Are we moving the dial? An evaluation of sex- and gender-based analysis integration in Canadian Institutes of Health Research-funded research from 2009-2020

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Abstract

Sex and gender impacts health outcomes and disease risk throughout life. Women and Two-Spirit, Lesbian, Gay, Bisexual, Transgender, Queer or Questioning, Intersex, and Asexual (2S/LGBTQIA+) health is often compromised as they experience delays in diagnosis. Distinct knowledge gaps in the health of these populations has prompted funding agencies to mandate incorporation of sex and gender into reearch. Sex- and gender-informed research perspectives and methodology increases rigor, promotes discovery, and expands the relevance of health research. The Canadian Institutes of Health Research (CIHR) implemented a Sex and Gender-based Analysis (SGBA) framework reccommending the inclusion of SGBA in project proposals in 2010 and in 2019, CIHR mandated the incorporation of SGBA into grant proposals. To examine whether these mandates resulted in increased SGBA uptake in research proposals, we searched the publicly available database of proposals funded by CIHR to analyze the amount of research that focused on sex and gender differences in health, as well as the 2S/LGBTQIA+ community. We categorized a total of 8,964 Project and Operating grant abstracts awarded from 2009-2020. Overall, under 10% of research funded by CIHR explicitly examined SGBA, with 1.94% of grants examining sex differences, 0.66% examining gender differences, 5.92% investigating female-specific outcomes, and 0.35% focusing on the 2S/LGBTQIA+ community. Although there was an increased number of grants funded for sex and 2S/LGBTQIA+ health across time, these increases were less than 2% between 2009 to 2020. The percentage of grants investigating female-specific health or gender differences did not change significantly. The percentage of funding dollars allocated to proposals analyzing SGBA also did not change substantially from 2009-2020, with grants examining sex differences or females increasing by 1.26% and 3.47% respectively, gender differences research funding decreasing by 0.49% and no change for

2S/LGBTQIA+-specific health. Our findings suggest more work needs to be done to increase researcher uptake in SGBA to advance health equity in research.

Highlights:

- Funded grants focusing on sex or gender differences in health research have largely remained unchanged from 2009 to 2020 with the largest increase of 1.57% for sex differences research.
- Total funding amounts for sex or gender differences in health research have stagnated or declined across 2009 to 2020.
- Grants focusing on female-specific health did not change across 2009-2020, but the percentage of funding dollars increased by 3.47%.
- The percentage of grants focused on, and funding allocated to, 2S/LGBTQIA+-specific health more than tripled across 2009-2020 but remained less than 1% of all funded grants.

Keywords: sex differences, gender differences, medical research, research funding, women's health, 2S/LGBTQIA+ health, CIHR

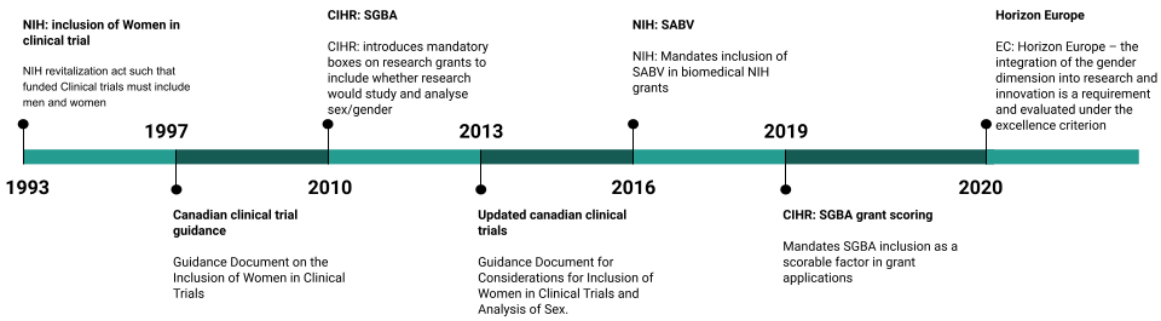
Background

Sex and gender play significant roles in health outcomes and disease risk (1). Sex refers to the biological attributes of females, males and intersex individuals, whereas gender is a psychosocial construct based on gender identity and society's expectations of roles and behaviours based on that construction. Examining the contribution of biological sex and gender in research is essential to our complete understanding of the mechanisms that contribute to the etiology, manifestation, and response to treatment of disease (1,2). The importance of inclusion cannot be overstated. For example, genetic polymorphisms related to asthma and transcriptomic signatures in major depressive disorder can show opposite patterns between males and females with the disorder (3,4), suggesting that any treatment could have disparate effects on the opposite sex. The European Gender Equality Index of 2021 highlights that access to power and resources based on sex, gender, and sexual orientation combined with intersecting social categories determines health outcomes (5). As health research in this area progresses, funding agencies must continue to incentivize and highlight the importance of sex and gender based analysis (SGBA).

