Social harms in female-initiated HIV prevention method research: state of the evidence

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Objectives: Assessment of safety is an integral part of real-time monitoring in clinical trials. In HIV prevention research, safety of investigational products and trial participation has been expanded to include monitoring for 'social harms', generally defined as negative consequences of trial participation that may manifest in social, psychological, or physical ways. Further research on social harms within HIV prevention research is needed to understand the potential safety risks for women and advance the implementation of prevention methods in real-world contexts.

Methods: Secondary analysis of quantitative data from three randomized, double-blind, placebo-controlled trials of microbicide candidates in sub-Saharan Africa was conducted. Additionally, we assessed data from two prospective cohort studies that included participants who became HIV-positive or pregnant during parent trials.

Results: Social harms reporting was low across the largest and most recent microbicide studies. Social harm incidence per 100 person-years ranged from 1.10 (95% CI 0.78–1.52) to 3.25 (95% CI 2.83–3.74) in the phased trials. Reporting differed by dosing mechanism (e.g. vaginal gel, oral tablet, ring) and study, most likely as a function of measurement differences. Social harms were most frequently associated with male partners, rather than, for example, experiences of stigma in the community.

Conclusion: Measurement and screening for social harms is an important component of conducting ethical research of novel HIV prevention methods. To date, social harm incidence reported in microbicide trials has been relatively low (<4% per 100 person-years), and the majority have been partner-related events. However, any incidence of social harm within the context of HIV prevention is important to capture and understand

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for the safety of individuals, and for the successful impact of prevention methods in a real-world context.

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Background

Assessment of safety is an integral part of real-time monitoring in clinical trials. In HIV prevention research, safety monitoring has been expanded to include 'social harms', generally defined as negative consequences of trial participation, that may manifest in social, psychological, or physical ways [1]. Participants may face social harms for being at risk of HIV, being perceived to have HIV, or for participating in research. A variety of factors, including cultural norms around sexuality and morality, local understandings of gender and sex roles, previous experience of violence within intimate partner relationships, and stigma contribute to and exacerbate social harm risk [2–4].

The concept of social harms in HIV prevention research was introduced in relation to vaccine studies in 1998 [5], and much of the research on social harms stems from these early HIV prevention studies. Little has been published about the frequency of social harms experienced during microbicide or oral preexposure prophylaxis (PrEP) studies. Although developed as biomedical technologies to provide women with agency to protect themselves from HIV, research has indicated that men's attitudes toward products influence women's acceptability and use [6–8]. Emerging evidence also suggests that microbicides in gel or ring formulations, or oral PrEP, may exacerbate women's risk for social harm, including intimate partner violence (IPV) [9,10]. Social harm experiences may also inhibit women's ability to consistently use HIV prevention products [9,11].

As more HIV prevention products are available, a greater number of women may be placed at risk of experiencing social harms. It is important to monitor whether, when and how prevention methods exacerbate experiences of social harm in a trial context, so as to mitigate risk and potential negative impact on product uptake and use. In this article, we review how social harms have been assessed in HIV prevention studies, report on their frequencies, and discuss best practices for monitoring and addressing social harms in future research and programmatic work.

Methods

Study design and sample

We conducted a secondary analysis of social harm data from three randomized, double-blind, placebo-controlled phase IIb and phase III trials of microbicide candidates in sub-Saharan Africa, two of which were sponsored by the Microbicide Trials Network (MTN) and one by the International Partnership of Microbicides (IPM). The purpose of this analysis was to understand how the largest and most current multisite microbicide trials with women were defining and measuring social harms, and to assess the frequency and scope of reported social harms.

Data included in this analysis were drawn from a convenience sample of studies from which colleagues and collaborators provided permission to access protocol-specified social harms procedures and data. Although not intended as a comprehensive review, all recent (post 2010) phase IIb and III microbicide candidate trials of which we had knowledge were invited to participate, and all but one were able to provide data at the time of request. Studies are summarized in Table 1.

