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# Sex and gender considerations in health research: a trainee and allied research personnel perspective

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The first step in precision health is the incorporation of sex and gender-based considerations and increasingly, a number of national organizations have instituted policies to support and encourage this practice. However, perspectives of trainees and allied research personnel on incorporation of sex and gender into research is lacking. We assessed trainee (undergraduate and graduate students, post-doctoral fellows, clinical trainees) and allied research personnel (study nurses, laboratory managers) perspectives on the barriers to incorporating sex and gender into their own university-based health research and recommendations to improve the process. Two separate focus groups were completed, and a qualitative analysis was employed to derive themes within perceived barriers and solutions. Participants described three overarching themes consistent with barriers including, lack of knowledge and skill, lack of applicability and feasibility, and lack of funding agency and institutional culture. Participants recommended: (1) increasing awareness and skill of incorporation of sex and gender considerations into health research; (2) implementing practical education curricula to facilitate understanding; and (3) fostering greater transparency and accountability by funding organizations and journal editors. Sex and gender considerations in research contribute to precision health, drive innovation and foster breakthroughs in science and medicine.

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## Introduction

Sex (biological attributes) and gender (social-cultural) considerations in research are important factors in precision health where diagnoses, treatment, and prevention strategies take individual variability into account (Collins and Varmus, 2015). Aspirin therapy, one of the most commonly used cardiovascular (CV) therapies, is effective at reducing the risk for CV events for both females and males (Berger et al., 2006), however, women with coronary heart disease are less likely to use aspirin than men, which may reflect gendered effects such as socio-economic position or type of health insurance (Opatowsky et al., 2007). COVID-19 infection rates are similar by sex, though globally mortality is notably greater in men compared to women (Global Health 5050, 2020). Sex likely plays a role in differences in disease severity as the female immune system demonstrates a stronger response to viral infection than that of males (Schurz et al., 2019). Conversely, handwashing (Johnson et al., 2003), compliance with public health measures (Hamel and Salganicoff, 2020) and mask-wearing (De La Vega et al., 2020) is less common in men compared to women, suggesting gendered behaviors may also contribute to differences in outcomes (Ahmed and Dumanski, 2020). Including both a sex and gender element to health research contributes to the understanding of different clinical manifestations, preventive and treatment strategies as well as outcomes of disease in women, men, and gender minorities (Mauvais-Jarvis et al., 2020). While there is increasing emphasis on the importance of incorporating sex-based and gender-based analysis (SGBA) in health research, little is known about trainee perceptions of barriers and opportunities for including sex and gender-based considerations in their work. It has been suggested that earlier exposure to new concepts is met with greater uptake; as such, targeting scientists in the training stages may have the potential for the greatest impact (Andrew, 2013; Murray and Haubl, 2007; Regensteiner et al., 2019; Song et al., 2018). We assessed trainee and allied research personnel perspectives on barriers to the incorporation of sex and gender considerations into health research and recommendations to improve the process.

## Methods

**Study design and setting.** We conducted focus groups of health research (biomedical, clinical, health services, population health) trainees (undergraduate, M.Sc. and Ph.D. students, post-doctoral fellows, clinical trainees) and allied research personnel on two occasions: first at the University of Calgary (19 March 2019, Calgary, Canada) and next at the 2019 Organization for the Study of Sex Differences (OSSD) and International Society of Gender Medicine Annual joint meeting (5 May 2019, Washington, DC, USA). This study was approved by the University of Calgary Conjoint Health Research Ethics Board (Ethics ID no. REB19-0321).

**Recruitment and participation.** We advertised the University of Calgary focus group participation through University of Calgary Graduate Students Association's newsletter ( $n = 6500$  subscribers), hard copies and electronic posters on University campus. Advertisement for OSSD focus group participation involved two emails, separated by one week, inviting all trainees registered to attend the general meeting ( $n = 152$ ) and to the Canadian Institutes of Health Research's Institute of Gender and Health national Sex and Gender Trainee Network ( $n = 50$ ) (Fig. 1). Informed consent was obtained from all participants. Following data analysis from these two focus groups, recruitment expansion was deemed unnecessary, as we identified several recurring

patterns in the data (barriers and recommendations presented by participants) with no new themes emerging (O'Reilly, 2012).

