

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Sex work and HIV in Cambodia: trajectories of risk and disease in two cohorts of high risk young women in Phnom Penh, Cambodia
<b>AUTHORS</b>	Page, Kimberly; Stein, Ellen; Sansothy, Neth; Evans, Jennifer; Couture, Marie-Claude; Sichan, Keo; Cockroft, Melissa; Mooney-Somers, Julie; Phlong, Pisith; Kaldor, John; Maher, Lisa

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Roger Detels Professor University of California, Los Angeles USA
<b>REVIEW RETURNED</b>	16-May-2013

<b>THE STUDY</b>	The authors give incidence figures, but provide very little information about how they were derived.
<b>RESULTS &amp; CONCLUSIONS</b>	The authors recognize that the second cross-sectional survey is likely to have missed a significant segment of the sex worker population.

<b>REVIEWER</b>	Dr. Kasumi Nishigaya Australian Demographic and Social Research Institute The Australian National University  I have no competing interests.
<b>REVIEW RETURNED</b>	18-May-2013

<b>THE STUDY</b>	This article offers important perspectives on how a shift in legal norms regulating sex work can impact upon health outcomes. I would like to highly recommend the editor to be published with one condition on ethics. I understand that the research project was approved by relevant ethics committees, but it will be good what have been the pertinent issues which are under consideration by the ethics committee and how they have been carried out in actual research processes.
<b>REPORTING &amp; ETHICS</b>	I signed No for the above questions, but what I meant was I do not NO. So, I would like to request the authors to please consider adding some sentences to answer the following questions:  Publication Standards: I do not know the publication standards of this journal. If necessary, I should be guided on this to make a final decision by the Editor.  Incentives to the Participants of Survey: Just like any other surveys in Cambodia, please explain whether

	there have been payments or in-kind gifts to the research participants.
--	---

<b>REVIEWER</b>	King K. Holmes, MD, PhD William H. Foege Chair, Department of Global Health Professor of Global Health and Medicine Adjunct Professor of Microbiology and Epidemiology Director, Center for AIDS and STD University of Washington Head, Infectious Diseases   Harborview Medical Center
<b>REVIEW RETURNED</b>	29-May-2013

<b>THE STUDY</b>	The authors define what they did, and why - but don't posit a hypothesis or research question, per se.
<b>REPORTING &amp; ETHICS</b>	IRB review was completed; I couldn't find how the sex workers consented - was it verbal?
<b>GENERAL COMMENTS</b>	<p>This manuscript compares a Young Women's Health Study survey conducted in 2007-2008 (YWHS-1) and a similar survey in 2009-2010 (YWHS-2) samples (not cohorts, that term is misused here) of female sex workers compared with the YWHS-1 sample (N=160), the YWHS-2 sample (N=153) had a higher percentage who were married/living together, and had more education, shorter duration of sex work, higher percentages working in entertainment-venues (especially selling/promoting beer) or as freelancers, or having a manager, boss, or supervisor: reported fewer sex partners, more alcohol consumption, and less ATS use; had lower HIV prevalence if employed in an entertainment venue; and more frequently had ever been tested for HIV.</p> <p>As the authors note, the results are critically dependent on sampling frame and sampling methods. The same eligibility criteria and outreach methods were used as described separately in Refs 5 and 39. However, participants were recruited via "information meetings in neighborhoods where sex work was prevalent." It does seem likely, that the new "law on suppression of human trafficking and sexual exploitation" that "banned brothel based sex work" and drove the direct sex trade "underground," could have influenced which sex workers chose to attend the information sessions—and hence could have profoundly influenced the characteristics of the 2009-2010 sample. The authors do address this possible impact of sampling in the discussion, but don't adequately discuss how this may influence results. The exclusion of 67 of 220 who consented to participate in 2009-2010 because they had already been participants in 2007, could help explain the shorter duration of sex work and lower prevalence of HIV in the 2009 sample. The authors report that in 1997 11,300 women worked as FSW; and that NCHADS estimated that 12,762 were working in sex work in 2008 (suggesting a fairly stable estimate of number of sex workers over an 11-year period), and estimated that the number engaged in entertainment based sex work then tripled to an estimated 41,622 women (year of the estimate not specified) after the law on the suppression of human trafficking was passed. The authors then assert in the discussion in a confusingly worded sentence "there is potential for amplified population attributable risk for HIV, given the significant increase in the population of women exposed to transactional sex as well as male partners who may bridge to the general population." The concept that FSW shifted from brothels to other entertainment venues when the 2008 law was passed seems plausible; however, the speculation that a tripling in the number of sex workers might in</p>