Biologically, female and male health outcomes differ in a host of diseases and across the entire spectrum of medicine. Sex differences in diseases exist in manifestation (6–9), diagnosis time (10), misdiagnosis (9), treatment efficacy (11), and progression of disease (10). For example, females demonstrate poorer outcomes and increased mortality due to cardiovascular disease compared to males (11). However, clinical trials in cardiovascular disease continue to recruit more males compared to females (12). Female deaths attributed to cardiovascular disease outnumber deaths by breast, ovarian, uterine, cervical, and vaginal cancers combined (13). Yet, diseases with the highest burden on women remain chronically underfunded, whereas diseases that afflict primarily men are more likely to be appropriately or overfunded relative to disease burden (14). Within women's health concerns, breast cancer

research receives an outsized proportion of funding compared to disease burden, whereas endometriosis receives proportionately fewer research dollars (14–16). Women's health research also needs to include more than health considerations between the boundaries of a bikini. Female sex-specific experiences, such as menses, menopause, and pregnancy, impact health outcomes and disease risk of conditions that target every organ including the heart, lung, kidney, and brain (17–20). Thus, the lack of health research in females perpetuates the disparities in duration of diagnoses, and the side effects due to treatments– resulting in devastating health effects for females compared to males (10,11,21).

Many of these health discrepancies can be attributed to the lack of female data collection in both animal models and clinical trials in North America. Starting in the late 1970's, all premenopausal females were banned from participating in drug trials for almost two decades in the United States due to concerns of causing harm to the reproductive process (22). The importance of considering sex and gender differences in research has prompted funding agencies, including the Canadian Institutes of Health Research (CIHR), to implement



SGBA frameworks for grant applications and adjudication. Figure 1 shows a timeline of

Figure 1. Timeline of mandates for inclusion and analysis of women/females in research from 1993 to 2020 from the National Institutes of Health (NIH) in the United States, the Canadian Institutes of Health Research (CIHR), and Horizon Europe.

funding agencies' changes in policy to encourage inclusion of sex and gender. In 1993, the National Institutes of Health (NIH) mandated the inclusion of women in clinical trials, but to

this day the inclusion of women in clinical trials is only a recommendation in Canada. Female health and sex differences continue to be overlooked in both clinical trials and basic research as women and female health are still routinely underrepresented (22–24). Even in research that includes women and females, the majority of these investigations (80%) do not use sex or gender as a factor in their primary outcomes, nor do they ask questions on whether female-specific factors influence these outcomes (25). This practice negates the benefits of diverse representation in research and does little to close the gap in our understanding of how sex and gender impact health.

Gender identity and sexual orienation are also key considerations for health research, as gender plays a role in healthcare seeking behaviour, symptom perception by clinicians, disease diagnosis, and treatment (1,10,26,27). Sexual orientation or being a member of the Two-Spirited, Lesbian, Gay, Bisexual, Transgender, Queer or Questioning, Intersex, and Asexual (2S/LGBTQIA+) community is a driving factor for poor health outcomes (28). 2S/LGBTQIA+ community members often face discrimination and trauma based on their gender, sexual, and racial identities when accessing health and social services and experience poorer health outcomes as a result (28,29). Despite ample literature demonstrating that gender-affirming healthcare improves health outcomes and mitigates risk of stigma and discrimination (30–32), evidence continues to suggest that 2S/LGBTQIA+ community members experience increased disease risk and poorer health outcomes (29,33,34).

Although more research is being conducted using both sexes and considering gendered health experiences as well as sexual orientation, little headway has been made to increase the analysis or examination of potential sex and gender differences in published research (23,35–38). In the wake of the COVID-19 pandemic and subsequent vaccine trials, these problems persist as sex and gender differences continue to be overlooked. Only 4% of COVID-19 clinical trials explicitly reported a plan to include sex/gender as an analytical

variable (38). Further, during the initial COVID-19 vaccine trials, questions on menstrual, menopause disturbances or the effects on pregnancy were not specifically probed, likely leading to greater vaccine hesitancy among women (39). COVID-19 vaccine uptake is just one example of how neglecting sex differences, gender differences, and female-specific health in research can directly hinder public health efforts.

Research funding bodies have also acknowledged the lack of progress. The European Commission reported a mere 3% increase in grant applications with a gender dimension from 2015-2017 (40) and the NIH put out a call to action saying the improved inclusion of women in clinical trials has not done enough to improve Sex as a Biological Variable (SABV) integration in the design, analysis, and reporting of clinical data (41). Conversely, CIHR reports that they met their target of 67% of proposals addressing sex or gender considerations in the 2019-2020 grant cycle (42). It is worth noting, however, that the CIHR report used mandatory reporting boxes in their analysis rather than the content of the final proposals, which may indicate why their SGBA intake seems higher relative to other funding agencies.