**Data collection.** After a 10-min presentation to give an overview on the definitions of sex and gender, focus groups were utilized to explore trainee experiences with incorporation of sex and gender-based considerations into health research. A priori, we decided to analyze the data in aggregate only to ensure the anonymity of our participants given the small sample size and the open group concept of our data collection gatherings. Standardized questions were posed to focus groups and were pilot tested with 15 local stakeholders (12 graduate trainees, 2 clinical trainees, 1 laboratory manager) at the University of Calgary and refined based on their feedback. We posed questions about participants' experiences with integrating sex and gender considerations in their research. We provided sheets of paper for participants to record their personal and group discussion answers to the following questions: (1) "What are the major barriers you face when it comes to incorporating sex and gender considerations into your research?"; (2) "What changes would help you incorporate sex and gender considerations into your research?"; and (3) "What else can be done to develop your ability to incorporate sex and gender considerations in your research?".

**Qualitative analysis.** Following the pilot test, three researchers (CZK, JPL, SBA) analyzed the written responses from the University of Calgary workshop ( $n = 15$ ) independently and in duplicate to identify prominent themes and amended questions and probes to ensure discussion of key themes at the OSSD focus group. Final data analysis involved two researchers (CZK and SBA) analyzing the responses independently and in duplicate to fracture the data using an open coding methodology to identify emerging themes without the use of software (Strauss, 2003). Coded quotes were organized by themes and subthemes. In order to achieve agreement, researchers compared open coding and developed a codebook of emerging themes. Each investigator analyzed the remaining data sheets independently using open, axial and selective coding to expand and collapse themes (Strauss, 2003).

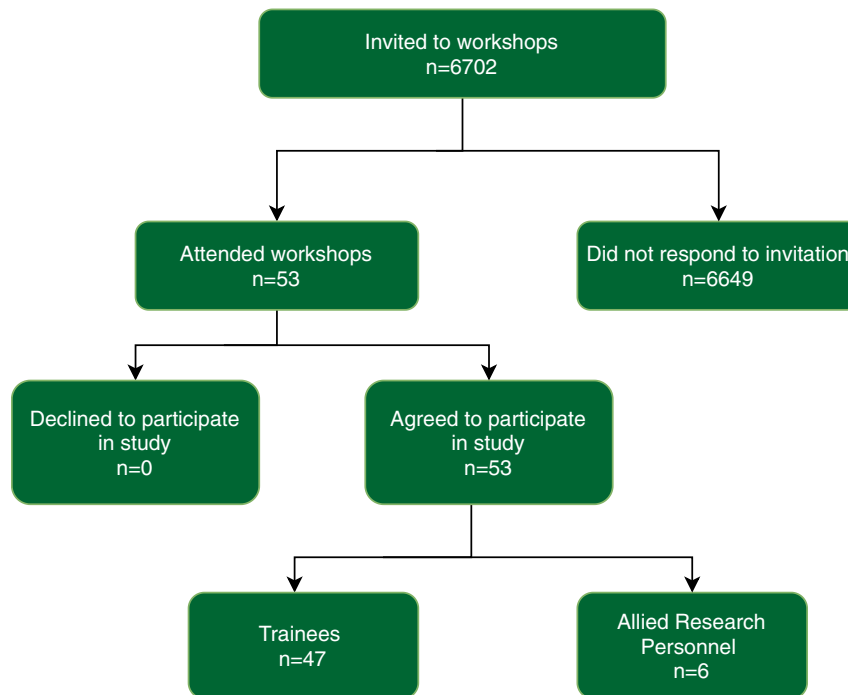
## Results

Email invitations were sent to 202 individuals and an estimated 6500 individuals had access to electronic and paper copy recruitment posters. Fifty-three individuals attended the two focus groups. Two-thirds were self-identified women (62%) (Table 1). The majority of participants were graduate students (58%) or post-doctoral trainees (26%) and approximately three quarters were involved in biomedical (55%) and clinical (17%) research. All allied research personnel self-identified as women and were involved in biomedical (33%) and clinical (67%) research.

Qualitative analysis demonstrated three overarching themes of perceived barriers to integrating sex and gender considerations in health research: (1) lack of knowledge and skill; (2) lack of applicability and feasibility; (3) lack of funding agency and institutional culture. The themes were strongly entrenched in participant responses and categorized by subthemes to capture the variety of participant perspectives. Exemplar quotations are illustrated in Table 2.