Study settings

All trials were conducted with women in sub-Saharan Africa. The VOICE and ASPIRE studies had sites in Uganda (Kampala); Zimbabwe (Chitungwiza, Harare); Malawi (Blantyre, Lilongwe) and South Africa (Cape Town, Durban, Johannesburg, Klerksdorp, Soweto). The Ring Study was conducted in Uganda (Masaka) and South Africa (Brits, Cape Town, Edendale, Ladysmith, Limpopo, Pinetown). The MTN-015 and MTN-016 cohort studies include data from global MTN sites, but only data from the aforementioned MTN sites were included in this analysis.

Measures and procedures

Trial-specific definition and measurement of social harms

The definition of 'social harm' and the process by which social harms were measured differed across studies. In MTN studies, social harms were defined as 'nonmedical adverse consequences experienced by participants as a result of their participation in the study.' Examples of social harm in MTN study-specific procedure manuals included difficulties in personal relationships with partners, family members, and friends, as well as stigma or discrimination because participants could become known as HIV-positive or at 'high risk' for HIV infection.

In the VOICE Study [13], data about experiences of social harm were systematically collected on Case Report Forms (CRF) from all participants as part of behavioral

Table 1. Summary of microbicide studies included in this analysis.

Name	Study design	*N*	Location	Duration
IPM 027/The Ring Study [12]	Phase III randomized, placebo-controlled trial of the safety and effectiveness of a vaginal ring containing the antiretroviral dapivirine	1959	South Africa Uganda	2012–2016
MTN-003/VOICE [13]; Vaginal and Oral Interventions to Control the Epidemic	Phase IIb randomized, placebo-controlled trial to assess the safety and effectiveness of daily use of an antiretroviral (ARV) tablet (tenofovir or Truvada) or daily use of a vaginal gel (tenofovir gel)	5029	South Africa, Uganda, Zimbabwe	2009–2012
MTN-015 [14]	Multisite, prospective, observational cohort study of women following HIV-1 seroconversion in microbicide trials of ARV-based microbicides or oral preexposure prophylaxis (PrEP)	409	Malawi, South Africa, Uganda, Zimbabwe	2009–2016
MTN-016/EMBRACE [15]; Evaluation of Maternal and Baby Outcome Registry After Chemo-prophylactic Exposure	Prospective observational cohort study of maternal exposures to investigational HIV prevention agents	550	Malawi, South Africa, Uganda, Zimbabwe	2010–2015
MTN-020/ASPIRE [16]; A Study to Prevent Infection with a Ring for Extended Use	Phase III randomized, placebo-controlled safety and effectiveness trial of a vaginal ring containing the antiretroviral dapivirine	2629	Malawi, South Africa, Uganda, Zimbabwe	2012–2015

assessments administered by interviewers quarterly, at the product use end visit, and at the termination visit. Social harms data were captured in a two-tier system. First, participants were read structured questions about whether they had experienced any 'problems' since the last visit as a result of being in this study and presented with a list of potential people including an open-ended 'other' response. If any problems were reported, they were asked whether the problem resulted in emotional, physical, or economic harm, or harm to their children. Participants could also spontaneously report study-related issues and problems to staff at any visit.

The social harm reporting policy for VOICE was revised for the ASPIRE Study [16]. Interviewers asked women a standardized question about social harms quarterly and at the product use end visit: *'At any time during the past 3 months, have you experienced a social harm related to your study participation?'* Staff were permitted to clarify the language if it was not understood. Social harms reported through this structured mechanism, or through any spontaneous report, triggered the completion of a *Social Impact Log* CRF, which captured a description of the event, the onset date, whether it involved physical harm to her or her children, and the impact on her quality of life (minimal disturbance, moderate disturbance with no significant impact, or major disturbance with significant impact). Each social harm was characterized as being related to family, a sex partner, other personal relationships, travel/immigration, employment, education, medical/dental, housing, or other.

