

Viewpoints

Absence of evidence is not evidence of absence: encouraging gender analyses in scholarly publications

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Abstract Sex and gender differences influence health risks, disease progression and treatment outcomes. Owing to the underrepresentation of females as subjects in medical research, current clinical management of women is less evidence-based than for men. Gender analysis is also underrepresented in the scientific literature. The dissemination of sex-specific results is critical for ensuring that women and men equally attain the highest standards of health. Editors and publishers can play a major role in making the paradigm of scientific publishing more comprehensive. Guidelines on manuscript preparation, instructions for authors and peer reviewers set the bar for good standards of reporting, and inclusion of a policy on sex-disaggregated data and gender analysis should not be amiss here.

Keywords Gender analysis; sex differences; editorial policies; peer reviewers; editors' role; publishers' responsibility.

Sex matters in health

Differences between men and women affect health risks, disease progression and treatment outcomes that span the breadth of human physiology. For example, HIV-infected women are reported to progress at lower viral load compared with men, and present higher CD4+ T-cell counts at seroconversion, AIDS diagnosis and AIDS-related death.^{1,2} Variations also exist in treatment response. A systematic review and meta-analysis of studies into the effects of aspirin on the risk of myocardial infarction supported the concept that women are less responsive to aspirin than men and that sex influences the efficacy of aspirin in reducing myocardial infarction rate.³ Many of the drug-related differences can be explained by differences in pharmacokinetics and pharmacodynamics. In practice, however, treatment strategies and drug dose adjustments often neglect sex differences.⁴

The social realm of wellbeing

Many of the observed differences are a result of not only sex-specific physiological and biological differences, but also social and behavioural factors. "Sex" is often used to differentiate males and females based on specific biological characteristics. "Gender", on the other hand, refers to the social determinants associated with acquired identity of femininity and masculinity, which are shaped by the cultural and social environment.⁴

Several studies suggest an impact of gender on health. In a study from Nigeria, gender affected access to HIV treatment. The study showed how women's ability to make

health-related decisions was shaped by structures of financial inequality, authority relations and social norms.

Gender analysis is of particular importance to the settings and populations with marked gender differences. Extrapolation and generalization of study results obtained from male-dominated cohorts to women as well as the absence of gender analysis may lead to suboptimal clinical management and potentially less favourable health outcomes. Medicine as it is practised today is less evidence-based when applied to women than to men.

Data analysis and reporting

The scientific literature is marked by the low inclusion of gender analyses in published studies. An analysis of randomized controlled clinical trials published in nine leading medical journals in 2004 showed that roughly 13% of the articles presented sex-disaggregated data or included sex as a covariate in multivariable statistical models.⁶ A follow-up study in 2009 revealed that this trend had improved marginally: 75% of the analyzed articles still failed to report data disaggregated by sex.⁷ Similar trends have been reported in specialist fields, such as cardiovascular medicine, where sex differences have a profound effect.^{3,8} In fact, of 645 cardiovascular trials published in 2004, only 24% reported sex-specific results. Interestingly, those studies funded by the National Institutes of Health, which have a clear mandate on gender inclusion and reporting, were significantly more likely to report outcomes disaggregated by sex.⁸ The same lack of gender analysis is observed in reports presented as conference abstracts. For example, of 34,000 abstracts submitted to 17 HIV/AIDS conferences between 2003 and 2009, only 13.7% were specifically related to women.⁹ It is, however, encouraging to see an increase of abstracts addressing the needs of women and girls for the International AIDS Society and International AIDS Conferences from 15% to 33.5% between 2009 and 2011, possibly due to the implementation of a gender policy and a women's research award (personal communication, International AIDS Society 2011).

One of the underlying factors for the lack of reporting on sex and gender differences is the underrepresentation of women in clinical trials, and the fact that most studies are not sufficiently powered from the outset to allow significant sex differences to be detected. Historically, a common reason for excluding women from clinical trials have been a risk of potential harm to the foetus and avoiding menstrual hormonal variations, thereby minimizing heterogeneity of the study population, which affects the size and complexity of a study impacting on cost and time requirements.¹⁰ A study

of phase I trial data for new molecular entities approved by the US Food and Drug Administration in 2006 and 2007 confirmed that women remain underrepresented.¹¹

Despite increasing efforts to encourage women's participation in clinical trials, investigators either fail to carry out gender analysis or do not report available data. Moreover, international guidelines and instructions for authors of scholarly publications do not specify how gender differences should be reflected in the submissions. Manuscript preparation guidelines can serve as a vital source of support for this cause. As d'Arminio Monforte and colleagues emphasize in their recent opinion piece in AIDS "the incorporation of a recommendation for including women in clinical trials and reporting female subanalyses in the CONSORT guidelines would encourage the transparent reporting of clinical trials... CONSORT should also recommend that a minimum percentage of female participants be included in studies that are not related to sex-specific problems".¹²

Time for editorial action

Investigators, ethical review boards, funding bodies, the pharmaceutical industry, regulators, peer reviewers and journal editors should facilitate equality for subpopulations involved in research studies. An active commitment in this direction is needed at all stages of research, from study design to the development of guidelines and reporting. Editors and publishers can play a major role through professional leadership.

