Submission to the House of Commons Health Committee Study on Women's Health

Prioritizing Women's Health Research Will Improve Health For All

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Women's health research has been undervalued, understudied, and underfunded for decades, which leads to disparities in health for everyone [1,2]. Although human females live longer than human males, they are also more likely to live with chronic disease, and a recent world economic forum report suggested that females spend 25% more time across their lifetime in poorer health compared to males[3]. For many disorders, there are sex differences in prevalence, as women are twice more likely to be diagnosed with depression and Alzheimer's disease than men[4]. Not only are sport concussions twice more likely to occur in women than in men, women show poorer outcomes than men[5]. Women have a unique physiology and experiences that impact their health differently compared to men, and many mental health conditions affect women differently and at different times in their lives than men[6]. Indeed, the time of greatest risk for first-time depression in a female's lifetime is during the postpartum [7,8]. And yet, despite these known differences we found that only 3% of over 3000 neuroscience and psychiatry studies considered women's health variables questions [9]. Indeed, there were nine times more studies in males than in females[9].

A large study found that for over 900 different disorders, women were diagnosed an average of 3.7 years later than men [10]. It is important to understand that this was true for many neurological and neuropsychiatric disorders. A fundamental reason for these disparities is the limited knowledge we have about women's health. Most of our medical knowledge - including diagnoses criteria - has been based on data collected in males and on the experiences of men. This has led to the labeling of symptoms in women as "atypical" across many disorders [11,12] and likely adds to the dismissal of symptoms and delay of treatment for many health conditions in women, including coronary heart disease [13] and obstructive sleep apnea[14]. By ignoring those differences, it becomes more difficult to accurately diagnose and treat these conditions in women, and earlier diagnosis leads to earlier interventions and improved health outcomes [15,16]. Although the National Institute of Health (NIH) in the United States mandated the inclusion of women in clinical trials in 1993, Canada has yet to follow suit.

Women's health research is underfunded and unprioritized in Canada, as well as globally[17,18]. In 2010, the Canadian Institutes of Health Research (CIHR) implemented sex and gender-based analysis (SGBA) frameworks for grant applications and adjudication. Despite this effort, research dedicated to women's health remains overlooked. In 2023, we published a study that examined over 8000 CIHR grants, across 11 years, and found that less than 6% of federal funding went to women's health research[19] . The reasons for this disparity are unclear, but are likely related to the undervaluing of women's health questions and little understanding that women's health questions can be studied <u>without</u> the inclusion of other sexes or genders. *Many of my colleagues, including myself, have received the feedback to "add males" on CIHR grants that study pregnancy, the placenta, or female-specific cancers.* We need to prioritize research <u>*in* women *for* women</u>. Although we need changes to healthcare and training of our health care providers it is vital that we have the **research**. Why? If we think of healthcare as our boat, health care providers as our crew, the **research discoveries are our guiding compass and map**. Without the research we do not know where to steer the boat. Without evidence-based women's health research, we cannot provide evidence-based information. One recent example of the underrepresentation of women in research is early trials of COVID-19 vaccines[6,20,21]. These

trials did not include pregnant persons or consider women's health-related side effects (e.g., changes to the menstrual cycle, menopausal symptoms, etc.)[21]. This lack of knowledge fuelled fear, and likely contributed to the greater vaccine hesitancy among women[21]. Later research revealed that pregnant females who contract COVID-19 have a 2.5 times greater risk of mortality, and getting the COVID-19 vaccine confers a benefit for the pregnant person as well as the fetus[6,20,21]. Prioritizing this research could have life-saving implications for women.

Although attention to the lack of equity in health research is improving, most of it has been directed to understanding sex and gender *differences* in disease and health; meaning, understanding how males and men *differ* from females and women. This is not enough to close the decades-long gap in our medical knowledge. A targeted, focused approach is needed to understand women's health and female-specific variables across the lifespan, which in turn drives discovery and improves health outcomes. This means not comparing to the "male standard", as well as extending our research focus beyond understanding sex influence on disease. In other words, prioritizing studying how female-specific experiences, such as pregnancy, menopause, menopausal hormone therapy and hormonal contraceptives influence health in the short and long term. Worldwide, only 3% of neuroscience studies examine women's health questions, excluding female breast cancer, only 4.4% of CIHR grants are dedicated to women's health questions [19], underscoring the lack of attention to women's health questions in medical research.