In this paper, we analyzed publicly available data from the CIHR funding database from 2009-2020 to determine whether proposal abstracts were considering SGBA, female-specific health, or 2S/LGBTQIA+ health. We hypothesized that these variables would increase over time as awareness improved and institutional requirements changed. Further, we hypothesized that following CIHR's SGBA mandates in 2019, 2020 abstracts would have increased uptake of SGBA.

Methods

We examined the published public abstracts of all Operating and Project Grants funded by the Canadian Institutes of Health Research (CIHR) from 2009 to 2020 using the CIHR Funding Decisions Database (43). From 2009-2015, CIHR held an Operating Grant program, which was renamed Project Grants in 2016. These programs fund individual research projects investigating fundamental and applied health research (44). To identify relevant grants, we used search terms "male, female, sex, gender, woman, women, uterus, uter, pregnan, breast, ovary, ovarian, ovariers, girl, boy, menopause, postpartum, maternal, placenta, prostate, cervi, testic, testes, vagin, penis, penial, binary, lesbian, gay, bisexual, MSM, FSF, queer, LGBT, LGBTQ, LGBTQIA, LGBTQIA+, LGB, transgender, transsex, trans, 2S, two spirit, 2 spirit, indigi (indigiqueer)" and then proceeded to manually code grants into appropriate categories (described below) based on the content of the abstract. For example, if an abstract mentioned comparing disease outcomes between males and females, it was coded as sex differences. Grant abstracts that did not clearly fall into one or more categories (n=12) were discussed between the three lead coding team members (ABN, TNS, TFLS) and were coded appropriately once a unanimous decision was met.

Inclusion Criteria

All Operating and Project Grants that were awarded to Canadian institutions by CIHR from 2009 to 2020 were included in our analysis (n= 8,964). Grants in both English (n=8,928) and French (n=36) were examined. French abstracts were translated using the Google translate tool, and then coded.

Categorization of Grants

Abstracts published with awarded grant information were examined and designated into the following categories (if relevant): sex differences (any grant that would investigate differences between sexes), gender differences (any grant that would investigate differences

between genders), female-specific grants (any grant that would include only female participants or investigate female-specific conditions), 2S/LGBTQIA+ (any grant that would investigate differences in outcomes of any 2S/LGBTQIA+ individuals). Any abstracts or grants that did not fit in the above definitions were categorized as SGBA omitted.

Statistical Analyses

To examine funding trends over time, we ran simple regression analyses on both the percentage of grants awarded as well as the percentage of funding dollars awarded across the twelve years (2009-2020). We also presented the data by binning the grants into 4 year intervals (2009-2012, 2013-2016, 2017-2020). As cancer research in female health (breast, ovarian, cervical, uterine, etc.) receives greater research funding than other female-specific health conditions (15,16), we did a sensitivity analysis by removing those grants from the overall female-specific analysis. Statistics were calculated using Statistica statistical analysis software (v. 9, StatSoft, Inc., Tulsa, OK, USA). Significance was set at $\alpha=0.05$.

Results

Overall, 8,964 Operating and Project Grants were awarded between 2009-2020, totaling $611,807,644 in research funding. Of these, 91.65% of grants omitted SGBA. Grants that mentioned studying sex differences totaled 1.94%, gender differences totaled 0.66%, female-specific totaled 5.92%, female-specific without cancer totaled 4.07%, and 2S/LGBTQIA+ totaled 0.35% (Figure 2a).

