Briefing Note: HIV/AIDS Group

Addressing Sex and Gender in Systematic Reviews

The purpose of this topic-specific briefing note is to provide systematic review authors with information and guidance on sex and gender analysis.

1. Why address sex and gender in systematic reviews?

- The safety and effectiveness of health interventions can differ within and between populations of men and women for many reasons including issues of sex and gender.
- There is consensus amongst various stakeholders (e.g., journal editors, research funders, policy makers) that the consideration of sex and gender in research is not only essential for scientific rigour but also for informed decision-making, for reduction of harm and for addressing inequities in health.
- There is, however, a lack of consistent analysis and reporting about sex and gender in health research (including primary studies and systematic reviews), and continued underrepresentation of women in clinical trials (Pinnow et al., 2014; Health Canada, 2013; Doull et al., 2010; Jagsi et al., 2009; Pinnow et al., 2009).
- Review authors and editors have identified a need for guidance on the integration of sex and gender analysis (SGA) into systematic review methods.
- As a leader in systematic review methodology, the Cochrane Collaboration must continue to advance the evidence-base and its applicability by integrating sex and gender analysis into its reviews.

2. What are 'sex', 'gender', and 'sex/gender analysis'?

- **Sex** refers to the biological, genetic and physiological processes that generally distinguish females from males.
- **Gender** refers to the roles, relationships, behaviours, relative power, and other traits that societies generally ascribe to women, men, and people of diverse gender identities (e.g., transgender persons).
- Although often categorized as binary for analysis, (e.g., male/female; masculine/feminine), attributes of sex and gender are multidimensional, dynamic and interactive. The term **sex/gender** is used to highlight this 'entanglement' of the biological and the social (Kaiser et al, 2009; Springer et al, 2011; Tudiver et al, 2012).
- **Sex/gender analysis is** an analytical framework that is used to explore possible biological and social similarities and differences between and among men and women. In the context of health care systems, SGA explores the interrelationships of sex and gender within or between groups in order to identify how these may affect health experiences, access to care, and health outcomes.

Applying sex/gender analysis: 'A few pointers'

- **The terms 'sex' and 'gender' are not interchangeable,** but rather, the pathways between these processes should be explored and documented.

- At an individual level, one's **sex** is "embedded" within one's **gender**. Explanations of **sex** differences must therefore consider the intersection of sex/gender.

- Even when health issues are sex-specific (e.g., prostate cancer, ovarian cancer), dynamics of **gender** may affect prevention, how and when care is sought, diagnosis, treatment and outcome.

- **Sex-disaggregation** (reporting results for males and females separately) **is a necessary but not sufficient step** for sex/gender analysis.

- Sex/gender can interact with **other determinants of health** (PHAC, 2013) to influence health status and the effectiveness of interventions.

- Gender/sex is part of the acronym **PROGRESS-**Plus (Evans & Brown, 2003; Welch et al., 2012) used by the Campbell and Cochrane Equity Group to list socio-demographic factors across which differences in health or therapies may be considered inequitable.

3. Why does addressing sex and gender in systematic reviews of HIV/AIDS interventions matter?

- Sex/gender differences have been reported to influence a wide spectrum of HIV/AIDS-related health outcomes ranging from risk of exposure, risk of seroconversion once exposed, immunological and virological responses, adverse effects of therapy, differences in opportunistic infections or other complications of HIV/AIDS including those that arise in the long-term, to differences in access to or utilization of health care.
- Sex/gender can also affect adherence, the ability to access health care, health care provider responses to individuals (including diagnosis and treatments offered) and social support networks.
- Overall quality of life and the way HIV/AIDS is experienced can be influenced by sex/gender.
- Social and behavioural factors such as gendered power dynamics and violence intersect with sex/gender and differentially affect women's and men's risk of infection and outcomes once infected (Pantalone et al., 2013).
- Differences in immunity, other pathophysiologic mechanisms, or pharmacokinetics and pharmacodynamics may result in differential responses of men and women to interventions (Prins et al., 1999; Castelnuovo et al., 2011).
- The presentation of sex-disaggregated data often illuminates differences and similarities as a starting point but a contextual analysis that considers the intersections between sex, gender and other health determinants is needed.
- There is growing consensus about the importance of considering sex/gender in HIV research (Heidari et al., 2011).

4. What can – and should – be done about it?

- Reviewers should **consider and document whether and in what ways sex and/or gender are relevant** to their review question.
- **Depending on the review question, different (or multiple) methods may be appropriate.** The following table provides some strategies to address issues of sex/gender in reviews and examples to illustrate some of the ways in which sex and/or gender can play a role in HIV/AIDS.
- In the table, sex/gender are dichotomized intentionally for clarity but emerging theory highlights the intersections between the two.