In the MTN-015 study [14], a prospective cohort study for women who seroconverted on VOICE, ASPIRE or other MTN investigational drug-related studies, participants were asked, similarly to VOICE, whether they had 'any problems with the following people [list] as a result of being in the study' at their month 3 and month 6 visits, and every 6 months thereafter including the final study visit. Questions were read from a questionnaire by a staff member. Participants were asked to specify the type of harm experienced. In this study, the traditional definition of social harm as being 'related to study participation' was expanded to measure harms related to being recently infected with HIV.

In the MTN-016 study [15], a prospective cohort registry of women who became pregnant during trials of microbicide or oral PrEP products and their infants, participants were asked about experiences of social harm at all follow-up visits, including quarterly during pregnancy; at pregnancy outcome; at 1, 6, and 12 months after birth; and at interim visits. MTN 016 study staff were instructed to 'inquire about social harms' on visit checklists but did not administer structured questions to participants. If a social harm was reported, a CRF was completed about the social harm, including whether it impacted the woman, the infant, or both, whether problems with a list of people had occurred, and whether the problem resulted in emotional, physical, economic/financial, or harm to children.

The Ring Study defined social harm as 'an untoward event that causes physical, emotional or financial harm to a trial participant'. Social harms were assessed and documented at every visit during HIV counseling sessions. In IPM study operating manuals social harms were further defined as: *'social harm means literally a social interaction that has caused harm to the participant',* which might encompass nontrial-related harms. If social harms were reported, a three-part CRF was completed. The first section included questions for the participant to establish the social harm type, her opinion of its relatedness to trial participation and if the social harm was resolved. The second section required the staff member to classify the harm as physical, emotional or

financial, and to document any follow-up required. The third section was a follow-up form that documented any additional or new information to a previously reported social harm.

Analysis

For each of the studies, we reviewed study protocols, procedural manuals and data collection forms to identify how social harms were defined, measured, referred (if applicable) and reported to protocol teams and ethics committees. For the MTN studies, raw individual-level data were obtained from the MTN Statistical and Data Management Center (SCHARP) and analyzed in Stata. Incidence of overall social harm (from any perpetrator) was computed as each participants' time from enrolment to reported onset of the first social harm or end of study, and incidence of partner-related social harm was computed as time to first partner-related social harm or end of study for each participant. Frequencies of social harm type, perpetrator and outcome were tabulated. For IPM 027, computed statistics, using SAS, were provided by ClinData, an IPM external service provider for biostatistics.

Results

Frequency, perpetrators and types of social harms

In VOICE, 218 social harms were reported by 195 women, representing an incidence of 3.25 (95% confidence interval (CI) 2.83–3.74) first social harm events per 100 women-years (Table 2). The incidence of partner-related social harm was 1.85 (95% CI 1.53–2.22), with just over half (112, 51.4%) of reported social harms being partner-related. The proportion of social harms reported did not differ by arm assignment (tablet vs. gel). The majority of social harms (98%) were described as causing emotional harm, with a smaller number, in addition to causing emotional harm, reported as causing economic harm (12%) or harm to children (2%). Eleven social harms (5%) were reported to cause physical harm (Table 3). The majority of social harms experienced by participants in the gel arm resulted from misconceptions about the study as well as a disapproval of physical effects of the gel that affected intercourse, such as vaginal wetness. Outcomes varied from general disapproval, forced removal from the study, to incidences of sexual violence. The majority of social harms in the tablet arm were perpetrated by male partners, most frequently because of misconceptions about the study (e.g. partners believed their female partners were participating because they were HIV-positive). Accusations, judgment or shaming around HIV status by friends, colleagues and community members were also frequently reported by those in the tablet arms.