	<p>one year (which is startling, and raises the question of how the NCHADS estimates were done) have an amplified PAR for HIV doesn't appear to be supported by the data in table 1, which suggests that although the number of sex partners in the last month per sex worker was at least 3 times higher in the YWHS-1 sample than in the YWHS-2 sample (grouped data can't be precisely analyzed). Although the authors state "alcohol use can be a barrier to condom use, and women working in the entertainment sector drink more alcohol," table one shows that reported condom use was not less common in the YWHS-2 sample than in the YWHS sample. At that time 40% of 437 brothel-based FSW were HIV seropositive. This present manuscript examines the interesting question of how the new 2008 anti-trafficking laws in Cambodia may be influencing female sex work and HIV risk. A balanced presentation and discussion of results could note that, 1) the composition of sex workers in the two samples differed; 2) the new law may have influenced sampling; 3) the estimated increase in numbers of sex workers in 2 years is astounding, not totally implausible, but warrants more information; 4) categories of FSW sampled in the two surveys differed; 5) to the extent entertainment-based sex workers have increased in number, I agree that increased attention to disease prevention and treatment services should address this growing population. The most interesting question is what impact—good or bad—that a law like this might have on female sex work and/or HIV/STI transmission. The data presented are a beginning, but don't warrant the over speculation advanced in this draft. Qualitative data —from FSW and from random samples of clients— e.g., the military— and from establishment managers, would be very interesting.</p>
--	---

### VERSION 1 – AUTHOR RESPONSE

Reviewer 1 (RD):

1. The authors give incidence figures, but provide very little information about how they were derived.

The method for calculating HIV incidence is provided in the Methods section, "Analyses" subsection (page 13). The HIV incidence rate calculated using the number of seroconversions per 100 person-years of observation (PYO) assuming a Poisson distribution.

2. The authors recognize that the second cross-sectional survey is likely to have missed a significant segment of the sex worker population.

We agree with the reviewer and noted such in the Discussion, where we discuss the challenges and limitations of researching this hard to reach population.

No changes are made to the manuscript with respect to this reviewer's comments.

Reviewer 2 (KN):

1. This article offers important perspectives on how a shift in legal norms regulating sex work can impact upon health outcomes.... [I]t will be good [to know] what have been the pertinent issues which are under consideration by the ethics committee and how they have been carried out in actual research processes.

We very much appreciate this consideration by the reviewer. As noted in the Methods section, Ethical

review of the study protocols were reviewed and approved by Institutional Review Boards from each of the participating Universities (UCSF, and UNSW), as well as the the Cambodian National Ethics Committee. All research procedures were carried out in adherence to recognized international and institutional standards for ethical conduct of human research practices (Helsinki Declaration of 1975, as revised in 2000). Written informed consent (in Khmer) was obtained from all participants after information meetings held in a community based setting (See page 11, where we added the term “written” to the description of the informed consent). Women who were unable to read assisted by and all study materials were read and explained to them. All study staff, both clinical and community-based, including anyone who had contact with any study subjects or study data received training in the Ethical Conduct of Human Subjects Research as well as Good Clinical Practice. All women received client-centered counseling for HIV and STI testing, and those with positive tests were referred to services for treatment and follow up (see sections on Data Collection and Laboratory testing of the manuscript). The strong involvement of a community based partner (the Cambodian Women’s Development Agency) helped to ensure that women had help in securing free or subsidized medical assistance. No changes were made to the manuscript in response to this comment as most of this information has already been detailed (Methods section).

2. Incentives to the Participants of Survey: Just like any other surveys in Cambodia, please explain whether there have been payments or in-kind gifts to the research participants.

Women who participated in the study were remunerated for their time: US\$5 at each visit. We added this to the manuscript in the Methods section in the Study Population and Recruitment subsection (page 11).

Reviewer 3 (KH)

1. The authors define what they did, and why - but don't posit a hypothesis or research question, per se. Question not well articulated.