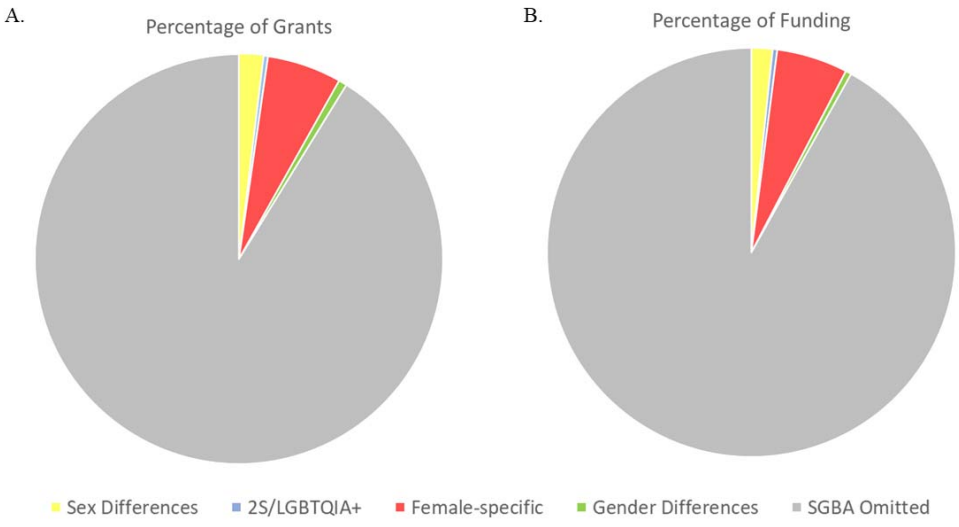


Figure 2. Mean percentage of grants and percentage of funding awarded to each category of health research. A) Pie chart of Canadian Institutes of Health Research (CIHR) grants in each category (% of total grants) from 2009-2020. Sex differences: 1.94%; 2S/LGBTQIA+: 0.35%; female-specific: 5.92%; gender differences: 0.66%; SGBA omitted: 91.65%. Additionally, 4.07% of the grants were female-specific excluding cancer grants. B) Pie chart of Canadian Institutes of Health Research (CIHR) funding (% of total funding amounts) for categorized grants from 2009-2020. Sex differences: 1.67%; 2S/LGBTQIA+: 0.36%; female-specific: 5.65%; gender differences: 0.46%; SGBA omitted: 92.27%. Additionally, 3.81% of the grants were female-specific excluding cancer grants.

Both the percentage of grants focusing on sex differences, and percentage of funding dollars for sex differences grants, more than doubled across 2009-2020

Overall, from 2009-2020, the percentage of funded grants that investigated sex differences was 1.94% (Figure 2a). This percentage increased from 1.30% in 2009 to 2.86% in 2020 (R^2 = 0.56, F (1, 10) = 12.91, p = 0.005, □ = 0.75). After the SGBA evaluation criteria were adopted in 2019, grants focusing on sex differences research in 2020 comprised 2.86% of funded grants, which was a decrease from 3.21% in 2018 and 4.43% in 2019.

Results indicated that grants focusing on sex differences were awarded 1.67% of all funding dollars from 2009-2020 (Figure 2b), which increased significantly from 1.07% in 2009 to 2.33% in 2020 (R^2 = 0.37, F (1, 10) = 5.99, p = 0.03, □ = 0.61).

The percentage of grants focusing on gender differences did not change from 2009-2020 and funding amounts dropped

Grants that focused on investigating gender differences were 0.66% of total CIHR-funded grants from 2009-2020 (Figure 2a) and 0.57% of projects funded in 2020. Although the percentage of grants that were funded decreased from 0.64% in 2009 to 0.57% in 2020 (see Figure 3), this was not statistically significant ($R^2 = 0.18$, $F(1, 10) = 2.20$, $p = 0.17$, □ = -.042).

The percentage of funding dollars awarded to grants focused on gender differences remained below 1% (0.46%) of the total amount of funding awarded by CIHR from 2009-2020 (Figure 2b). This percentage significantly decreased from 0.80% in 2009 to 0.31% in 2020 ($R^2 = 0.46$, $F(1, 10) = 8.55$, $p = 0.02$, □ = -0.68). This indicates that although the percentage of grants awarded to study gender differences did not change, funding dollars awarded to such grants decreased over time (Table 1).