### Overarching themes

**Lack of knowledge and skill.** Lack of knowledge and skill was a dominant theme among participants. We define knowledge as the theoretical or practical understanding of a subject, and skill as abilities acquired through experience (e.g., critical appraisal of



**Fig. 1** Flow diagram of recruitment of participants.

**Table 1** Characteristics of participants.

Characteristics	No. of participants (n = 53)
Undergraduate student	2 (4%)
Graduate student	31 (58%)
M.Sc.	13 (25%)
Ph.D.	18 (34%)
Post-doctoral fellow	14 (26%)
Physician	3 (6%)
Registered nurse	1 (2%)
Other	2 (4%)
<i>Self-identified gender</i>	
Woman	33 (62%)
Man	20 (38%)
<i>Pillar of research</i>	
Biomedical	29 (55%)
Clinical	9 (17%)
Health services	2 (4%)
Population health	7 (13%)
Not applicable/not reported	6 (11%)

performing research) or education (e.g., seminars or courses). Participants described they lacked an approach to critically appraise existing research with a sex and gender lens. Subthemes included an inability to apply sex and gender-based analysis to qualitative analysis and limited literature that included more than one sex or gender.

**Lack of applicability and feasibility.** A perceived lack of applicability and feasibility of sex and gender in health research was the second theme that emerged in participant groups. We define applicability as the quality of being relevant or appropriate, while feasibility refers to the facility and practicality of incorporating sex and gender-based considerations. Due to the nature of some animal models used in health research (e.g., hermaphroditic or asexual organisms), some participants did not feel integrating sex and gender-based considerations was necessary or even relevant

to their research. A prevalent subtheme was the notion that incorporation of sex considerations into research was not feasible given that more resources would be needed to accommodate a larger sample size that contains both males and females, particularly in animal studies. Participants also reported difficulty in understanding how to quantify and measure gender.

**Institutional culture and lack of funding agency.** Institutional culture and lack of funding support for sex and gender considerations in research were perceived to be important barriers among participants. We define institutional culture as the norms, beliefs, and values that influence processes and protocols within health research in an academic setting. We define funding agencies as any external organization, public or private, which undertakes a contractual agreement with a university to sponsor research. Participants described that in order to incorporate sex and gender considerations into research, additional resources such as animal care, space allotment, and increased sample size would be necessary; however, these additional required resources were not perceived by participants to be priorities for funders or institutions. A prominent subtheme highlighted by participants was the lack of support for incorporation of sex and gender-based considerations from primary supervisors.

**Suggestions to improve incorporation of sex and gender considerations in health research.** Participants were asked to offer solutions to improve the incorporation of sex and gender considerations into health research (Table 3). The following were the most common recommendations provided by participants:

The first, increase the awareness and development of SGBA skills in order to have widespread acceptance and consistent incorporation of SGBA into health research. Some participants described feeling limited by the capacity of their mentors in this domain, who may be cognizant of sex and gender considerations in research but lacked confidence accessing relevant resources or expertise.

Next, implement practical education curricula to facilitate understanding and provide methodological framework for incorporation of sex and gender-based considerations. Participants

**Table 2 Perceived barriers and facilitators to incorporating sex and gender into health research, identified by trainees.**

Theme and subtheme	Quote
<i>Lack of knowledge and skill</i> Lack of awareness of its application	"Knowledge of its application. How does it apply?" "Unaware of biological differences that could arise between sexes"
Understanding the statistics and methodology behind accounting for differences in sex	"Lack of knowledge about what the implications of a significant effect of sex means scientifically"
Finding literature that includes males and females in the study	"Finding studies that incorporate and describe sex of animals in animal models (e.g. proportion of males and females used. Lack of interest in sex as a variable"
Interpreting statistics	"Difficulty understanding the statistics"
<i>Lack of applicability and feasibility</i> Doesn't apply to/not relevant to research topic	"Not relevant to my research topic" "Our current study lacks a measure of gender so although we consider sex, we aren't able to look at gender in our participants"
More resources to accommodate greater sample size	"Cannot determine gender of early fish embryos. Doesn't really apply to my project." "In animal models, it doubles the number of experiments or increases internal variability"
Difficulty applying a measure for gender	"Non-significant results based on lack of power" "Our current study lacks a measure of gender so although we consider sex, we aren't able to look at gender in our participants"
Non-binary concepts	"My worms are hermaphroditic"
<i>Lack of funding agency and institutional culture</i> Lack of recognition from peer reviewers, publishers and funding agency	"Peer reviewers (grants) don't care" "Lack of recognition in my field that SGBA can influence clinical research outcomes" "Lack of funding/grants specifically for sex and gender specific research proposal as most do not understand it is important"
Lack of supervisor support	"Convincing a senior PI that it is important"

SGBA sex and gender-based analysis.