The YWHS-1 and -2 studies were prospective observational studies, the principal study aims were to estimate HIV prevalence and incidence, and associated risk factors (See Introduction, last paragraph). Both studies had additional specific research questions: (1) assess the association between Amphetamine-type stimulant (ATS) use and HIV and STI infections in YWHS-1), and; (2) assess the prevalence of HPV and association with HIV (YWHS-2), as detailed in published papers of these primary analyses (See Couture et al., 2010; Couture et al., 2011, and Couture et al., 2013). As noted by the reviewer, we did not describe these primary research questions in this paper, as they have been previously published on. In this paper, we do theorize that demographic characteristics and HIV risk of FSW has shifted as a result of socio-legal changed induced by the implementation of the new legislation. We added this information to the Introduction section (page 10; last sentence) of the paper. We note to the reviewer that we used the word “theorize” since we did not test a hypothesis in this paper.

2. IRB review was completed; I couldn't find how the sex workers consented - was it verbal?

Written informed consent was obtained from all participants (see response to Reviewer 2, item#1 above). We also clarified this in the Methods section (page 11) of the manuscript.

3. The exclusion of 67 of 220 who consented to participate in 2009-2010 because they had already been participants in 2007, could help explain the shorter duration of sex work and lower prevalence of HIV in the 2009 sample.

Analyses including the 67 women who participated in both shows a somewhat higher proportion of

HIV-positive women (15.45% vs. 9.2% when excluded) and longer duration of sex work (median of 3.5 years; [IQR 2, 5.75] vs. 3 years [IQR 1.7, 5] when excluded), however these are remains below that found in YWHS1 and are not significantly different. We have included information on this with respect to HIV prevalence in the manuscript (Results section, page 15), maintain that there are real differences between the two samples that cannot be attributed to the exclusion of the 67 women.

4. The authors report that in 1997 11,300 women worked as FSW; and that NCHADS estimated that 12,762 were working in sex work in 2008 (suggesting a fairly stable estimate of number of sex workers over an 11-year period), and estimated that the number engaged in entertainment based sex work then tripled to an estimated 41,622 women (year of the estimate not specified) after the law on the suppression of human trafficking was passed.

We regret not providing the necessary information for this important data. The number of women estimated to be working in the entertainment industry – 41,622, was enumerated in 2012. This (the year) is clarified in the Introduction (page 9). The reviewer is correct that there appeared to be some stability in the number of women working in the sex and entertainment industry up until 2008. After that date, the number of women has grown substantially (in 2009, NCHADS estimated that there were 35,000). We do not intend to imply that the number of FSW grew as a result of the legislation. We believe that this was more a result of secular economic forces during the years of 2008-2012. To clarify this, and the effects of the anti-trafficking legislation we edited the introduction slightly (see page 9). Many sources to support that there was an exodus of women from brothel-based work to entertainment-based work or 'underground' after the anti-trafficking legislation.

5. The authors then assert in the discussion in a confusingly worded sentence “there is potential for amplified population attributable risk for HIV, given the significant increase in the population of women exposed to transactional sex as well as male partners who may bridge to the general population.” .... Amplified PAR for HIV doesn't appear to be supported by the data in table 1, which suggests that although the number of sex partners in the last month per sex worker was at least 3 times higher in the YWHS-1 sample than in the YWHS-2 sample (grouped data can't be precisely analyzed).

We understand the reviewers concern, and the confusion regarding this. We disagree that there is not potential for amplified population attributable risk for HIV in association with transactional sex in this context most significantly in association with the numbers of women involved in transactional sex. However, given the limitations of the data, and sampling, we modified the statement, which we hope the reviewers will find both less confusing and more balanced in suggesting the potential increased risk. On page 17 in the Discussion section we write: “Despite the lower prevalence of HIV and the lower number of male sex partners reported by this growing group of FSW, there is significant potential for amplified transmission of HIV at a population level, given the extraordinary growth in the size of the population, especially if male partners bridge to women who are not involved in transactional sex.”

6. Although the authors state “alcohol use can be a barrier to condom use, and women working in the entertainment sector drink more alcohol,” table one shows that reported condom use was not less common in the YWHS-2 sample than in the YWHS sample.