During ASPIRE, 91 participants reported 94 social harm events, representing an incidence of 2.00 per 100 women-years (95% CI 1.63–2.46; Table 2) [9]. Eighty-five women reported partner-related social harms during the study, including two women who reported two social harm events each (incidence of first partner-related event: 1.87, 95% CI 1.51–2.31). These constituted 92.6% of all social harm events reported during the study. Twenty-six (28.9%) social harm events resulted in physical harm to the participant; there were no reports of harm to the participant's children. The majority of partner-related social harms were reported to have minimal impact on quality of life (51 social harms or 58.6%), with 27 (31.0%) classified as moderate disturbance and nine (10.4%) causing a major disturbance with significant impact. Those with major impact were often related to the participant's partner threatening divorce or separation or no longer wanting to have sex with the participant if she did not leave the study. Participants also reported physical violence from male partners when the ring was discovered during sex and relationship dissolution after partner notification for STI treatment (data not shown). At the end of the study, seven social harm events were unresolved or unable to be resolved ($n = 4$) because of participants being lost to follow-up.

Table 2. Frequency and incidence of social harms reported in microbicide studies.

Study	N[a]	Women reporting social harms	Social harms reported	Person-years	Social harm incidence per 100 person-years	Partner-related social harms[b] (%/social harms)	Partner-related social harm incidence per 100person-years[b]
IPM 027/The Ring Study [12]	1958	37	39	3359.09	1.10 (95% CI 0.78–1.52)	34 (87.2%)	0.95 (95% CI 0.65–1.34)
MTN-003/ VOICE [13]	4943	195	218	5992.75	3.25 (95% CI 2.83–3.74)	112 (51.4%)	1.85 (95% CI 1.53–2.22)
Tablet	2963	113	125	3729.51	3.03 (95% CI 2.52–3.64)	65 (52.0%)	1.72 (95% CI 1.35– 2.19)
Gel	1980	82	93	2263.24	3.62 (95% CI 2.92–4.50)	47 (50.5%)	2.05 (95% CI 1.54–2.73)
MTN-015 [14]	400	2	2	1183.96	0.17 (95% CI 0.04–0.68)	1 (50.0%)	0.08 (0.01–0.60)
HIV-related	400	12	13	1160.37	1.29 (95% CI 0.78–2.14)	11 (84.6%)	0.94 (0.52–1.71)
MTN-020/ ASPIRE [16]	2622	91	94	4548.34	2.00 (95% CI 1.63–2.46)	87 (92.6%)	1.87 (95% CI 1.51–2.31)

[a]Analysis sample size.
[b]Partner-related person-years at risk is slightly higher because the person-years includes only time to the first partner-related social harm.

Table 3. Social harm classifications, perpetrators and outcomes, by study.

	VOICE		ASPIRE	MTN 015		MTN 016	IPM 027
	Gel	Tablet		Study-related	HIV-related		
Number of 'problems' reported[a] (*n*)	168	225	NA	8	22	1	NA
Unique participants reporting a 'problem'[a] (*n*)	138	201	NA[b]	8	20	1	NA
Number of social harms reported (*n*)	93	125	94	2	16	1	39
Unique participants reporting a social harm or experiencing social harm from a reported problem[a] (*n*)	82	113	91	2	15	1	37
Classification of harm experienced[c]: *n* (%)							
Emotional	91 (98)	122 (98)	NA	2 (100)	16 (100)	1 (100)	33 (85)
Physical harm	3 (3)	8 (6)	26 (28)	0	2 (1)	0	14 (36)
Economic harm	15 (16)	12 (70)	NA	0	4 (3)	0	7 (18)
Harm to children	2 (2)	2 (2)	1 (1)	0	4 (3)	0	2 (5)[d]
Perpetrator or source of problem/ social harm[e]: *n* (%)							
Partner	53 (60)	70 (61)	87 (93)	1 (50)	11 (69)	1 (100)	34 (87)
Family/people at home (not partner)	11 (13)	18 (16)	2 (2)	0	1 (6)	0	3 (8)
Friend/personal relationships	8 (9)	8 (7)	1 (1)	1 (50)	2 (13)	0	0
Employment-related/co-workers	9 (10)	10 (8)	2 (2)	0	2 (13)	0	1 (3)
Landlord or property owner	1 (1)	0	1 (1)	0	0	0	NA
Healthcare provider or medical-related	2 (2)	5 (4)	0	0	0	0	0
Education-related	1 (1)	1 (1)	0	0	0	0	NA
Travel or Immigration-related	NA	NA	0	NA	NA	NA	NA
Church members	NA	NA	NA	NA	NA	NA	0
Community members known to you[f]	3 (3)	2 (2)	1 (1)	0	NA	0	0
Strangers	NA	NA	NA	NA	NA	NA	1 (3)
Reported impact on quality of life							
Minimal disturbance	NA	NA	54 (57)	NA	NA	NA	15 (38)
Moderate disturbance, no significant impact[g]	NA	NA	29 (31)	NA	NA	NA	13 (33)
Major disturbance with significant impact[g]	NA	NA	11 (12)	NA	NA	NA	10 (26)

