Sampling bias in transgender studies

Stefan Baral and colleagues[1] reported an international meta-analysis of HIV seroprevalence among transgender women. This work shares a common methodological weakness with past meta-analyses on this topic, one that unfortunately Baral and colleagues are unable to remedy. Sampling bias is common in studies of transgender women, in which convenience samples are primarily drawn from urban sites over-representing street-active women, including HIV testing sites. Although such studies are important in reporting HIV vulnerabilities experienced by segments of the transgender population, we caution against broadly extrapolating to transgender women.

Evidence for greater heterogeneity has emerged in new population studies with large samples and self-reported data. In North America, three studies[2–4] have observed self-reported HIV prevalences in transgender women of between 2·2% and 3·8%. These results contrast by a factor of four with the summary statistic of 11·8% from Herbst's meta-analysis of US studies with self-report measures,[5] studies that were similar in design to those used by Baral and colleagues. The consistency of results across larger, more representative samples contrasts with the consistently higher prevalences observed in urban convenience and clinic samples, suggesting that sampling bias has a potentially large role in shaping these results. We suspect that when new studies are able to provide seroprevalence estimates for broad population samples of transgender women, the results will probably challenge the "remarkable" consistency observed by Baral and colleagues.

Moreover, contrary to Baral and colleagues' assertion that transgender women "have been consistently identified as engaging in receptive anal sex with men",[1] data for sexual behaviour reported for one of the broader population studies showed that about half of transgender women have no past-year sex partners, and most reported no anal sex.[2] Thus, urban and clinic samples might not represent the sex lives of transgender women in less urban areas, of higher economic positions, or those who are not primarily sexually attracted to men.

Although high HIV prevalences can serve as an advocacy instrument in drawing attention to the health of transgender women, labelling a group that experiences stereotypes of hypersexuality as a high risk group for HIV has the potential to add to stigma. We support Baral and colleagues' arguments for greater inclusion of transgender women in HIV surveillance, research, and interventions, and for structural changes to increase social inclusion. However, we caution that the consistency that they observe might be, at least in part, a function of consistent sampling bias.

We declare that we have no conflicts of interest.

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1 Baral SD, Poteat T, Stromdahl S, Wirtz AL, Guadamuz TE, Beyrer C. Worldwide burden of HIV in transgender women: a systematic review and meta-analysis. *Lancet Infect Dis* 2013; **13:** 214–22.

2 Bauer GR, Travers R, Scanlon K, Coleman TA. High heterogeneity of HIV-related sexual risk among transgender people in Ontario, Canada: a province-wide respondent-driven sampling survey. *BMC Public Health* 2012; **12:** 292.

3 Grant JM, Mottet LA, Tanis J, Herman JL, Harrison J, Keisling M, for the National Center for Transgender Equality and the National Gay and Lesbian Task Force. National transgender discrimination survey report on health and health care, 2010. http://transequality.org/PDFs/NTDSReportonHealth_final.pdf (accessed May 2, 2013).

4 Iantaffi A, Bockting WO. Views from both sides of the bridge? Gender, sexual legitimacy, and transgender people's experiences of relationships. *Cult Health Sex* 2011; **13:** 355–70.

5 Herbst JH, Jacobs ED, Finlayson TJ, McKleroy VS, Neumann MS, Crepaz N. Estimating HIV prevalence and risk behaviors of transgender persons in the United States: a systematic review. *AIDS Behav* 2008; **12:** 01–17.

Authors' reply

We thank Greta Bauer and Ayden Scheim for highlighting concerns about selection bias in studies of transgender women and the generalisability of estimates of HIV burden in these women. As described in our study,[1] the sampling strategies that are most pragmatic in most settings tend to oversample higher risk transgender women, which could overestimate the actual burden of HIV in all transgender women in a city, country, or region. This is a challenge for studies in any populations in which denominators are scarce and population-based sampling is problematic. Our study called for improved sampling frames of transgender women through inclusion of transgender identities in government censuses or formal recognition of transgender people in the context of government documentation.

Given these realities, however, we do not agree with Bauer and Scheim's assessments. Our study specifically excluded self-reported HIV prevalence data because of the well known limitations of self reports of HIV status. Bauer and Scheim quoted three studies in which self-reported HIV prevalence ranged from 2·2 to 3·8% in transgender populations;[2–4] however, these studies also had remarkably high numbers of transgender women who had not been tested recently or had never been tested. In the study from Ontario,[2] only 27% of transgender women had been tested for HIV in the previous year, and 42% had never been tested for HIV. Moreover, although 3% reported living with HIV, 25% reported being unsure of their status. The highest self reported HIV prevalence of 17% (+24% unsure) was in Aboriginal populations who also reported the highest testing rates.[2] In the National Transgender Discrimination survey,[3] 2·6% of all participants (4·3% in transgender women) reported living with HIV, but more than three-times as many reported being unsure of their status and coverage of HIV testing was not assessed. Additionally, in the online

survey from Iantaffi and Bockting,[4] the estimate of 2·2% self-reported HIV prevalence included 43% female-to-male transgender people (who have much lower HIV prevalence in most samples) and again coverage of HIV testing was not reported. A more recent publication, also from the USA, showed an HIV prevalence of 40% and annual HIV incidence of 2·8% in transgender women.[5] HIV in this group was strongly associated with gender abuse and depressive symptoms.[5] These data suggest that in a population affected by multilayered stigma and limited access to clinically and culturally competent health care, self-reported HIV prevalence data is not a valid marker of the actual burden of HIV.

