

Monica Gandhi¹, Laura M. Smeaton², Christina Vernon³, Eileen P. Scully⁴, Sara Gianella⁵, Selvamuthu Poongulali⁶, Anandi N. Sheth⁷, Marije Van Schalkwyk⁸, Karin L. Klingman⁹, William R. Short¹⁰, Valarie S. Opollo¹¹, Susan E. Cohn¹², Kimberly K. Scarsi¹³, Rosie Mngqibisa¹⁴, Elizabeth Connick¹⁵

1. ¹University of California San Francisco, San Francisco, CA, USA, ²Harvard T.H. Chan School of Public Health, Boston, MA, USA, ³Social & Scientific Systems, Silver Spring, MD, USA, ⁴Johns Hopkins University, Baltimore, MD, USA, ⁵University of California San Diego, La Jolla, CA, USA, ⁶YR Gaitonde Center for AIDS Research and Education, Chennai, India, ⁷Emory University, Atlanta, GA, USA, ⁸Stellenbosch University, Cape Town, South Africa, ⁹NIH, Bethesda, MD, USA, ¹⁰University of Pennsylvania, Philadelphia, PA, USA, ¹¹Kenya Medical Research Institute, Kisumu, Kenya, ¹²Northwestern University, Chicago, IL, USA, ¹³University of Nebraska, Omaha, NE, USA, ¹⁴Enhancing Care Initiative, Durban, South Africa, ¹⁵University of Arizona, Tucson, AZ, USA

BACKGROUND

- Over 50% of world's HIV infections are in women
- Sex differences in HIV acquisition, pathogenesis, reservoir, treatment response, antiretroviral pharmacokinetics and toxicities seen¹
- But adequate sex representation not always achieved in studies, nor sex-specific analyses performed
- NIH "expects that sex as a biological variable will be factored into research designs, analyses, and reporting"

NIH Policy on Sex as a Biological Variable

The 4 Cs of Studying Sex to Strengthen Science



Consider
Design studies that take sex into account, or explain why it isn't incorporated



Collect
Tabulate sex-based data



Characterize
Analyze sex-based data



Communicate
Report and publish sex-based data

- CROI 2018 program committee requested investigators to consider sex as a biological variable and asked oral presenters specifically to include sex-specific analyses when feasible

Boston | March 4-7, 2018

- This analysis examined compliance with this recommendation



METHODS

- CROI 2018 held in Boston, MA, March 4-7, 2018; each oral presentation video-taped with the talk and slides made available as a webcast
- Instructions to oral abstract presenters: *Please consider whether there is substantive evidence of differences in effect by sex or other key demographic groups. If so, a stratified analysis should be made available during the presentation of the abstract at CROI*
- Women's Health Inter-Network Scientific Committee (WHISC) is a working group of two NIH-funded clinical trials networks -the AIDS Clinical Trials Group (ACTG) and International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT)- focused on HIV among girls and women
- At least 2 WHISC members reviewed each of the CROI 2018 oral sessions
 - 1) Whether the abstract's scientific question/objective was relevant to both sexes
 - 2) Whether the study included human participants, animals, or was pre-clinical, but still included specimens from humans or animals
- If both criteria met, reviewers assessed
 - 1) Whether the reported study demographics included sex
 - 2) If sex-delineated outcomes or sex-stratified analyses were presented
 - 3) If results by sex not presented, whether an explanation for omission was provided

RESULTS

- Of 83 original oral abstracts presented at CROI 2018, 16 (19%) deemed relevant to one sex only and were excluded from this analysis.
- Of the remaining 67 oral abstracts relevant to both sexes, 35 (52%) included the distribution of the study sample by sex; 7 (10%) presented sex distributions, albeit mislabeled as "gender"; and 25 (37%) did not present or address sex distributions
- Sex distribution was reported in human observational studies and clinical trials the majority of the time (41/54, 76%) but only 1/13 of pre-clinical studies included sex-distribution
- **Only 16 (24%) of all oral abstracts presented at CROI 2018 relevant to both sexes included sex-stratified analyses or sex-delineated outcomes**

TABLE : Proportion of abstracts at CROI 2018 presenting sex-specific results

Type of abstract	Number of total (%)	Presented sex distribution	Presented sex-specific results
Relevant to one sex only	16 of 83 (19%)	NA	NA
Relevant to both sexes	67 of 83 (81%)	42 of 67 (63%)	16 of 67 (24%)*
Human studies	54 of 67 (81%)	41 of 54 (76%)	16 of 54(30%)
Animal/cell-based studies	13 of 67 (19%)	1 of 13 (8%)	0 of 13 (0%)

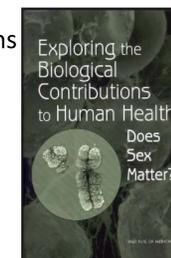
Of 51 which did not present sex-specific results, only 8 provided an explanation of why this wasn't done

KEY POINTS.

- **Sex-specific analyses can provide insight into whether HIV prevention, treatment, cure and the management of HIV-associated conditions should be tailored by sex.**
- **NIH, FDA, Institute of Medicine all recommend sex-specific reporting**
- **Over 52% of HIV infections worldwide are in women**
- **Despite CROI 2018 providing guidelines on reporting by sex, more than a third of oral presentations at this conference last year failed to report sex demographics and only a quarter included sex-stratified analyses**

DISCUSSION

- Sex differences in HIV exist when examined
- CROI program committee has aligned its recommendations to abstract presenters with NIH, Institute of Medicine and FDA policies
- Despite recommendations, paucity of sex-specific reporting at this major HIV conference highlights missed opportunities to contribute to the knowledge base on sex differences in HIV infection
- Sex rarely reported for animal or cell-based studies, but genetic differences by sex even in somatic cells and epigenetic effects of hormones may influence HIV responses
- Sex and gender, ideally, should be reported separately



Conclusion: Researchers should incorporate NIH recommendations on sex inclusion/sex-reporting into study design and conferences/journals should enforce these guidelines

REFERENCES and ACKNOWLEDGEMENTS

1. Scully E et al. *Current HIV/AIDS Rep* 2018
2. National Institutes of Health. NIH Policy on Sex as a Biological Variable; <https://orwh.od.nih.gov/sex-gender/nih-policy-sex-biological-variable>
3. Institute of Medicine. *Does Sex Matter?* Exploring the Biological Contributions to Human Health. 2001
- NIAID/NIH funding to ACTG: UM1 AI068634, UM1 AI068636, UM1 AI106701
- Co-author KLK is an employee of the NIH, but the views expressed in this paper do not necessarily represent those of the NIH
- We acknowledge and thank the other members of the WHISC and ACTG leadership (Drs. Judy Currier and Joe Eron) for supporting this analysis