**Table 3 Suggestions to incorporate sex and gender into health research.**

Theme and subtheme	Quote
<i>Increase awareness</i> Greater acknowledgement of the importance of sex and gender	"To be aware of biological differences that could arise between sexes" "Increased recognition of its importance" "More introductory literature"
Support from primary supervisors	"Convincing a primary investigator that it is important" "Educating primary investigators"
<i>Implement practical education curricula</i> Incorporate SGBA in current courses	"Biostatistics grad courses should incorporate sex and gender"
Leverage existing training	"[Completion of CIHR training modules] should be part of grad school registration and training" "Encourage training for lab members e.g CIHR training modules"
Institute SGBA as part of journal clubs	"Make it part of journal clubs and teach it in biostatistics courses" "Show/teach examples of papers who do it well"
Provide support with the methods	"More information on how to measure gender characteristics"
<i>Greater transparency and accountability by researchers</i> Disaggregate data by sex	"Also, papers should segregate effects of both males and females so we can use that data to make sure if sex/gender is relevant in our research"
Change in messaging around SGBA	"Reframing this as an opportunity for growth, better science, more accurate outcomes"
Increasing transparency	"Be transparent about [sex and gender] inclusion in research"

believed that academic institutions should be at the forefront of providing practical guidance in this area. Participants stated that courses at all levels (undergraduate, graduate, and medical school) in fields such as biostatistics and epidemiology should include SGBA as part of the syllabus. Participants described the importance of strong foundational knowledge of sex and gender considerations, starting with the ability to accurately define the terms "sex" and "gender" which are often erroneously used interchangeably, and educating researchers on the appropriate incorporation of sex and gender considerations where relevant, from study design through to publication and knowledge translation.

Lastly, encourage greater transparency and accountability by the research community. Commonly referred to as "change agents",

participants described how funding agencies and journal editors may be harnessed to encourage incorporation of sex and gender in research. Participants described that funding agencies could play a greater role in ensuring appropriate incorporation of sex and gender-based considerations, and that journal Editorial Boards should make it mandatory for investigators to report this information and require that at minimum, data be disaggregated by sex.

**Interpretation**

While there is increasing global recognition of the importance of considering sex and gender differences in health research (Del Boca, 2016; Hankivsky et al., 2018; Wald and Wu, 2010), little is

known about the experiences and perspectives of scientists in the formative years of training or allied research personnel. Our study provides a qualitative investigation of trainee and allied study personnel perceptions on why sex and gender considerations are not consistently incorporated into health research and suggestions on how to improve. The detailed description of scientists-in-training presented here adds to the existing literature on sex and gender-based incorporation that has been developed using quantitative and qualitative methods (Hankivsky et al., 2018; Norris et al., 2019; Ramirez et al., 2017; Tannenbaum et al., 2017). This study identified three overarching themes representing perceived barriers, including the lack of knowledge and skill, lack of perceived applicability and feasibility, and lack of funding agency and institutional culture. Participants highlighted the need for increased awareness of sex and gender considerations in health research, implementation of educational curricula on sex and gender considerations, and greater transparency and accountability by funding organizations and journal editors of the importance of sex and gender in research.

**Lack of knowledge and skill.** The integration of sex and gender considerations into health research has the potential to encourage new perspectives, pose new questions and improve social equity to make the results of research more inclusive (Avery and Clark, 2016; Hankivsky et al., 2018; Heidari and Bachelet, 2018; Regensteiner et al., 2019; Tannenbaum et al., 2019). A lack of awareness and knowledge of sex and gender-based considerations has resulted in health research that has historically focused on male populations (Bartz et al., 2020), with the results of these studies being used to inform diagnosis and treatment of health conditions for the general population, and at times to the detriment of understudied groups (Santema et al., 2019). Among the 10 prescription pharmaceuticals withdrawn from the US market between 1997 and 2001, eight caused greater harm to women than men (U.S. Government Accountability Office G.-.-R, 2001). Previous research has highlighted that the terms “sex” and “gender” are often erroneously used interchangeably (Hammarstrom and Annandale, 2012). However, interactive online learning, combined with feedback and self-assessment, has been shown to result in improved knowledge and self-efficacy (Tannenbaum and van Hoof, 2018). This underscores the effectiveness of teaching methods to incorporate sex and gender considerations into health research.