The reviewer is correct, and we have modified the Discussion to note that we did not find differences in reported inconsistent condom use between the two samples (See Discussion section, page 18).

7. A balanced presentation and discussion of results could note that, 1) the composition of sex workers in the two samples differed; 2) the new law may have influenced sampling; 3) the estimated increase in numbers of sex workers in 2 years is astounding, not totally implausible, but warrants more information; 4) categories of FSW sampled in the two surveys differed; 5) to the extent

entertainment-based sex workers have increased in number, I agree that increased attention to disease prevention and treatment services should address this growing population. The most interesting question is what impact—good or bad—that a law like this might have on female sex work and/or HIV/STI transmission. The data presented are a beginning, but don't warrant the over speculation advanced in this draft. Qualitative data —from FSW and from random samples of clients— e.g., the military— and from establishment managers, would be very interesting.

We agree with the reviewer regarding these points. We believe that the Discussion largely made the points elucidated, however we do add some edits to avoid 'over-speculation'. In paragraph 1 of the Discussion (Page 16), we believe we covered points #1-4, but add a sentence at the end regarding point #5. In the final paragraph of the Discussion (page 20) we include edits that note the need for more research on the effects of the law, and note the "potential" of the effects (rather than asserting as we did in the previous draft).

### VERSION 2 – REVIEW

<b>REVIEWER</b>	King Holmes Chair, Department of Global Health University of Washington Seattle, WA USA
<b>REVIEW RETURNED</b>	24-Jul-2013

<b>RESULTS &amp; CONCLUSIONS</b>	<p>The strengths of this study are the documentation of the shifts in patterns of sex work following the criminalization of prostitution in Cambodia; the characterization of differences in sex workers surveyed before and after the criminalization; the call for new approaches to HIV/STI prevention, given the changes; and the brief discussion of potential new approaches; this warrants publication.</p> <p>The weaknesses include the speculation that with the changes in sex work following criminalization "there is significant potential for amplified transmission of HIV at the population level" which does not necessarily follow from the data presented. For example, the mean number of partners in last month fell from 30 to 5; HIV prevalence in sex workers fell from 23.1% to 9.2%; and numbers of sex workers increased from 12,762 enumerated in 2008 to 41,622 in 2012 (from 2012 estimates, methodology not described).</p> <p>Thus, from the data presented, assuming condom use was unchanged, the number of sex workers x median number of partners per sex worker x proportion of sex workers with HIV represents 88,441 exposures through commercial sex to HIV in 2008 and 19,146 in 2012. These numbers suggest 78% reduction in HIV exposures through commercial sex.</p> <p>Neither the authors nor I like the concept of criminalization of sex work, but the data for this study does make the case for how this might increase risk of HIV transmission. The data suggest the opposite. The authors cite their own qualitative research, and that of others, that "negative impacts of criminalization include displacement and harassment and reduced access to condoms and health care... raising concerns about increased risks of HIV transmission as a result of the increasingly clandestine nature of sex work." However, the sex workers education, income, amount of sex work, and women per partner increased for the women surveyed.</p> <p>A real issue is what is happening to the women not surveyed in 2012</p>
----------------------------------	--

	– who weren't reached because they are now clandestine? Also, a comparison to the Thai approach, with the evidently successful 100% condom use in brothels – vs the nearby Cambodian criminalization approach could be made.
<b>GENERAL COMMENTS</b>	If the authors don't want to address my comments, but my review is published - which I believe is what you do - that's fine with me. If my comments are not published, then I recommend they modify the discussion.

### **VERSION 2 – AUTHOR RESPONSE**

We agree with Dr. Holmes, the reviewer that the situation is complex and that inferring causality to increased risk to the implementation of new anti-trafficking laws is beyond the scope of the paper. We see his point regarding the potential for cumulative reduced risk exposure based on the calculations made, but respectfully disagree with the conclusion. We feel that the addition of new low risk women to the population pool of FSW - ADDS to the higher risk group, who have not disappeared. They are not in our sample and may be poorly represented in government census figures as well. We did modify our manuscript to address his point, which is important. Our edits are in the discussion section, in blue font. We thank the editors and Dr. Holmes for their careful assessment of the implications of the data in this paper. We believe that the final product is greatly improved as a result.