

SUBMISSION

AMA submission on the development of a joint NHMRC/MRFF statement on sex, gender, variations of sex characteristics and sexual orientation in health and medical research

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Introduction

The AMA supports the development of a joint National Health and Medical Research Council (NHMRC)/Medical Research Future Fund (MRFF) Statement on Sex, Gender, Variations of Sex Characteristics and Sexual Orientation in Health and Medical Research.

A framework or checklist for scientific and medical researchers to ensure sex, gender, variations of sex characteristics and sexual orientation are incorporated into study design, across all stages of health and medical research, will undoubtedly increase our understanding of the cause of disease and how best to prevent and manage these conditions.

Consideration of these variables is long overdue in Australia. Thirty years ago, the NIH stipulated that women and people of different ethnicity should be included in phase 3 clinical trials so that valid analyses of differences in intervention effects could be performed¹. Numerous countries, including Canada, Ireland and Germany, have introduced policies and practices that require the integration of sex and gender analyses in competitive research grants and publications in journals. In the UK, *The Lancet* has “published a commentary on editorial policies with respect to sex and gender analyses that proposed guidelines for medical journals, including accurate use of sex and gender terms and reporting of sex, gender or both in study participants and the sex of animals and cells”².

¹ <https://www.ncbi.nlm.nih.gov/books/NBK236531/>

² <https://www.mja.com.au/journal/2019/sex-and-gender-health-research-australia-lags-behind>

The AMA recommends that the Statement be recognised not only by the funders (NHMRC and MRFF) but also by Universities and Research Institutions, Human and Animal Ethics Committees, CROs, Editors and Peer-Reviewers. In addition, as Australian research is conducted overseas, an expectation that the Australian standards on the use of that data (with appropriate recognition of sex, gender, variations of sex characteristics and sexual orientation) should receive the same scrutiny.

Sex and Gender in Health and Medical Research

Sex and gender differences are often over-looked in research design and over- and under-representation can result in health harm and the invisibility of certain health outcomes. Despite complex sex differences in rodents, pre-clinical experiments typically use male mice³. It may be that for some experimentalists, any reduction in variability is considered a good thing. Female mice add an extra level of complexity because of the menstrual cycle and variable hormone levels. However, by not having a framework in place to ensure, that consideration of sex differences is included throughout all phases of health research, differences in treatment responses are bound to be observed moving through to human clinical trials.

Imbalances in sex and gender also adversely impact clinical trials. The fundamentals of different pharmacokinetics and pharmacodynamics within males and females must be considered. For example, women who take beta blockers, used to treat heart problems, have higher concentrations in their blood. The reasons for this are multiple but include factors as simple as differences in blood volume. Women also metabolise many medicines differently to men, because of sex hormone levels and enzyme activity⁴. Due to these and other factors, the lack of consideration given to and reporting of sex balance in trials can lead to significant limitations in the generalisability of research findings and applicability to clinical practice.

Variations of Sex Characteristics and Sexual Orientation in Health and Medical Research

Biological and social differences between women, men, girls, boys, and gender-diverse people contribute to differences in their health. Sex (biological attributes), gender (sociocultural factors), and other related variables can influence the environmental and occupational risks, risk-taking behaviours, access to health care, health-seeking behaviour, health care utilisation, and perceived experience with health care, and thus disease prevalence and treatment outcome.

³ <https://theconversation.com/science-experiments-traditionally-only-used-male-mice-heres-why-thats-a-problem-for-womens-health-205963#:~:text=Meanwhile%2C%20it%20has%20taken%20a,and%20female%20cells%20and%20animals.>

⁴ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7218117/>

Transgender and gender diverse populations (including non-binary, cis-gender, trans-gender and gender-diverse (trans) people) are more at risk for chronic somatic diseases and psychiatric disorders (e.g., because of minority stress and related (mental) health problems)⁵. Omission of sex, gender, and sexual orientation in studies also reinforces the unintentional notion of irrelevance of these concepts to health research.

Recognition of the Statement by Universities, Research Institutions, CROs and Publishers

The Statement must be supported by not only the funding bodies (NHMRC and MRFF) but also the wider medical research community. All institutions over a particular size who seek to conduct research in Australia should have a published inclusion policy applicable across all segments of their institutions and not only their research division. The policy ought to reflect objective best-practice. Specifically, any institution that engages in research and delivers education or healthcare services ought to have up-to-date policies, practices and procedures that reflect current evidence and best-practice. These policies should be implemented at all levels of research co-ordination- animal and human ethics committees, CROs, and pharmaceutical sponsored trials.

There is also an onus on editors and peer-reviewers of scientific and medical journals to ensure that Sex, Gender, Variations of Sex Characteristics and Sexual Orientation are considered, and every attempt has been made by the researchers to demonstrate an inclusive study population to increase the rigor of medical research leading to improvements in health.

Conclusion

The AMA supports the development of a NHMRC/MRFF joint statement on Sex, Gender, Variations of Sex Characteristics and Sexual Orientation in Health and Medical Research. The AMA would also like to see the adoption of the Statement by the wider research community. If Australia does not move swiftly to implement the Statement, there is a real risk Australian research will lose its competitiveness to attract funding and partner with international bodies. Australia needs to step up and align with other nations to improve health research and practice for all Australians.

⁵ <https://psycnet.apa.org/record/2018-45577-001>