# **CIHR Project Grant: Sex and Gender Textbox Considerations Guidelines**

Last updated on July 10, 2023 for the Fall 2023 CIHR Project Grant competition.

Sex and/or gender considerations are queried via two questions (<u>Task 2: Enter proposal information;</u> <u>Subtask: Details</u>), however a single 2,000-character explanation is required, covering sex **and** gender. If there are no sex and/or gender considerations, there should still be an explanation (*i.e.*, strong justification as to why not); "N/A" is **not** an acceptable response. If only sex **or** only gender are applicable, start with the explanation for the one that is relevant, then explain why the other is not.

Use the textbox to provide a summary of all relevant sex and/or gender information contained within the Research Proposal, including your research design, methods, analysis and interpretation, and/or dissemination of findings. Specifically, for projects with sex and/or gender considerations, information must be provided in both this textbox **and** the proposal; it is insufficient to only use the textbox.

- Consider expanding on background or preliminary data to further describe sex differences, potential mechanisms, etc. or to highlight a unique approach/strength for sex and/or gender.
- Include phrases such as "results will be analyzed/reported disaggregated by sex", as relevant.
- Provide an estimated n/sex to show you will have statistical power to explore sex differences.
- Re: "gender identity", consider other possible gender-related variables (e.g., occupation, responsibility for child care, income level) since research now shows that these can provide more insight than gender identity.

**Tips:** (1) Ensure all information included in the textbox is expanded upon in detail in the Research Proposal. (2) Write this textbox after you've written your Research Proposal to ensure that it captures all relevant aspects covered in the 10-page document. (3) Maximize use of the 2,000-character textbox to provide strong justification.

Note for applicants selecting Gender, Sex & Health as their preferred committee: The textbox can be edited between the Registration and Application stages. However, the Gender, Sex & Health peer review committee uses the textbox at the Registration stage to determine 'committee fit'. Ensure you have included a comprehensive justification for your selection at this stage.

#### **Corresponding SPARC Services:**

- 1) A review of sex and/or gender content located in the Response to Previous Reviews document can be done as part of our **Response to Previous Reviews**.
- 2) A review of the sex and/or gender content located in the Research Proposal document can be performed as part of our **Research Proposal Review**.

**Note:** The remaining pages contain examples of effective text from successful Project Grant applications, generously shared by UBC researchers, including both those with and without relevant sex and/or gender considerations. For additional ideas, consult SPARC's <u>Sample Grant Library</u> (CWL required).

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#### One Example of an Effective No Sex or Gender Considerations Textbox

### 1) Sex/gender information does not affect research design and sex/gender biases are out of scope:

The proposed study creates bioinformatics tools and data specifications modeled on existing / available datasets that are anonymized. So while our data specifications will attempt to capture gender and sex information, the information does not affect our research design per se. There does appear to be sex biases associated with our proposed use cases (TB and food-borne pathogens) that we will include in this study to model the data field specifications of public health surveillance data. For example, there are far more men infected with TB than women and there are more women infected with Salmonella than men. Indeed, public health researchers will be able to use the results of our data model to design studies to address factors influencing sex/gender biases but these experiments are outside of the scope of our study.

### One Example of an Effective Sex (only) Considerations Textbox

#### 1) Given possible impact of sex hormones, sex will be accounted for in a sub study and analysis:

Inconclusive evidence suggests that males have more severe disease and have increased risk of ACE related events compared to women. This is born out by a stem cell derived cardiomyocyte-based ARVC model suggesting sex hormones affect outcome. There is also evidence to support that some of the apparent risk may be mediated by physical activity. These factors will be accounted for in the analytic strategy as outlined above, as well as planned sub studies focused on exercise effects.

The study will collect data on ethnicity, family history and sex. We will not formally collect gender, though extensive patient perspective studies are planned as outlined in the proposal which may include gender-related topics.