[a]VOICE, MTN 015 and MTN 016 were the only studies that systematically first asked about 'problems' before probing further into experience of harms.
[b]'NA' in this table is used to indicate that the item was not measured
[c]Social harms could be classified in all categories that applied. The denominator in percentages is the total number of social harm.
[d]Categorized as harm to others, including children.
[e]For VOICE there are 16 of 218 social harms for which the data are unclear as to the perpetrator. These have been excluded from these tabulations.
[f]In VOICE and ASPIRE these were captured under 'other' and defined as community members or neighbors
[g]Significance of impact not captured on Case Report Forms (CRFs) for The Ring Study.

In the IPM Ring Study, 37 participants reported 39 social harm events, representing an incidence of 1.10 per 100 women-years (95% CI 0.78–1.52). Thirty-two women reported 34 partner-related social harms during the study, with an incidence of 0.95 per 100 women years (95% CI 0.65–1.34). The majority (33; 85%) of social harms were reported as emotional harm to the participant and 14 (36%) social harms resulted in physical harm. Two (5%) participants reported harm to others including children and family members. The perpetrators included the sex partner for 34 (87%) of the participants, family members for three (8%), co-workers in one (3%) and a stranger for one (3%) participant. Partner-related social harms were mostly reported as a minor disturbance (15 social harms; 38%), with 13 (33%) classified as a moderate disturbance and 10 (26%) causing a major disturbance.

In the MTN-015 study, nine participants (2.3%) reported partner-related social harms associated with being HIV-positive and one (0.3%) reported a partner-related social harm associated with study participation (Table 2). The social harm from study participation was because of the partner complaining about her absence from home during study visits. The majority of harms related to the participants' HIV status were emotional and occurred when the relationship dissolved or there was anger and blame over who infected whom within the partnership. There were also several reports of withdrawal of financial support after the participant's HIV status disclosure, and one report of physical violence.

In the MTN-016 study, one social harm was reported (data not shown), and it was an emotional harm associated with the male partner. The participant reported her husband did not believe she was planning to attend an ultrasound appointment, but thought she was going to meet another man.

Discussion

Monitoring of social harms in HIV prevention research is an important strategy to assess and address adverse consequences of study participation or product use that

go beyond clinical adverse events. Unlike adverse events, 'social harms' are not clearly defined or recognized by an international regulatory body, and in microbicide and other HIV prevention studies, their measurement and definition (and recognition of the importance thereof) has evolved over the past two decades. Although numerous HIV prevention studies have noted the importance of understanding and mitigating social harms related to study participation, few studies have conducted in-depth explorations of social harms, including how social harms might differ by dosing platform (e.g. vaginal gel, oral tablet, vaginal ring); and few have explored the incidence of social harms in the African context [1,4,10,17–20]. In this analysis of secondary data, we identified several key findings. First, social harm reporting was low across the largest and most recent microbicide studies. Second, reporting differed by dosing mechanism and study, most likely as a function of measurement differences. Third, social harms were most frequently associated with male partners.

