. B., Bruno, K. A., Dumanski, S. M., Galea, L. A. M., Kundakovic, M., Raznahan, A., Tronson, N. C., & Cunningham, R. L. (2026). Twenty years of sex and gender science in health research: A policy statement from the Organization for the Study of Sex Differences. Biology of Sex Differences, 17(1), 85. https://doi.org/10.1186/s13293-026-00894-w

Al Hamid, A., Beckett, R., Wilson, M., Jalal, Z., Cheema, E., Al-Jumeily OBE, D., Coombs, T., Ralebitso-Senior, K., & Assi, S. (2024). Gender bias in diagnosis, prevention, and treatment of cardiovascular diseases: A systematic review. *Cureus*, *16*(2), e54264. https://doi.org/10.7759/cureus.54264

Alcalde-Rubio, L., Hernández-Aguado, I., Parker, L. A., Bueno-Vergara, E., & Chilet-Rosell, E. (2020). Gender disparities in clinical practice: Are there any solutions? Scoping review of interventions to overcome or reduce gender bias in clinical practice. *International Journal for Equity in Health*, *19*(1). https://doi.org/10.1186/s12939-020-01283-4

Aulakh, A. K., & Anand, S. S. (2007). Sex and Gender Subgroup Analyses of Randomized Trials: The Need to Proceed With Caution. Women's Health Issues, 17(6), 342–350. https://doi.org/10.1016/j.whi.2007.04.002

Bartz, D., Chitnis, T., Kaiser, U. B., Rich-Edwards, J. W., Rexrode, K. M., Pennell, P. B., Goldstein, J. M., O'Neal, M. A., LeBoff, M., Behn, M., Seely, E. W., Joffe, H., & Manson, J. E. (2020). Clinical Advances in Sex- and Gender-Informed Medicine to Improve the Health of All: A Review. JAMA Internal Medicine, 180(4), 574. https://doi.org/10.1001/jamainternmed.2019.7194

Ballering, A. V., Rosmalen, J. G. M., & Hartman, T. C. (2022). Differences between women and men are present in the rate of diagnosed diseases after a diagnostic intervention is conducted in primary care. *The Journal of the American Board of Family Medicine*, *35*(1), 73–84. https://doi.org/10.3122/jabfm.2022.01.210289

Berardi, R., Liguori, C., & Rossi, F. (2026). Gender Oncology: Rethinking Cancer Through a Sex- and Gender-Based Lens. Journal of Clinical Medicine, 15(14), 5435. https://doi.org/10.3390/jcm15145435

Brabete, A. C., Greaves, L., Maximos, M., Huber, E., Li, A., & Lê, M.-L. (2022). A Sex- and Gender-Based Analysis of Adverse Drug Reactions: A Scoping Review of Pharmacovigilance Databases. Pharmaceuticals, 15(3), 298. https://doi.org/10.3390/ph15030298

Burgess, S., Zaman, S., Towns, C., Coylewright, M., & Cader, F. A. (2025). The under-representation of women in cardiovascular clinical trials: State-of-the-art review and ethical considerations. American Heart Journal, 282, 81–92. https://doi.org/10.1016/j.ahj.2024.12.011

Carland, C., Hansra, B., Parsons, C., Lyubarova, R., & Khandelwal, A. (2022). Adequate enrollment of women in cardiovascular drug trials and the need for sex-specific assessment and reporting. American Heart Journal Plus: Cardiology Research and Practice, 17, 100155. https://doi.org/10.1016/j.ahjo.2022.100155

Carey, J. L., Nader, N., Chai, P. R., Carreiro, S., Griswold, M. K., & Boyle, K. L. (2017). Drugs and Medical Devices: Adverse Events and the Impact on Women's Health. *Clinical Therapeutics*, *39*(1), 10–22. https://doi.org/10.1016/j.clinthera.2016.12.009

Chen, N., Kendall, T., Zhang, W., & Brotto, L. A. (2016). Women-related cardiovascular research funding under Canada's Sex- and Gender-Based Analysis policy from 2000 to 2024: An interrupted time series analysis.

Cottingham, M. D., & Fisher, J. A. (2022). Gendered Logics of Biomedical Research: Women in U.S. Phase I Clinical Trials. Social Problems, 69(2), 492–509. https://doi.org/10.1093/socpro/spaa035

Delgado, J., Abadía, M. C., Akyüz, K., Goisauf, M., & Rodríguez-Arias, D. (2025). Uncovering the persistent gap: The ongoing challenge of integrating sex and gender in biomedical

research. Journal of Biomedical Research, 39(1), 18. https://doi.org/10.7555/JBR.38.20240157

Duma, N., Vera Aguilera, J., Paludo, J., Haddox, C. L., Gonzalez Velez, M., Wang, Y., Leventakos, K., Hubbard, J. M., Mansfield, A. S., Go, R. S., & Adjei, A. A. (2018). Representation of Minorities and Women in Oncology Clinical Trials: Review of the Past 14 Years. Journal of Oncology Practice, 14(1), e1–e10. https://doi.org/10.1200/JOP.2017.025288

Health Canada. (2022, October 3). Guide: Disaggregated data questionnaire for drug submissions in Canada [Guidance]. https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/clinical-trials/disaggregated-data-questionnaire-submissions.html

Health Canada. (2025, December 19). Draft guidance document for clinical trial sponsors: SGBA plus demographics action plan in clinical trial applications [Consultations]. https://www.canada.ca/en/health-canada/programs/consultation-modernizing-framework-clinical-trials/draft-guidance-document-sponsors-sgba-plus-demographics-action-plan-applications.html

Khadraoui, W., Meade, C. E., Backes, F. J., & Felix, A. S. (2023). Racial and Ethnic Disparities in Clinical Trial Enrollment Among Women With Gynecologic Cancer. JAMA Network Open, 6(12), e2346494. https://doi.org/10.1001/jamanetworkopen.2023.46494

Liu. (2025). Sex differences in cardiovascular disease risk and the role of biological aging pace.