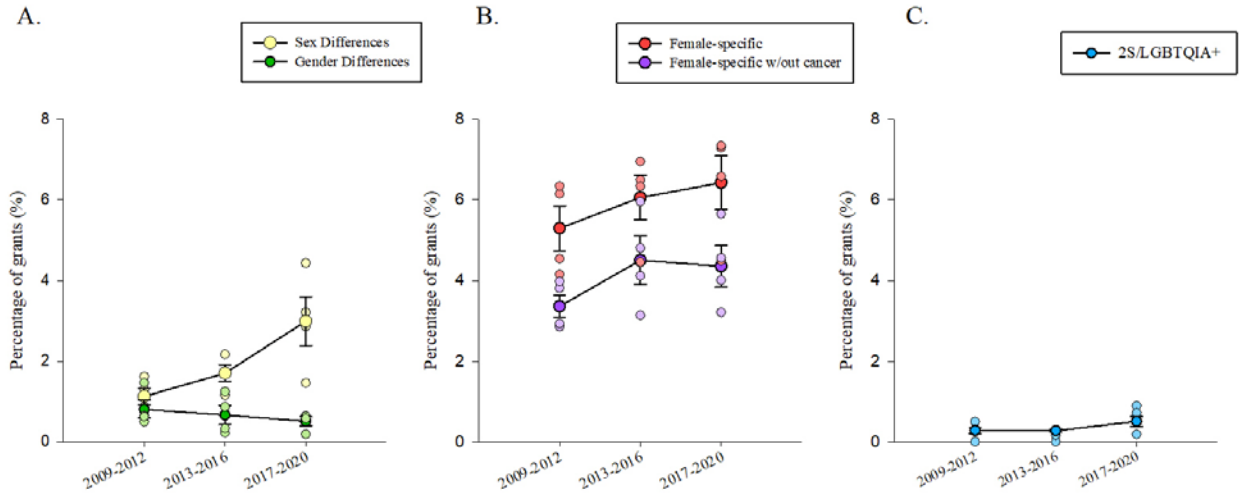


Figure 3. Mean percentage of grants awarded to each category of health research. A-C) Percentage of total grants funded by CIHR binned in three time points: 2009-2012, 2013-2016, and 2017-2020. Data points indicate individual years within the range and error bars represent standard error of the mean (SEM). A) Percentage of grants funded by year that focused on sex differences (yellow) and gender differences (green) remained below 2% throughout the years. Sex differences grants increased over time but gender differences grants did not. B) Percentage of grants funded by year that focused on female-specific health or disease factors (red), and female-specific health when grants related to cancer research were removed (purple). The percentage of grants awarded in either

category did not increase over time. C) The percentage of grants funded by year that focused on 2S/LGBTQIA+ health (blue) remained below 1% across all years but increased significantly over time.

Grants focusing on female sex did not change across 2009-2020, but the percentage of funding dollars increased by more than 3%

Our results indicate that from 2009-2020, 5.92% of funded grants were allocated to female-specific health research (Figure 2a). There was no significant difference in the percentage of grants that focused on female-specific research over time (from 4.54% in 2009 to 6.58% in 2020) ($R^2 = 0.08$, $F(1, 10) = 0.82$, $p = 0.39$, □ = 0.28). Furthermore, 5.65% of CIHR funding dollars were awarded to female-specific proposals from 2009-2020 (Fig. 3b), which did significantly increase across the years from 3.37% in 2009 to 6.84% in 2020 ($R^2 = 0.32$, $F(1, 10) = 4.75$, $p = 0.05$, □ = 0.57).

We next performed a sensitivity analysis by removing grants awarded for "female" cancers, which receive an outsized proportion of funding compared to other health research (15,16). After removing these grants, grants awarded to female-specific research comprised 4.07% of total grants awarded from 2009-2020. There was no significant change in the percentage of female-specific grants, excluding cancer, over time (from 2.85% in 2009 to 4.01% in 2020) ($R^2 = 0.10$, $F(1, 10) = 1.15$, $p = 0.32$, □ = 0.32; Figure 3b).

In terms of research funding dollars, the percentage of funding allocated to female-specific health, excluding cancer research, was 3.81% from 2009-2020 (Table 1). There was no significant difference in the amount of funding dollars awarded across years for female-specific health excluding cancers (1.95% in 2009 to 4.00% in 2020) ($R^2 = 0.12$, $F(1, 10) = 1.34$, $p = 0.27$, □ = 0.34). Comparing the slopes of the two funding regression lines (0.19 for female-specific and 0.11 for female-specific without cancer) reveals that nearly half of the

gains in funding for female-specific projects over time are attributable to cancer research, despite cancer projects representing only 31.3% of female-specific grants funded.

The percentage of grants focused on 2S/LGBTQIA+-specific health and funding allocated to these projects more than tripled across 2009-2020, but remained less than 1% of all funded grants

Grants that focused on 2S/LGBTQIA+-specific health comprised less than 1% (0.35%) of total grants funded by CIHR from 2009-2020 (Figure 2a). There was a significant increase in the percentage of grants funded throughout the years, from 0.13% in 2009 to 0.43% in 2020 (R^2 = 0.36, F (1, 10) = 5.53, p = 0.04, □ = 0.60; Figure 3c). The percentage of grant money awarded to 2S/LGBTQIA+-specific health grants also remained below 1% (0.36%) from 2009-2020 (Figure 2b), increasing from 0.05% in 2009 to 0.46% in 2020, which was not significant (R^2 = 0.22, F (1, 10) = 2.82, p = 0.12, □ = 0.47).

The percentage of grants funded and funding dollars awarded to grants omitting SGBA decreased by roughly 3% across 2009-2020

Grants omitting SGBA comprised 91.65% of total grants overall from 2009-2020 (Figure 2a). This percentage significantly decreased over time, from 93.51% in 2009 to 90.41% in 2020 (R^2 = 0.41, F (1, 10) = 7.07, p = 0.02, □ = -0.64; data not shown). Grants omitting SGBA in their abstracts received 92.27% of funding dollars from 2009-2020 (Figure 2b). This percentage also decreased significantly over time, from 93.58% in 2009 to 91.09% in 2020 (R^2 = 0.46, F (1, 10) = 8.49, p = 0.02, □ = -0.68).

Table 1. Funding data in four-year bins. Total funding amounts in CAD and average percentage of total funding amount (%) for female-specific grants, female-specific grants without cancer grants (excluding any grants related to female-specific cancers), sex

differences grants, gender differences grants, and 2S/LGBTQIA+ grants by year awarded by CIHR.