**Lack of applicability and feasibility.** While participants involved in biomedical research described an appreciation for the importance of sex and gender considerations in research involving human participants, they did not feel SGBA was applicable or even relevant to preclinical models (e.g., hermaphroditic or asexual organisms). It is important to note that sex and gender factors still play important roles in many of these models (Koene, 2016). For example, the sex-ratio hypothesis suggests that hermaphroditic organisms assess the relative fitness payoffs for each sexual role, and thus the incentive to perform a specific sex role is flexible (Anthes et al., 2006). Many species of fish and reptiles demonstrate temperature-dependent sex determination (Conover and Kynard, 1981; Honeycutt et al., 2019; Ospina-Alvarez and Piferrer, 2008), a finding that may have implications for humans (Fukuda et al., 2014). Unfortunately, a lack of perceived applicability leads to a lack of reporting inclusive of sex and gender-related variables, limiting reproducibility and generalizability (Sugimoto et al., 2019). Participants also described a prevalent subtheme that in order to incorporate SGBA in research, the sample size must be doubled; therefore, requiring more funding and resources to accommodate a larger sample size.

Using conventional single-factor design, there would indeed be a need for duplication of sample size; however, using a (balanced) factorial design offers the possibility of analyzing the impact of more than one categorical variable on the primary outcome (Buch et al., 2019; Dayton et al., 2016). Factorial design is an efficient experimental design (Festing, 1992, 1994) that would allow the gathering of sex-specific information while only modestly increasing sample size (Buch et al., 2019; Miller et al., 2017). Others have called for mixed cohorts without increasing sample size as a first step to determining if sex differences exist in mouse research models (Shansky, 2019).

**Lack of funding agency and institutional culture.** Participants highlighted the important role funders and academic institutions play in the incorporation of sex and gender considerations in health research. As of 2010, the Canadian Institutes of Health Research (CIHR) required that grant and graduate award applications indicate how sex and gender have been incorporated into the research project (Health Canada, 2009). In 1993, the United States Congress passed the National Institutes of Health (NIH) Revitalization Act to mandate inclusion of women as participants in clinical research (National Institute of Health), and since 2016 the NIH has required investigators to account for sex as a biological variable in all NIH-funded research (National Institutes of Health, 2015). The European Commission’s Horizon 2020 research program (Directorate-General for Research and Innovation, 2016) has made similar requirements for sex and gender incorporation, and a growing number of other funding agencies are increasingly supporting SGBA in research (Schiebinger et al., 2020). While a growing list of medical journals are adopting the Sex and Gender Equity in Research (SAGER) guidelines, the incorporation of sex and gender considerations in research remains insufficient (Heidari and Bachelet, 2018).

One of the key mechanisms for change in an organizational culture is to model the leader (Schein, 1990). As such, targeted education to senior leaders in health and science-related faculties may prove to be an effective method to influencing institutional approaches to incorporating sex and gender considerations into research. Publications with female first and last authors have an increased probability of sex-related reporting (Sugimoto et al., 2019); increasing gender diversity in the scientific workforce may thus contribute to greater incorporation of sex and gender considerations in health research.

**Limitations.** First, our study sample was limited; however, recruitment material was sent to almost 7000 potential participants. In addition, some participants may have been motivated to participate as a result of a previous positive or negative experience related to the incorporation of sex and gender in health research and thus some perspectives may have been missed. Next, the majority of comments reflect the perspective of trainees involved in biomedical research and thus our results may not accurately reflect those who are doing more participant-centered research. Furthermore, given the nature of our study design, whereby participants demographics were separate from their comments for the purposes of protecting anonymity, we were unable to stratify our data by the sex, gender, discipline, career stage (i.e. research personnel or trainee) or by geographical region (i.e. US, Canada, or Europe). Nevertheless, given the scope of our sample (i.e., perspectives from trainees and allied research personnel from the US, Canada, and Europe) and the distinct similarities of reported perceived barriers and recommendations across pillars of research, we believe that our results are worthy of consideration by all academic institutions. Finally, while we did not quantify the themes that emerged in the coding, we followed

a rigorous approach consistent with qualitative research standards (Strauss, 2003) wherein the goal is theoretical (i.e., developing in-depth insight) not statistical (i.e., inferring the results from a sample to the broader population) generalizability. As qualitative research involves the collection, analysis, and interpretation of data that are not easily reduced to numbers and to quantify themes or emphasize how many people noted each particular theme is not largely accepted as an indicator of rigor in qualitative data. As such, we refrained from taking this approach and instead focused on identifying emergent and prominent themes across the dataset as opposed to measuring the appearance of thematic concepts.