Liu, K. A., & DiPietro Mager, N. A. (2016). Women's involvement in clinical trials: Historical perspective and future implications. Pharmacy Practice, 14(1), 708–708. https://doi.org/10.18549/PharmPract.2016.01.708

Mauvais-Jarvis, F., Bairey Merz, N., Barnes, P. J., Brinton, R. D., Carrero, J.-J., DeMeo, D. L., De Vries, G. J., Epperson, C. N., Govindan, R., Klein, S. L., Lonardo, A., Maki, P. M.,

McCullough, L. D., Regitz-Zagrosek, V., Regensteiner, J. G., Rubin, J. B., Sandberg, K., & Suzuki, A. (2020). Sex and gender: Modifiers of health, disease, and medicine. The Lancet, 396(10250), 565–582. https://doi.org/10.1016/S0140-6736(20)31561-0

McClain, A. K., Monteleone, P. P., & Zoldan, J. (2024). Sex in cardiovascular disease: Why this biological variable should be considered in in vitro models. Science Advances, 10(19), eadn3510. https://doi.org/10.1126/sciadv.adn3510

Ritz, S. A. (2025). Limitations of the Male/Female Binary for Studying the Influences of Sex- and Gender-Related Factors on Health. American Journal of Human Biology, 37(5), e70064. https://doi.org/10.1002/ajhb.70064

Rotz, S., Rose, J., Masuda, J., Lewis, D., & Castleden, H. (2022). Toward intersectional and culturally relevant sex and gender analysis in health research. Social Science & Medicine, 292, 114459. https://doi.org/10.1016/j.socscimed.2021.114459

Ruben, M. A., & Stosic, M. D. (2024). Documenting Race and Gender Biases in Pain Assessment and a Novel Intervention Designed to Reduce Biases. The Journal of Pain, 25(9), 104550. https://doi.org/10.1016/j.jpain.2024.104550

Samulowitz, A., Gremyr, I., Eriksson, E., & Hensing, G. (2018b). “Brave Men” and “Emotional Women”: A Theory-Guided Literature Review on Gender Bias in Health Care and Gendered Norms towards Patients with Chronic Pain. *Pain Research and Management*, *2018*, 1–14. https://doi.org/10.1155/2018/6358624

Steinberg, J. R., Turner, B. E., Weeks, B. T., Magnani, C. J., Wong, B. O., Rodriguez, F., Yee, L. M., & Cullen, M. R. (2021a). Analysis of Female Enrollment and Participant Sex by Burden of Disease in US Clinical Trials Between 2000 and 2020. JAMA Network Open, 4(6), e2113749. https://doi.org/10.1001/jamanetworkopen.2021.13749

Steinberg, J. R., Turner, B. E., Weeks, B. T., Magnani, C. J., Wong, B. O., Rodriguez, F., Yee, L. M., & Cullen, M. R. (2021b). Analysis of Female Enrollment and Participant Sex by

Burden of Disease in US Clinical Trials Between 2000 and 2020. JAMA Network Open, 4(6), e2113749. https://doi.org/10.1001/jamanetworkopen.2021.13749

Sun, T. Y., Hardin, J., Nieva, H. R., Natarajan, K., Cheng, R.-F., Ryan, P., & Elhadad, N. (2023). *Large-scale characterization of gender differences in diagnosis prevalence and time to diagnosis* [Preprint]. *medRxiv*. https://doi.org/10.1101/2023.10.12.23296976

Tobb, K., Kocher, M., & Bullock-Palmer, R. P. (2022). Underrepresentation of women in cardiovascular trials- it is time to shatter this glass ceiling. American Heart Journal Plus: Cardiology Research and Practice, 13, 100109. https://doi.org/10.1016/j.ahjo.2022.100109

Upadhyay, V., Gangwar, R., Chappuis, G. L., & Kohli, M. (2025). Lack of sex- and gender-disaggregated data in diagnostics: Findings from a scoping review of five tracer conditions. *Frontiers in Public Health*, *12*. https://doi.org/10.3389/fpubh.2024.1484873

Warren, A., Garrett, K., & Frame, L. A. (2025). Disparities in women's health and clinical considerations from a translational science perspective: A narrative review and framework for future directions. *Women's Health*, *21*. https://doi.org/10.1177/17455057251399009

Westergaard, D., Moseley, P., Sørup, F. K. H., Baldi, P., & Brunak, S. (2019). Population-wide analysis of differences in disease progression patterns in men and women. *Nature Communications*, *10*(1). https://doi.org/10.1038/s41467-019-08475-9

Zhao, M., Woodward, M., Vaartjes, I., Millett, E. R. C., Klipstein-Grobusch, K., Hyun, K., Carcel, C., & Peters, S. A. E. (2020). Sex Differences in Cardiovascular Medication Prescription in Primary Care: A Systematic Review and Meta-Analysis. Journal of the American Heart Association, 9(11), e014742. https://doi.org/10.1161/JAHA.119.014742