### Six Examples of Effective Sex and Gender Considerations Textboxes

### 1) Focuses on gender considerations and how results may also vary by sex:

Gender, a social construct that is classified based on the perception of a bystander, may impact a bystander's decision to perform CPR. Previous studies have shown that bystanders are less willing to perform CPR on women than on men, which may play a role in observed lower rates of survival among women with out-of-hospital cardiac arrest. It is uncertain whether bystanders are more or less willing to perform critical interventions such as naloxone administration, chest compressions, and rescue breathing (ventilations) on women versus men with opioid-related cardiac arrest. We will acquire gender data from paramedic records, in which they classify patients as male or female based on their perceptions and bystander reports (records are not linked to a central electronic medical record). We will test the association of gender and several variables (demonstrating bystander interventions): bystander chest

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compressions, bystander ventilations, and naloxone administration. We will also examine whether gender is associated with paramedic treatment choices including intra-arrest naloxone, number of epinephrine doses, and resuscitation duration attempts.

It is possible that the optimal medical management may vary by sex—that the physiological and biological differences between the sexes may influence the effectiveness of treatments provided. We will dichotomize the study cohort based on sex (using provincial health records which classify by sex at birth) and will examine whether the association of chest compression-plus-ventilation CPR (reference: chest compression-only CPR) and outcomes (survival and survival with favourable neurological status) vary between strata defined by sex, by using a sex interaction term into the analysis. We will repeat these analyses looking at the effectiveness of paramedic-delivered naloxone and time-to-naloxone administration.

# 2) Describes how sex considerations play a role, and how age and education may also play roles:

Sex differences play a role among the population of individuals with lower limb amputation (LLA). Studies consistently demonstrate that the incidence of LLA is higher among males (~68%) in Canada, however, a substantial part of the population are females. Therefore, we will ensure to recruit both sexes. Recruiting females will be crucial because evidence suggests that they are more likely to: be readmitted to hospital post LLA; have compromised physical and mental health status; have greater morbidity and mortality after amputation; and have a greater incidence of falling and fear of falling. The role of gender in the amputee literature is unknown. While some studies report on gender it is unclear how they derived the variable. In our qualitative exploratory study in support of SMART development we asked separate questions regarding the sex and gender of our LLA participants (n=19; 68% males) and found no self-reported difference. However, our clinician participants (2/31) did selfidentify as having a sex/gender difference. While we cannot make any conclusive comments, it is plausible that the generational (age) and education level difference between these two cohorts may have contributed to these results. Regardless, in our proposed project we will disaggregate outcomes data by both sex and gender, as we speculate that sex and gender may play an important role in the impact of SMART. We will avoid exploring the sex/gender differences, however, because the sample size is too small to allow for this type of analysis. We will document sex and gender at enrolment using the Canadian Institute of Health Research (CIHR) definition and the Best Practices for Asking Questions to Identify Transgender and Other Gender Minority Respondents on Population-Based Surveys.

### 3) Discusses understudied female sex:

Pregnancy and motherhood (parity) are unique female experiences that need to be taken into account to better understand female brain function and aging. This proposal centres on understanding how parity affects brain aging. As such, this proposal examines females, the understudied sex. A major impetus for establishing SGBA has been due to the under studied field of women's health. There are very few female-only studies (please see <a href="https://www.eneuro.org/content/4/6/ENEURO.0278-17.2017">https://www.eneuro.org/content/4/6/ENEURO.0278-17.2017</a> and

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https://doi.org/10.1016/j.yfrne.2020.100835) with data showing that female-only studies are under 5% of all studies, while male-only studies are ~35%. Not all studies need to examine SGBA, and we do not examine males here, as male rats are not actually "fathers". If placed in the cages they will often be infanticidal and thus, it is not ethically appropriate to house them together. If we were to add males to the study, it is not an appropriately group to compare against either of the female groups as we would have males that have sexual experience without pup exposure. Our females on the other hand, consistent of nulliparous (without sexual experience) or parous (females with sexual experience, pregnancy and pup experience). Women's and/or men's health needs to be studied but should not always be studied with respect to the differences between them and compared to the opposite sex. Given that females are the understudied sex, and that the comparison to males is not scientifically appropriate in rodents, we do not consider males as a comparison group in these studies. Because we are interested in the biological underpinnings of how reproductive experience influences metabolic and immune responses, as such our examination of gender is limited, as it is a psycho-social construct. However, part of gender can be "gendered experiences" and as such environmental differences (such as diet) could be loosely construed an environmental/"gender" effect.