## Conclusion

To ensure the success of precision medicine, incorporation of sex and gender-based factors into all aspects of health research is essential. Despite the increased attention on sex and gender considerations in health research, it is clear that trainees and allied research personnel perceive barriers to its implementation. Addressing these barriers requires a multipronged approach through the action of institutions, funding organizations and journal editors to increase awareness, implement sex and gender methodology into education curricula and require greater transparency by researchers. Creating opportunities for scientists-in-training to integrate sex and gender considerations into their work will ultimately result in excellence in health research and better outcomes for all.

## Data availability

All data generated or analyzed during this study was included in this published article.

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## References

- Ahmed SB, Dumanski SM (2020). Sex, gender and COVID-19: a call to action. *Can J Public Health* (2020). <https://doi-org.ezproxy.lib.ualgary.ca/10.17269/s41997-020-00417-z>.
- Andrew N (2013) Clinical imprinting: the impact of early clinical learning on career long professional development in nursing. *Nurse Educ Pract* 13 (3):161–164. <https://doi.org/10.1016/j.nepr.2012.08.008>
- Anthes N, Putz A, Michiels NK (2006) Sex role preferences, gender conflict and sperm trading in simultaneous hermaphrodites: a new framework. *Animal Behav* 72(1):1–12
- Avery E, Clark J (2016) Sex-related reporting in randomised controlled trials in medical journals. *Lancet* 388(10062):2839–2840. [https://doi.org/10.1016/S0140-6736\(16\)32393-5](https://doi.org/10.1016/S0140-6736(16)32393-5)
- Bartz D, Chitnis T, Kaiser UB, Rich-Edwards JW, Rexrode KM, Pennell PB, ... Manson J E (2020). Clinical advances in sex- and gender-informed medicine to improve the health of all: a review. *JAMA Intern Med*. <https://doi.org/10.1001/jamainternmed.2019.7194>
- Berger JS, Roncaglioni MC, Avanzini F, Pangrazzi I, Tognoni G, Brown DL (2006) Aspirin for the primary prevention of cardiovascular events in women and men: a sex-specific meta-analysis of randomized controlled trials. *JAMA* 295 (3):306–313. <https://doi.org/10.1001/jama.295.3.306>
- Buch T, Moos K, Ferreira FM, Frohlich H, Gebhard C, Tresch A (2019) Benefits of a factorial design focusing on inclusion of female and male animals in one experiment. *J Mol Med* 97(6):871–877. <https://doi.org/10.1007/s00109-019-01774-0>
- Collins FS, Varmus H (2015) A new initiative on precision medicine. *N Engl J Med* 372(9):793–795. <https://doi.org/10.1056/NEJMp1500523>
- Conover DO, Kynard BE (1981) Environmental sex determination: interaction of temperature and genotype in a fish. *Science* 213(4507):577–579. <https://doi.org/10.1126/science.213.4507.577>
- Dayton A, Exner EC, Bukowy JD, Stodola TJ, Kurth T, Skelton M, Cowley Jr AW (2016) Breaking the cycle: estrous variation does not require increased sample size in the study of female rats. *Hypertension* 68(5):1139–1144. <https://doi.org/10.1161/HYPERTENSIONAHA.116.08207>
- de la Vega R, Ruíz-Barquín R, Boros S, Szabo A (2020) . Could attitudes toward COVID-19 in Spain render men more vulnerable than women? *Global Public Health* 15(9):1278–1291
- Del Boca FK (2016) Addressing sex and gender inequities in scientific research and publishing. *Addiction* 111(8):1323–1325. <https://doi.org/10.1111/add.13269>
- Directorate-General for Research & Innovation (2016). H2020 programme: guidance on gender equality in Horizon 2020. European Commission
- Festing MF (1992) The scope for improving the design of laboratory animal experiments. *Lab Anim* 26(4):256–268. <https://doi.org/10.1258/002367792780745788>
- Festing MF (1994) Reduction of animal use: experimental design and quality of experiments. *Lab Anim* 28(3):212–221. <https://doi.org/10.1258/002367794780681697>
- Fukuda M, Fukuda K, Shimizu T, Nobunaga M, Mamsen LS, Yding Andersen C (2014) Climate change is associated with male:female ratios of fetal deaths and newborn infants in Japan. *Fertil Steril* 102(5):1364–1370 e1362. <https://doi.org/10.1016/j.fertnstert.2014.07.1213>