Like many other people, transgender people report a broad range of sexual practices throughout their lives. In terms of the sexual transmission of HIV, unprotected receptive anal intercourse with non-virally suppressed HIV serodiscordant partners is associated with the highest risk of HIV acquisition and is the most probable driver of the very high HIV prevalence in transgender women.[6] Contextualising sexual practices by use of a life course approach will help with the development of evidence-based HIV prevention, treatment, and care services for these women that will also affirm their human rights.

Although risks for transgender populations might be lower in some settings with broader access to appropriate health care (including surgical options) such as Canada,[7] HIV is a public health emergency in transgender women throughout the world; driven, at least in part, by both biology and stigma. Moreover, it is an emergency that has been too long overlooked throughout the HIV response. That needs to change if we are ever to reach an AIDS-free generation.

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1 Baral SD, Poteat T, Strömdahl S, Wirtz AL, Guadamuz TE, Beyrer C. Worldwide burden of HIV in transgender women: a systematic review and meta-analysis. *Lancet* 2013; **13:** 214–22.
2 Bauer GR, Travers R, Scanlon K, Coleman TA. High heterogeneity of HIV-related sexual risk among transgender people in Ontario, Canada: a province-wide respondent-driven sampling survey. *BMC Public Health* 2012; **12:** 292.
3 Grant JM, Mottet LA, Tanis J, Harrison J, Herman JL, Keisling M. Injustice at every turn: a report of the National Transgender Discrimination Survey. Washington: National Center for Transgender Equality and National Gay and Lesbian Task Force, 2011. http://endtransdiscrimination.org/PDFs/NTDS_Report.pdf (accessed Sept 9, 2013).
4 Iantaffi A, Bockting WO. Views from both sides of the bridge? Gender, sexual legitimacy and transgender people's experiences of relationships. *Cult Health Sex* 2011; **13:** 355–70.
5 Nuttbrock L, Bockting W, Rosenblum A, et al. Gender abuse, depressive symptoms, and HIV and other sexually transmitted infections among male-to-female transgender persons: a three-year prospective study. *Am J Public Health* 2013; **103:** 300–07.
6 Baggaley RF, White RG, Boily MC. HIV transmission risk through anal intercourse: systematic review, meta-analysis and implications for HIV prevention. *Int J Epidemiol* 2010; **39:** 1048–63.
7 Radix A. Hormones = health. Health outcomes among transgender clients in an urban health center. https://apha.confex.com/apha/140am/webprogram/Paper271247.html (accessed Sept 9, 2013).

Antibiotics in acute non-pneumonic lower-respiratory tract infection

We read with interest the study by Paul Little and colleagues[1] that confirmed the findings of previous smaller studies[2] and support the present recommendations that acute bronchitis should not be treated with antibiotics. Because the authors used a threshold of 1% for statistical significance, we wonder why one of the secondary outcomes—that fewer individuals experienced new or worsened symptoms in the amoxicillin group—was interpreted as significant (p=0·043). We think that, according to the methods of the authors, none of the primary or secondary outcomes reached statistical significance, which would further corroborate the authors' conclusions to discourage the use of antibiotics in patients with acute non-pneumonic lower-respiratory tract infection. Moreover, these data emphasise the need to develop strategies to identify which patients with lower-respiratory tract infections need antibiotic treatment and which do not. For example, the use of biomarkers such as procalcitonin has been suggested to provide such a discriminative method,[3] and thus it might be interesting to know whether the patients included in the present study had low procalcitonin concentration.

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1 Little P, Stuart B, Moore M, et al. Amoxicillin for acute lower-respiratory-tract infection in primary care when pneumonia is not suspected: a 12-country, randomised, placebo-controlled trial. *Lancet Infect Dis* 2013; **13:** 123–29.
2 Evans AT, Husain S, Durairaj L, Sadowski LS, Charles-Damte M, Wang Y. Azithromycin for acute bronchitis: a randomised, double-blind, controlled trial. *Lancet* 2002; **359:** 1648–54.
3 Christ-Crain M, Stolz D, Bingisser R, et al. Procalcitonin guidance of antibiotic therapy in community-acquired pneumonia: a randomized trial. *Am J Respir Crit Care Med* 2006; **174:** 84–93.

Authors' reply

We are grateful for the comments of Simon Müggler and Lars Huber who query whether our interpretation of the modest benefit of antibiotics for new or worsening symptoms as significant at 5% matches the original assumptions in the power calculation. However, the outcome new or worsening symptoms was the limiting element in the sample size calculation, and the paper states that an α of 0·05 was chosen for this outcome, so our interpretation is consistent with this.[1] Findings should also be put in context of previous work: the modest symptomatic benefit is less likely to result from chance because it is in line with the previous systematic review.[2] Our study shows with precision