# 4) Discusses how analyses will be assessed with data disaggregated by sex:

Canadians no longer die from stroke; 83% will survive at least one year. Yet 80% will suffer from long term-disability. Canadian women are disproportionately affected by stroke. Women suffer from more severe strokes, have less access to rehabilitation and show overall poorer recovery. There is a critical need to develop new approaches to recovery for the nearly 350,000 Canadians, over half of whom are women, living with disability after stroke.

One approach is to pair non-invasive brain stimulation with rehabilitation. Responses to this intervention are varied. Differences in response to non-invasive brain stimulation could be due to a number of factors, including sex. But, we know little about response patterns to non-invasive brain stimulation in women. The impact of sex on response to brain stimulation has only been considered in 5 papers; only 2 employed repetitive stimulation as is proposed here. Both of these papers reported less capacity for neuroplasticity in women. Currently there is no clear neurobiological rationale for these findings; the proposed work will consider one possible source of sex differences, patterns of interneuron excitability. As women have poorer functional outcomes after stoke and no work has considered how interneuron excitability or other neurobiological factors may differ by sex we will enroll equal numbers of men and women. Each specific aim will be assessed with data from the whole group and also disaggregated by sex. Because there is little data to guide our investigation of sex, our analyses are exploratory. As we will be among the first to report whether neurobiology after stroke differs by sex we will report this data in papers and at conferences. Given the novelty of our study we will target conferences that speak directly to women's health (e.g. Women's Health Symposium). Despite the preliminary nature of these analyses they are an essential first step in understanding how outcomes after stroke may differ by sex.

# 5) <u>Includes participants irrespective</u> of sex or gender:

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As oligometastatic disease affects all individuals, all patients presenting with 1-3 metastatic cancer lesions, irrespective of their sex or gender, will be offered the opportunity to participate in this trial. While we do not expect that gender will be relative to this study, a review of the literature indicates a knowledge gap currently exists with respect to gender influences in radiation therapy clinical trials. As such, the trial case report forms will collect both sex and gender data to enable sensitivity analyses to detect any differences in survival and progression-free outcomes, quality of life, and resource utilization. Furthermore, sex and gender of participants, and findings from sex and gender analyses, will be disaggregated and reported to funding agencies, as well as included in all knowledge translation materials and in publications and presentations of results.

### 6) <u>Discusses inclusion of women:</u>

The proposed project will focus on individuals who identify as women who have experienced intimate partner violence (IPV). This is justified because 2-3% of women, or 276,000 women in Canada, experience IPV resulting in physical injuries each year with the large majority of them likely suffering a traumatic brain injury as a consequence. In addition, public health statistics report far greater incidence of IPV resulting in injury in women compared to men (Sinha, 2013) with this disparity being even more exaggerated in the LGBTQ population (Valentine et al., 2017). In addition, the number of community agencies available to individuals who identify as women and who have experienced IPV is far more substantial than that for individuals who identify as men. Finally, in alignment with the BC government's framework for transition houses (BC Housing, 2015), the community agency with which we are partnering (Kelowna Women's Shelter) provides services for all women irrespective of sexual orientation and/or gender identity. Thus, as part of the proposed project, we will collect demographic data including information on sexual orientation and gender identity (see Demographic questionnaire in Appendix B.1) and will seek appropriately matched controls. If there is sufficient power, this information will be used to perform an exploratory intersectional analysis of the potential modulating effect of these variables on IPV-related brain dysfunction.