- Global Health 5050 (2020). COVID-19 sex-disaggregated data tracker. <http://globalhealth5050.org/covid19>
- Hamel L, Salganicoff A (2020). Is there a widening gender gap in coronavirus stress? <https://www.kff.org/policy-watch/is-there-widening-gender-gap-in-coronavirus-stress/>
- Hammarstrom A, Annandale E (2012) A conceptual muddle: an empirical analysis of the use of ‘sex’ and ‘gender’ in ‘gender-specific medicine’ journals. *PLoS ONE* 7(4):e34193. <https://doi.org/10.1371/journal.pone.0034193>
- Hankivsky O, Springer KW, Hunting G (2018) Beyond sex and gender difference in funding and reporting of health research. *Res Integr Peer Rev* 3:6. <https://doi.org/10.1186/s41073-018-0050-6>
- Health Canada (2009). Health portfolio sex and gender-based analysis policy. <https://www.canada.ca/en/health-canada/corporate/transparency/corporate-management-reporting/health-portfolio-sex-gender-based-analysis-policy.html>
- Heidari S, Bachelet VC (2018) Sex and gender analysis for better science and health equity. *Lancet* 392(10157):1500–1502. [https://doi.org/10.1016/S0140-6736\(18\)32619-9](https://doi.org/10.1016/S0140-6736(18)32619-9)
- Honeycutt JL, Deck CA, Miller SC, Severance ME, Atkins EB, Luckenbach JA, Godwin J (2019) Warmer waters masculinize wild populations of a fish with temperature-dependent sex determination. *Sci Rep* 9(1):6527. <https://doi.org/10.1038/s41598-019-42944-x>
- Johnson HD, Sholcosky D, Gabello K, Ragni R, Ogonosky N (2003) Sex differences in public restroom handwashing behavior associated with visual behavior prompts. *Percept Mot Skills* 97(3 Pt 1):805–810. <https://doi.org/10.2466/pms.2003.97.3.805>
- Koene JM (2016) Sex determination and gender expression: Reproductive investment in snails. *Mol Reprod Dev* 84(2):132–143
- Mauvais-Jarvis F, Bairey Merz N, Barnes PJ, Brinton RD, Carrero JJ, DeMeo DL, Suzuki A (2020) Sex and gender: modifiers of health, disease, and medicine. *Lancet* 396(10250):565–582. [https://doi.org/10.1016/S0140-6736\(20\)31561-0](https://doi.org/10.1016/S0140-6736(20)31561-0)
- Miller LR, Marks C, Becker JB, Hurn PD, Chen WJ, Woodruff T, Clayton JA (2017) Considering sex as a biological variable in preclinical research. *FASEB J* 31(1):29–34. <https://doi.org/10.1096/fj.201600781R>
- Murray KB, Haubl G (2007) Explaining cognitive lock-in: the role of skill-based habits of use in consumer choice. *J Consum Res* 34:77–88
- National Institute of Health. Including women and minorities in clinical research background. <https://orwh.od.nih.gov/research/clinical-research-trials/nih-inclusion-policy/including-women-and-minorities-clinical>
- National Institutes of Health (2015). Consideration of sex as a biological variable in NIH-funded research. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-102.html>
- Norris CM, Tannenbaum C, Pilote L, Wong G, Cantor WJ, McMurtry MS (2019) Systematic incorporation of sex-specific information into clinical practice guidelines for the management of st-segment-elevation myocardial infarction: feasibility and outcomes. *J Am Heart Assoc* 8(7):e011597. <https://doi.org/10.1161/JAHA.118.011597>
- O'Reilly MPN (2012) ‘Unsatisfactory Saturation’: a critical exploration of the notion of saturated sample sizes in qualitative research. *Qual Res* 13:190–197
- Opatowsky AR, McWilliams JM, Cannon CP (2007) Gender differences in aspirin use among adults with coronary heart disease in the United States. *J Gen Intern Med* 22(1):55–61. <https://doi.org/10.1007/s11606-007-0116-5>
- Ospina-Alvarez N, Piferrer F (2008) Temperature-dependent sex determination in fish revisited: prevalence, a single sex ratio response pattern, and possible effects of climate change. *PLoS ONE* 3(7):e2837. <https://doi.org/10.1371/journal.pone.0002837>
- Ramirez FD, Motazedian P, Jung RG, Di Santo P, MacDonald Z, Simard T, Hibbert B (2017) Sex bias is increasingly prevalent in preclinical cardiovascular research: implications for translational medicine and health equity for women: a systematic assessment of leading cardiovascular journals over a 10-year period. *Circulation* 135(6):625–626. <https://doi.org/10.1161/CIRCULATIONAHA.116.026668>