Years	**female-specific grants funding**	**female-specific w/out cancer grants funding**	**Sex differences grants funding**	**Gender Differences grants funding**	**2S/LGBTQIA+ grants funding**	**Total for all grants funding**
2009-2012	$88,176,847 (4.76%)	$53,590,011 (2.91%)	$19,471,838 (1.07%)	$10,587,955 (0.58%)	$4,689,111 (0.25%)	$1,838,500,442
2013-2016	$97,552,417 (6.00%)	$70,813,456 (4.55%)	$21,339,244 (1.42%)	$8,441,267 (0.50%)	$4,782,071 (0.27%)	$1,731,993,160
2017-2020	$123,992,008 (6.19%)	$78,583,385 (3.97%)	$53,585,969 (2.51%)	$6,486,435 (0.31%)	$12,219,729 (0.58%)	$2,002,035,786
Total (2009-2020)	$309,721,272 (5.65%)	$203,682,822 (3.81%)	$94,397,051 (1.67%)	$25,515,657 (0.46%)	$21,690,911 (0.36%)	$5,714,297,846

Discussion

Overall, our analysis of CIHR research funding allocation revealed that, from 2009-2020, 91.65% of grants did not have sex or gender considerations outlined in their abstract of proposed research. Across all groups examined, the percentage of grants awarded and the funding dollars allocated to projects investigating female-specific health, 2S/LGBTQIA+-specific health, and sex or gender differences was low—below 10%— and slightly lower for funding dollars compared to percentage of grants funded. Although the percentage of grants that focused on sex differences or 2S/LGBTQIA+-specific health doubled over the 12 years, both remained under 3% of grants funded in 2020 (Figure 4a). The percentage of CIHR grants that focused on female-specific health or gender differences in health did not significantly change across the years. However, the percentage of grants omitting SGBA from their abstracts of proposed research declined by approximately 3% over the twelve years but still remained at more than 90% of grants in 2020. Overall, we found that incorporating mandatory SGBA reporting in applications in 2010 and scoring in 2019 has been successful in increasing the amount of funded health research that considered two of the specified groups in our analysis (2S/LGBTQIA+ and sex; see Figure 4b). However, the gains have been modest (increasing by 0.3% and 1.5%, respectively). Moreover, overall funding allocated to sex differences, gender differences, female-specific health, and 2S/LGBTQIA+-specific health research remains below 10% of all funded Project/Operating grants at CIHR after 10 years of SGBA adoption. These findings suggest that additional incentives must be introduced to convince researchers to adopt SGBA into their grant proposals.