Methods	**Guidance**
Question formulation	▪ **Consider whether there are known or possible differences by sex/gender across: baseline risk, prevalence, vulnerability, implementation, response to intervention and plan objectives and methods accordingly.** ▪ Example: Women in sub-Saharan Africa make up 57% of those living with HIV/AIDS (UNAIDS, 2013). ▪ Example: In a study examining first line ARV treatment researchers found that toxicities in women were the most common reason for drug substitutions (Castelnuovo et al., 2011).
Context	▪ **Consider sociocultural understandings of sex/gender as part of context** [e.g. how gender roles, norms, identity, and gender relations can influence symptoms, implementation and health] ▪ This may include developing an **analytic framework/logic model** to define assumptions about sex/gender across intervention, comparator and outcomes.
Population	▪ **Specify if sex/gender will be used as a basis for exclusion or inclusion of studies.** ▪ **Consider ways in which other inclusion criteria at the review or primary study level, such as age or**

	ethnicity, may interact with sex/gender. For example, age of onset of disease or complications related to a condition may differ for men and women – thus age-based inclusion criteria may favour one sex.
Intervention **C**omparator	▪ **Consider whether sex/gender interacts with aspects of the intervention (e.g. treatment delivery; likelihood of offering treatment; acceptability),** and whether this is important for the review question. ▪ **Example:** Meader et al (2010) conducted sex-disaggregated analyses and found that trials of psychosocial interventions that enrolled mainly females were more effective than trials that included both men and women in each group.
Outcomes	▪ **Consider whether the outcomes are relevant for both women and men. Does the condition or its complications manifest differently in men and women – and do the selected outcomes for the review capture both of these scenarios?** ▪ **Example:** At the same viral load, women have a higher risk of progression to AIDS as compared to men consider this if using thresholds or cut off points for viral load measures (Farzadegan et al., 1998). ▪ **Example**: Findings suggest a sex disparity in the pharmacokinetics of antiretroviral therapy, which has been shown to have pharmacodynamic effects for some drugs. Such findings call for adequate powering of trials to detect sex-based differences (Ofotokum et al., 2007).
Study design	▪ Consider **study design eligibility** according to the review question and objectives related to sex and gender. If non-randomized studies are considered, why, and what are their eligible features?
Searching for studies	▪ Indexing for studies that assess sex/gender is not consistent. Applying these terms to a search may unnecessarily limit the scope, unless the search terms have been validated. Searching beyond usual databases may be required to assess influence of gender and sociocultural context.
Data collection	▪ **Extract sex-disaggregated data** and contact authors for sex-disaggregated data and sex of participants if not reported. ▪ **Identify and report characteristics of the population that might intersect with sex/gender** (e.g. consider PROGRESS factors).
Risk of bias	▪ Be aware that a potential form of **reporting bias** would occur if only a subset of studies provided sex-disaggregated data so that findings were based only on the subset.
Data analysis	▪ **Subgroup Analysis:** Specify the method of **subgroup analysis** by sex/gender in the protocol, with attention to credibility criteria for subgroup analyses (see Cochrane Handbook; Sun et al., 2012). ▪ **Sensitivity Analysis:** Conduct pre-planned **sensitivity analysis** to assess the robustness of results across sex. ▪ **Heterogeneity:** Consider sex/gender as reasons for **heterogeneity** and explore with methods such as meta-regression techniques and subgroup analyses (see Cochrane Handbook). ▪ Consider the use of individual patient data meta-analysis to assess differences in effects across sex/gender. ▪ Be aware of ecological bias (aggregation bias, ecological fallacy) with meta-regression techniques. ▪ Consider effects of possible confounders of sex/gender differences (e.g., age, ethnicity, bone size and others).
Additional analyses	▪ Consider additional analyses and **qualitative methods** such as realist review (Thomas et al., 2008), meta-ethnography (Pawson et al., 2005), and thematic analysis (Atkins et al., 2008) to address or situate results within sociological understandings of gender, if relevant to the question of interest.
Presenting results	▪ **Report number and percentage of both female and male participants** in included studies and

and summary of findings	report if data are not available. ▪ Report **results of planned analyses related to sex/gender**, and justify why planned analyses were not conducted. ▪ Identify and **justify any post hoc, exploratory analyses** related to sex/gender. ▪ Consider whether a separate **summary of findings table** is needed to show differences/similarities in response or baseline event rate across sex/gender.
Interpreting results and drawing conclusions	▪ **Describe to whom the available evidence applies,** and the implications for the overall quality of the findings in relation to sex/gender and any intersecting characteristics. ▪ Outline **research gaps or unanswered questions** related to sex and gender analysis, and identify planned analyses that could not be conducted due to unavailable data.

Questions? Comments?

- The Sex/Gender Methods Group, affiliated with the Campbell and Cochrane Equity Methods Group, is available to support authors in implementing this guidance.
- This document may be used and distributed. We would appreciate the following citation: Doull M., Shea B., Puil L., Runnels V., Welch V., Tudiver S., Boscoe M for the Sex/Gender Methods Group. Addressing Sex/Gender in Systematic Reviews: Cochrane HIV/AIDS Group Briefing Note. Version 2014-01. Accessed at: http://equity.cochrane.org/sex-and-gender-analysis.
- Web link for resources: http://equity.cochrane.org/sex-and-gender-analysis
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