- Regensteiner JG, Libby AM, Huxley R, Clayton JA (2019) Integrating sex and gender considerations in research: educating the scientific workforce. *Lancet Diabetes Endocrinol* 7(4):248–250. [https://doi.org/10.1016/S2213-8587\(19\)30038-5](https://doi.org/10.1016/S2213-8587(19)30038-5)
- Santema BT, Ouwerkerk W, Tromp J, Sama IE, Ravera A, Regitz-Zagrosek V, Voors AA (2019) Identifying optimal doses of heart failure medications in men compared with women: a prospective, observational, cohort study. *Lancet* 394(10205):1254–1263. [https://doi.org/10.1016/S0140-6736\(19\)31792-1](https://doi.org/10.1016/S0140-6736(19)31792-1)
- Schein, E. H. (1990). Organizational culture. *American Psychologist*, 45(2), 109–119. <https://doi.org/10.1037/0003-066X.45.2.109>.
- Schiebinger L, Klinge I, Madariaga ISD, Paik HY, Schraudner M, Stefanick M (2020). Sex and gender analysis policies of major granting agencies. <http://genderedinnovations.stanford.edu/sex-and-gender-analysis-policies-major-granting-agencies.html>
- Schurz H, Salie M, Tromp G, Hoal EG, Kinnear CJ, Moller M (2019) The X chromosome and sex-specific effects in infectious disease susceptibility. *Hum Genom* 13(1):2. <https://doi.org/10.1186/s40246-018-0185-z>
- Shansky RM (2019) Are hormones a “female problem” for animal research? *Science* 364(6443):825–826. <https://doi.org/10.1126/science.aaw7570>
- Song W, Furco A, Maruyama G, Lopez I (2018) Early exposure to service- learning and college success beyond the freshman year. *Int J Res Serv-Learn Community Engagem* 6(1):Article 15
- Strauss AL (2003) *Qualitative analysis for social scientists*. Cambridge University Press, Cambridge
- Sugimoto CR, Ahn Y-Y, Smith E, Macaluso B, Larivière V (2019) Factors affecting sex-related reporting in medical research: a cross-disciplinary bibliometric analysis. *Lancet* 393(10171):550–559. [https://doi.org/10.1016/S0140-6736\(18\)32995-7](https://doi.org/10.1016/S0140-6736(18)32995-7)
- Tannenbaum C, Clow B, Haworth-Brockman M, Voss P (2017) Sex and gender considerations in Canadian clinical practice guidelines: a systematic review. *CMAJ Open* 5(1):E66–E73. <https://doi.org/10.9778/cmajo.20160051>
- Tannenbaum C, Ellis RP, Eyssel F, Zou J, Schiebinger L (2019) Sex and gender analysis improves science and engineering. *Nature* 575(7781):137–146. <https://doi.org/10.1038/s41586-019-1657-6>
- Tannenbaum C, van Hoof K (2018) Effectiveness of online learning on health researcher capacity to appropriately integrate sex, gender, or both in grant proposals. *Biol Sex Differ* 9(1):39. <https://doi.org/10.1186/s13293-018-0197-3>
- U.S. Government Accountability Office-01-286R. (2001). Drug safety: most drugs withdrawn in recent years had greater health risks for women. <https://www.gao.gov/products/gao-01-286r>
- Wald C, Wu C (2010) Biomedical research. Of mice and women: the bias in animal models. *Science* 327(5973):1571–1572. <https://doi.org/10.1126/science.327.5973.1571>

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## Competing interests

The authors declare no competing interests.

## Additional information

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