Guidelines on manuscript preparation, instructions for authors and peer reviewers set the bar for high standards of reporting and inclusion of a policy on sex-disaggregated data and gender analysis is overdue. As a first step, the *Journal of the International AIDS Society* has adopted an editorial policy strongly encouraging provision of data disaggregated by sex (and race if applicable) and gender analysis.¹³ Nature Publishing Group also considers sex and gender information mandatory for its scholarly publications.¹⁴ In addition, a recent Gender Summit held in Brussels highlighted gender issues in scientific research and publications, including how editorial policies can improve gender equality by increasing our knowledge on the impact of sex and gender on health.¹⁵

Conclusion

Both men and women are entitled to benefit equally from the highest attainable standards of healthcare. Collection, analysis and reporting of clinical data that takes differences between subpopulations into account are an integral part of ensuring this fundamental human right for all. Comparable inclusion and publication of relevant results remain an urgent health priority. Scholarly journals now exist that are entirely devoted to these issues, eg *Biology of Sex Differences* and *Gender Medicine*. However, gender mainstreaming throughout the scholarly literature is required.

Peer reviewers, editors and publishers are encouraged to put more efforts into implementing changes to increase reporting of differences between subpopulations in peer-reviewed publications. Learned associations may facilitate improvements in editorial policies and move from discussions to actions.

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References

- Prins M, Robertson JR, Brettle RP, Aguado IH, Broers B, Boufassa F, Goldberg DJ, Zangerle R, Coutinho RA, van den Hoek A. Do gender differences in CD4 cell counts matter? AIDS (London, England) 1999;13(17):2361-2364.
- Napravnik S, Poole C, Thomas JC, Eron JJ Jr. Gender difference in HIV RNA levels: a meta-analysis of published studies. Journal of Acquired Immune Deficiency Syndromes 2002;31(1):11-19.
- Yerman T, Gan WQ, Sin DD. The influence of gender on the effects of aspirin in preventing myocardial infarction. BMC Medicine 2007;5:29. doi: 10.1186/1741-7015-5-29
- Carrero JJ. Gender differences in chronic kidney disease: underpinnings and therapeutic implications. Kidney & Blood Pressure Research 2010;33(5):383-392. doi: 10.1159/000320389
- Mbonu NC, Van den Borne B, De Vries NK. Gender-related power differences, beliefs and reactions towards people living with HIV/AIDS: an urban study in Nigeria. BMC Public Health 2010;10:334. doi: 10.1186/1471-2458-10-334
- Geller SE, Adams MG, Carnes M. Adherence to federal guidelines for reporting of sex and race/ethnicity in clinical trials. Journal of Women's Health (Larchmt) 2006;15(10):1123-1131. doi: 10.1089/jwh.2006.15.1123
- Geller SE, Koch A, Pellettieri B, Carnes M. Inclusion, analysis, and reporting of sex and race/ethnicity in clinical trials: have we made progress? Journal of Women's Health (Larchmt) 2011;20(3):315-320. doi: 10.1089/jwh.2010.2469
- Blauwet LA, Hayes SN, McManus D, Redberg RE, Walsh MN. Low rate of sex-specific result reporting in cardiovascular trials. Mayo Clinic proceedings 2007;82(2):166-170. doi: 10.4065/82.2.166
- Lunny C, Shearer BD, Cruikshank J, Thomas K, Smith A. Women in HIV Conference Research: Trends and Content Analysis of Abstracts Presented at 17 HIV/AIDS Conferences from 2003 to 2010. Women's Health Issues 2011; Sep 2 [Epub ahead of print]. doi: 10.1016/j.whi.2011.06.009
- Berlin JA, Ellenberg SS. Inclusion of women in clinical trials. BMC Medicine 2009;7:56. doi: 10.1186/1741-7015-7-56
- Pinnow E, Sharma P, Parekh A, Gevorkian N, Uhl K. Increasing participation of women in early phase clinical trials approved by the FDA. Women's Health Issues 2009;19(2):89-93. doi: 10.1016/j.whi.2008.09.009
- d'Arminio Monforte A, González L, Haberl A, Sherr L, Ssanyu-Sseruma W, Walmsley SL; Women for Positive Action. Better mind the gap: addressing the shortage of HIV-positive women in clinical trials. AIDS (London, England) 2010;24(8):1091-1094. doi: 10.1097/QAD.0b013e3283390db3
- Heidari S, Eckert MJ, Kippax S, Karim QA, Sow PS, Wainberg MA. Time for gender mainstreaming in editorial policies. Journal of the International AIDS Society 2011;14:11. doi: 10.1186/1758-2652-14-11
- Putting gender on the agenda [Editorial]. Nature 2010; 465:665. doi:10.1038/465665a
- Theme D: GENDER ISSUES IN SCIENCE PUBLICATIONS How can editorial policies and writing on gender issues in science be improved to make the assessment and selection of research results for publication sensitive to gender and sex issues? Available at http://www.gender-summit.eu/index.php?option=com_content&id=56&Itemid=5 (accessed 21 September 2011).