Given these points, we propose the following recommendations.

1) **Dedicated ring-fenced funding for women's health research that extends beyond sexual and reproductive health research**. Our sex chromosomes (i.e. XX, XY) are located in *every* nucleated cell in our bodies and brain. Moreover, ovarian hormones act on hormone receptors located throughout the body and brain, not just in specific so-called "reproductive" areas. Knowing this, it is necessary to investigate the influence of ovarian hormones on *all* body systems and not just in relation to reproduction. Furthermore, when there is intentional, protected funding for a given cause, substantial discovery and health progress is made. A well-documented example of this is the ice bucket challenge that raised $115M for ALS (amyotrophic lateral sclerosis)[22]. This investment more than doubled the number of researchers, publications and clinical trials on ALS leading to at least 4 new approved treatments. A recent world economic forum report suggests that we would save $1T a year if we invest in women's health research[3]. Furthermore, the US government promised $12B for women's health research [23]. Canada should follow suit and provide protected funding for women's health research. Charities should also be encouraged to have dedicated funding for women's health that extends beyond SGBA.

2) Relatedly, **peer review committees dedicated for women's health research are needed** to increase funding opportunities for researchers**.** The CIHR does not have a dedicated review panel for women's health research. A Maternal and Child Health panel exists, however, even a cursory view of the funded grants indicates it prioritizes the

health of the child over the health of the mother/parent. Having knowledgeable panels dedicated exclusively to women's health would increase funding, and in turn knowledge generation. At least one committee per CIHR's four pillars would be welcome.

3) Furthermore, we propose **women's health training** along with sex and gender-based analysis (SGBA) training in medical and graduate schools across Canada, and to any researcher **applying for federal funding**. This training can help debunk mistaken beliefs and misconceptions, including that females are too complex due to their fluctuating hormones. Human males experience a *daily* decline of testosterone by approximately 50%[24], raising the question of why females were labeled as too hormonal compared to males. Moreover, this training can clarify that including males and men is often unnecessary when focusing on women's health questions (e.g., menstruation, ovarian cancer, pregnancy, menopause, etc.), and that *within* sex and *within* gender comparisons can be a more powerful approach to promote discovery. Proper SGBA training reduces barriers and facilitates discovery.

4) **Open data approaches and reduced provincial and federal privacy barriers to allow for amalgamated national databases with female-health related variables captured**. Along with smaller cohort studies, researchers need access to large databases with detailed information on female health variables. Large databases ensure sufficient statistical power to address women's health-related questions across intersectional variables such as race/ethnicity and socioeconomic status. However, female-specific information, including hormonal contraception use, menopause type, hormone therapy use, parity and pregnancy history, are not accessible or properly recorded. Therefore, our ability to address women's health related questions is severely limited by the lack of quality data that has been collected.

Discoveries in women, will lead to improved treatment options in men and gender diverse individuals. For example, "lazeroids", a series of compounds that were effective in limiting the brain damage in ischemic strokes, was rejected by the FDA in 1999 as it was "not effective" in a trial of both men and women[25]. It turns out that when analyzing the data by sex, "lazeroids" were beneficial but only for male patients, and had this been examined at the time could be in circulation today, improving the outcome from stroke in men[25]. Additionally, multiple sclerosis goes into remission during late pregnancy[26], and discovering why this occurs could lead to improvements for multiple sclerosis in men.

Prioritizing women's health research means prioritizing personalised medicine. It requires us to abandon a "one size fits all" approach that is outdated and limits the diagnosis and treatment of health conditions in women and gender diverse individuals. We must empower researchers investigating women's health questions and devote more attention to delineating the influence of female-specific factors on health outcomes and disease risk. Make no mistake, discoveries that lead to improvements in women's health will lead to discoveries to improve health for all, regardless of sex or gender. This is the promise of personalised medicine.

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