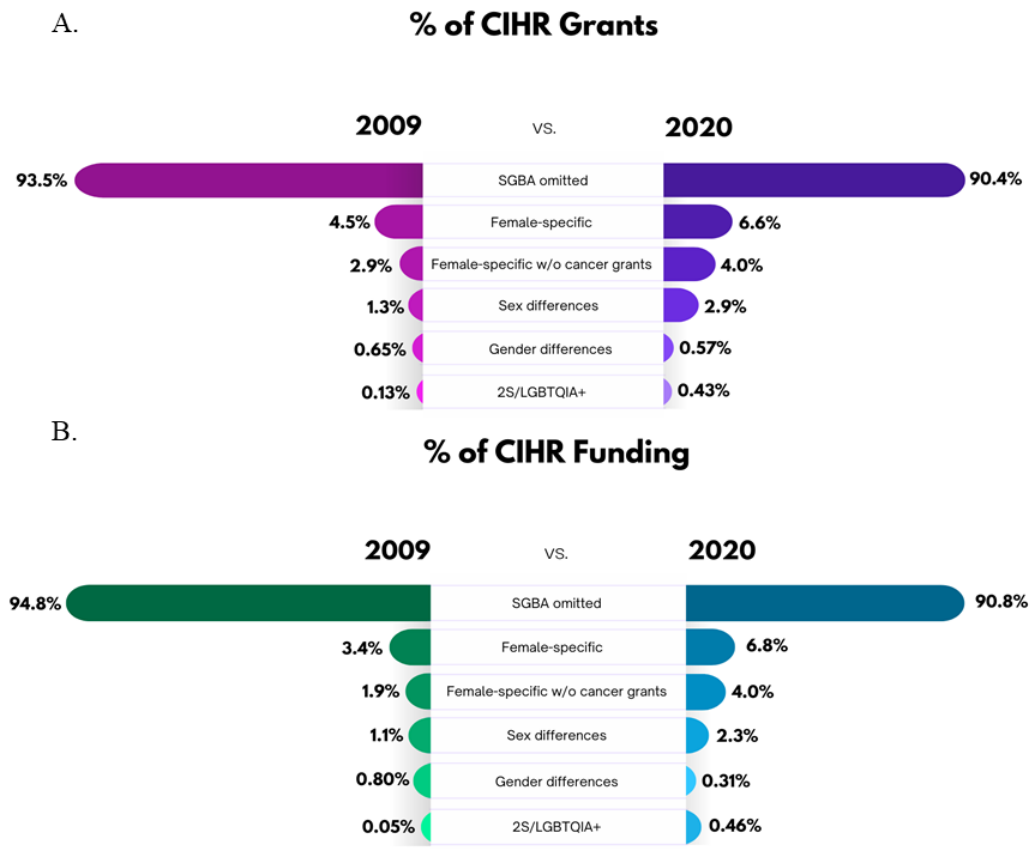


Figure 4. An infographic depicting the change in percentage of grants and funding between 2009 and 2020 for awarded Canadian institutes of Health Research (CIHR) grants.
The change in percentage (%) of grants (A) and funding amount (B) in the years 2009 and 2020 that omitted sex and gender based analysis (SGBA) in their grant proposal abstracts, focused on a female-specific health, female-specific health not including cancer based grants, sex differences, gender differences, and grants interested in 2S/LGBTQIA+ health.

Grants focusing on sex or gender differences have largely remained unchanged and funding amounts have stagnated or declined

In the current study, we found that sex and gender differences comprised 2.57% of grants funded and 2.13% of the research dollars dispersed from 2009-2020. Although the percentage of grants evaluating sex differences increased significantly between 2009 and 2020, the percentage of gender differences grants did not change. Yet, even though CIHR-funded sex differences research increased, it was only by 2% over 12 years with the funding amounts mirroring this trend. Moreover, when comparing the percentage of grants evaluating

sex differences with the funding allocated to these projects, we found that funding was disproportionately small (2.68% vs 3.12% of grants) and is increasing at a slower rate. Alarmingly, funding for gender differences research did not just fail to increase, but actually decreased.

Worldwide, research funding bodies have recognized the importance of bridging the gap in knowledge of sex and gender differences in health and implemented mandates to encourage its scientific inquiry. CIHR reports that as of 2020, 67% of research "addresses sex or gender considerations" (42). However, our results examining the published abstracts draw a starkly different conclusion. This paper, in line with previous reports, demonstrates that even though researchers are required to outline how SGBA will be investigated in their research, mandates alone may not be enough to substantially move the needle on SGBA uptake (23,24,45,46).

Cancer research received the bulk of funding awarded to female-specific health grants

In the current study, we found that female-specific research comprised 5.92% of grants funded from 2009-2020 and correspondingly 5.65% of research dollars disbursed, and neither measure increased significantly over time. Female-specific cancer research accounted for approximately 31.3% of this funding; removing these grants we found that only 4.07% of grants funded investigated female-specific health. Drawing a parallel to previous findings in the published literature, 5% of neuroscience publications (47), or 3-4% of neuroscience and psychiatry papers (23). This is disproportionately lower than male-specific studies that represented up to 50% of neuroscience publications in 2010-2014 (47), and 27% of neuroscience and psychiatry publications in 2009 and 2019 (23). Taken together, these findings suggest a good consensus between grants funded and published research, which is perhaps not surprising.

Gynecologic and breast cancer grants accounted for approximately 31% of the female-specific funded grants. This suggests that female cancer research initiatives received a third of the overall amount of funding dollars awarded for female-specific health inquiries. Of course, female health is more than gynecological cancers; this must be acknowledged to make progress. Not only are there diseases unique to female reproductive organs that do not involve cancer, but female-unique experiences alter disease outcomes. For example, disorders during pregnancy, such as preeclampsia and gestational hypertension elevate the risk of type 2 diabetes and cardiovascular disease later in life (48). Despite evidence of female-specific factors influencing health conditions, studies have neglected the adequate use of females in their research (25), contributing to poor health outcomes in females such as more adverse side effects to drugs (11,49).

2S/LGBTQIA+-Specific Health was awarded less than 1% of the funding dollars

Our findings indicate that grants investigating 2S/LGBTQIA+-specific health comprised less than 1% of overall funded grants and funding dollars from 2009-2020 at CIHR for Operating and Project Grants. Although the proportion of grants investigating 2S/LGBTQIA+-specific health did increase across the 12 years, this was only an increase of 0.3%, and the amount of funding dollars did not significantly increase across the same time. 2S/LGBTQIA+-specific health has been systematically excluded from health research resulting in greater health disparities for 2S/LGBTQIA+ community members (50). For example, lesbian women are less likely to access cancer prevention services (51) and gay men are at a higher risk of HIV, especially among communities of color (33). Furthermore, 2S/LGBTQIA+ individuals are at higher risk for poor mental health outcomes (52), psychological distress (53), and suicidal ideation (54) relative to heterosexuals. 2S/LGBTQIA+ community members have higher rates of disability (34) and poorer general health (54). Thus, 2S/LGBTQIA+ health requires explicit attention and funding dollars to

address these disparities. Although it is encouraging that 2S/LGBTQIA+ research is trending in the right direction, dedicated funding initiatives are required to help close the health disparity gap.

