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Integrating Sex and Gender in Medical Research: SAGER Guidelines

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Cisapride, a gastroprokinetic drug prescribed for gastroesophageal reflux at the time, was approved in 1993. While cisapride was in the market, until 1999, 341 patients experienced cardiac arrhythmias. Sixty percent of the cisapride users were women who are more susceptible to QT prolongation and torsades de pointes (1). In the end, cisapride was withdrawn from the market by the United States Food and Drug Administration in 2000; making it a symbolic case for the harmful consequences of preclinical research which neglects sex differences.

Highlights

- **Gender/sex bias persists in preclinical and clinical research.**
- **Ignoring gender/sex in research can lead to harmful clinical outcomes.**
- **SAGER Guidelines ensures research equity, transparency, and scientific rigor.**
- **SAGER Guidelines may help correct structural gaps in health-related evidence.**

In 1990s, despite several institutions' mandates for the inclusion of females in clinical trials, the practice of excluding female participants and failure to analyze the results by sex remained widely unchanged (2). In 2011, Beery and Zucker's study underlined the male bias in preclinical studies, showing that most studies reported only male animals (3). It was considered to be the main reason behind several drugs' asymmetrical harm to women, such as cisapride (2). After 2000s, sex differences in health drew more attention, with Legato saying "Women are not just small men." (4). Legato revealed how the male-centric bias in biomedical research had systematically compromised the diagnosis, treatment, and care of women. On the other hand, due to sex bias, diseases like osteoporosis were perceived as women's diseases, leaving men with osteoporosis underdiagnosed and undertreated (5).

In 2012 European Association of Science Editors (EASE) founded a Gender Policy Committee. After three years of hard work, the committee published the Sex and Gender Equity in Research (SAGER) Guidelines in 2015 (6). The guidelines proposed a comprehensive framework for reporting sex and gender information at all stages of research, including study design, data analysis, results, and interpretation (6). It emphasized the importance of sex-disaggregated data while stating the necessity of justifying the exclusion of one sex or the failure to perform sex-based analyses (6).

SAGER guidelines were created in response to a need. However, it was being underused. Thus, in 2022, Van Epps and colleagues published a review containing two checklists of the SAGER Guidelines, one for human studies and one for animal studies (7). The aim was to improve research transparency, promote research equity, and standardize the expectations of editors and reviewers.

First of all, SAGER Guidelines checklist requires the proper use of the terms "sex" and "gender" (7). Sex refers to the biological aspects of being female or male. Instead, gender is a social construct that is self-defined as woman, man, or non-binary. Gender interacts with sex, affecting both health and disease (2). Secondly, if only one sex and/or gender is included in the research, the Checklist requires a title and an abstract that specify the sex and/or gender of participants. For the introduction section of research papers, it calls for mentioning whether sex and/or gender differences are expected based on prior evidence. Methods section should state how sex and/or gender are defined and measured, and justify the inclusion or exclusion of sexes or genders. Results should be disaggregated by sex and/or gender whenever possible. Sex and/or gender-based analyses should be reported even if they are not statistically significant. Discussion section should address the implications of sex and/or gender specific findings. In case sex and/or gender-based analyses are not done, the discussion section should provide the rationale.

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The World Health Organization (WHO) formally adopted the SAGER Guidelines in 2023, along with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) Statement. This initiative was part of the WHO's broader Roadmap to Advance Gender Equality, Human Rights, and Health Equity (2023–2030). It aims to enhance the scientific quality, transparency, and relevance of global health data; by endorsing these frameworks. WHO now requires sex and gender-disaggregated data, recognizing that sex and gender are not secondary variables but essential to evidence-based, equitable healthcare. Inclusion of sex and gender enhances both scientific rigor and the generalizability of health research outcomes (8).

Unfortunately, major treatment guidelines of psychiatry, like the American Psychiatric Association's and National Institute for Health and Care Excellence, do not have sex/gender-based recommendations. However, scientific evidence shows that women and men often respond to psychopharmacological treatments differently. For instance, women may respond to lower doses of antipsychotics, whereas certain antidepressants may cause more side effects in men (9,10). The lack of systematic incorporation of these differences into clinical guidelines reflects a structural gap: the failure to integrate sex into treatment protocols. That is precisely where the SAGER Guidelines can offer a valuable framework—not only for scientific reporting but also for updating clinical standards. As SAGER emphasizes; disaggregating, analyzing, and interpreting data by sex is essential not only for scientific accuracy but also for treatment efficacy and patient safety. Given that clinical guidelines shape real-world medical decisions, the exclusion of sex-based evidence from these documents constitutes not merely a scientific omission but a silent driver of inequality in healthcare.

REFERENCES

1. Wysowski DK, Corken A, Gallo-Torres H, Talarico L, Rodriguez EM. Postmarketing reports of QT prolongation and ventricular arrhythmia in association with cisapride and Food and Drug Administration regulatory actions. Am J Gastroenterol. 2001;96(6):1698–1703. [Crossref]
2. Mauvais-Jarvis F, Bairey Merz N, Barnes PJ, Brinton RD, Carrero JJ, DeMeo DL, et al. Sex and gender: Modifiers of health, disease, and medicine. Lancet. 2020;396(10250):565–582. [Crossref]
3. Beery AK, Zucker I. Sex bias in neuroscience and biomedical research. Neurosci Biobehav Rev. 2011;35(3):565–572. [Crossref]
4. Legato MJ. Eve's rib: The new science of gender-specific medicine and how it can save your life. Harmony Books; 2002.
5. Watts NB, Adler RA, Bilezikian JP, Drake MT, Eastell R, Orwoll ES et al. Osteoporosis in men: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010;95(6):2056–2065. [Crossref]
6. Heidari S, Babor TF, De Castro P, Tort S, Curno M. Sex and Gender Equity in Research: rationale for the SAGER guidelines and recommended use. Res Integrity Peer Rev. 2016;1:2. [Crossref]
7. Van Epps H, Astudillo O, Del Pozo Martin Y, Marsh J. The Sex and Gender Equity in Research (SAGER) guidelines: Implementation and checklist development. Eur Sci Ed. 2022;48:e86910. [Crossref]
8. Heidari S, Fernandez DGE, Coates A, Hosseinpoor AR, Asma S, Farrar J et al. WHO's adoption of SAGER guidelines and GATHER: setting standards for better science with sex and gender in mind. Lancet. 2024;403(10423):226-228 [Crossref]
9. Seeman MV. The Pharmacodynamics of Antipsychotic Drugs in Women and Men. Front Psychiatry. 2021;12:650904. [Crossref]
10. LeGates TA, Kvarta MD, Thompson SM. Sex differences in antidepressant efficacy. Neuropsychopharmacology. 2019;44(1):140-154. [Crossref]