Limitations

Although the current study contributes to our understanding of the implementation of SGBA mandates in CIHR funded grants, there are some limitations to acknowledge. First, it is important to consider we were only able to look at publicly available abstracts rather than the full scientific summaries submitted with grant application packages. Having access to full summaries would have allowed us to better evaluate the use of SGBA in CIHR operating and project grants. However, we believe that if sex and gender considerations were central to a proposal's design, these would have been included in the abstract, and our results mirror those of analyses examining SGBA in published literature (23,47). Further, although we examined nearly 9000 Canadian project grants, it is crucial to understand worldwide health research funding trends. Future research should consider evaluating other funding agencies' uptake of SGBA and SABV, such as the NIH, Public Health Agency of Canada, Horizon Europe, the Council of Scientific and Industrial Research (CSIR, India), Nottingham China Health Institute (NCHI), and the African Academy of Sciences.

Perspectives and Significance

Given the importance of studying SGBA and 2S/LGBTQIA+ effects on all four pillars of research (biomedical, clinical, population health, and health services), we have developed recommendations for future promotion and evaluation of SGBA in health research. First, we recommend specific, ring-fenced funding for SGBA, female-specific health, and 2S/LGBTQIA+-specific health. Dedicated funding has a multifold effect to increase the number of investigators, and the number of publications which drives discovery into disease management and treatments. Recent examples of this can be seen with research funding

awarded to AIDS and ALS (55,56). Indeed, CIHR has held funding competitions dedicated to SGBA. For example, in 2017 a Catalyst Grant for Sex as a Variable in Biomedical Research awarded $4,315,370. However, this represents only 1.16% of research funding compared to that awarded by Project and Operating grants in the same year. It is also possible these catalyst funds spurred the increase in grants on sex differences in 2018-2020 as seen in Figure 3A. Dedicated funding amounts that matched the need for SGBA, female-specific health, and 2S/LGBTQIA+-specific health would not only encourage future research proposals to properly integrate SGBA, but also inspire the next generation of researchers to investigate the role of sex and gender in health, female-specific health, and 2S/LGBTQIA+ specific health.

For many granting agencies, once funds are awarded there is no reporting mechanism in place to determine if the awarded money was spent on the proposed project. Therefore, despite requiring a disclosure of how SGBA is represented in the grant application, there is no requirement for performing research with appropriate sex or gender considerations to receive funding, nor is there a requirement to report on SGBA findings at the end of the award. Funding agencies should consider introducing mechanisms of accountability for SGBA after funding has been awarded (45).

Publishers also play a critical role in advancing SGBA in health research. An academic publisher is tasked with the proper validation of scientific findings (57). As such, implementing rigorous standards for SGBA is an important step to enhance the uptake and utilization of SGBA. For example, as of June 2022, researchers who submit to certain Nature Journals are prompted to state why or why not SGBA was used in addition to noting if results are gender- or sex-specific in the title or abstract (58). This addition ensures that SGBA is monitored and enforced during another step in the academic research and dissemination process.

Although our understanding of the need for and recognition of SGBA in research may be improving, it has yet to be translated into increased research focus and funding. The research community needs to acknowledge that for publications, clinical trials, and grant funding applications, SGBA has not been integrated despite numerous attempts to support its integration. In line with previous reports (23,29,58), we found that grants awarded to research investigating sex and gender differences, female-specific health, and 2S/LGBTQIA+-specific health consistently represented a small percentage of awarded grants and funding from 2009-2020. The aspiration of SGBA is that widespread adoption of its principles will result in an equitable future for health where female-specific health, 2S/LGBTQIA+ health, racialized and gendered experiences, and more are considered. This study suggests that although SGBA mandates and frameworks are a first step in ensuring researchers contribute to a more representative body of knowledge, more work needs to be done to advance health equity in research.

As CIHR itself has noted (59), sex and gender meaningfully contribute to differences in health through differing disease risk and manifestation, treatment response, and healthcare seeking behaviour (1,10,26,27). However, sex and gender have been historically neglected in health research, leaving gaps in our knowledge of how best to diagnose and treat illnesses afflicting people of both sexes and any gender identity. These gaps contribute to ongoing sex and gender disparities in health outcomes that may begin to be rectified if more time and resources are devoted to such research.

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Ability of Data and Material – all material was from publicly available databases but is available upon request

Competing Interests

None.

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