Although no benchmarks exist, the included studies reported a low rate of social harms among a small proportion of participating women, and when measured, the majority of social harms did not negatively impact quality of life (Table 2). When reported, many social harms were acts of IPV, most commonly emotional IPV, but also physical. Given the high background rates of IPV in the region – the estimated lifetime IPV prevalence is 36.3% in Africa (95% CI 32.7–40.5) [21], in juxtaposition to the relatively low rates of social harm reported in these studies, several questions are raised, for example, *how are trial participants different than other women in their communities?* This is complex to measure, but it is likely that some women most vulnerable to social harm and HIV are not willing or able to join prevention trials, and implementation scientists and public health practitioners should preemptively prepare for monitoring social harms in prevention distribution programs. *Additionally, Do trial participants under-report social harms because they fear they will be exited from the trial or for other reasons?* In most cases, participants would not be exited and are told this during consent processes and counseling. However, qualitative studies have shown participants may report socially desirable behaviors about product adherence (i.e. do not report nonuse) so as not to be removed from the study [22,23]. Thus, it is likely some participants are fearful of reporting experiences that they think might jeopardize trial participation.

The overall incidence of social harm associated with participating in the dapivirine ring trials (ASPIRE and The Ring Study) was lower than what was reported in the tablet or gel arms of VOICE. However, the proportion of social harms that were *partner-related* in both ring trials was higher than in tablet or gel studies and the incidence of partner-related social harm was similar across all dosing platforms. Most social harms to date in HIV prevention trials have been partner-related problems associated with a study participant using an HIV-related or vaginal product, and the perceived implications of this on promiscuity, trust or HIV-status [9]. These findings are consistent with previous reports about the importance of male partners on women's microbicide use [8,22,24,25].

Importantly, it is unknown whether the partner-related differences between these studies are meaningful or a consequence of measurement. In studies, such as ASPIRE and The Ring Study, social harms were monitored systematically at every visit, and analogous to adverse events, a more in-depth description of events (e.g. onset, duration, severity) recorded. In ASPIRE, social harm reporting was triggered by overtly asking participants if they had experienced a social harm, or by participants spontaneously describing an event that was then recorded. It is unknown how well, or how consistently, participants understood the meaning of 'social harm' when asked this question, which may have introduced a classification bias. During The Ring Study, counselors assessed experiences of social harm during every HIV counseling visit, thus there was a less standardized and systematic application of a structured question. In other studies, like VOICE, participants were asked a more general question about experiencing 'problems' with different people in their lives, followed by detailed questioning to determine if a social harm had occurred. Although the use of a general term like 'problems' can also be subject to classification errors, it may be an effective screening question to explore potential social harms in more depth. Perhaps the best assessment of social harms in future studies would include a hybrid approach: enquiring about problems with various types of people (family, friends, partner, etc.) at every visit, then probing about, and documenting, social harms through counseling discussions and structured questionnaires. Additionally, data capture regarding the level of disturbance of social harms, and the impact on quality of life will provide important contextual information about each event.

Additional important questions raised through this analysis are: 'Do participants see social harms as everyday life experiences rather than social harm? Do the definitions of social harm used by researchers adequately address the experiences of harm and violence in women's lives?' Many harms may exist in women's lives, and with the exception of The IPM Ring Study and MTN-015, these would not get classified as social harms if they were not 'study-related'. Further, it may be difficult for women and researchers to know if an event is truly 'study-related', as the causal relationship is not always clear, particularly in abusive or controlling relationships. In MTN-015, social harms were categorized as 'definitely' or 'possibly' study-related, and in The Ring Study they were classified as 'study-related' or 'not study-related', which helps to acknowledge this ambiguity. Future projects may consider documenting all social harms and subsequently

quantifying, as with standard adverse event practice, the relatedness of social harms to the intervention. Integration of tools to measure and respond to IPV within the context of HIV prevention trials and demonstration projects may also expand beyond the study-related definition of social harms and better respond to women's needs. For example, addressing IPV/social harms could improve adherence and study outcomes, a hypothesis that several projects have aimed or are seeking to test [26–28]. However, addressing IPV is no small feat: it requires substantial time and resources in often over-burdened settings. There is a need for short, validated tools to measure IPV in prevention trial or public health clinics, as compared with longer questionnaires used in violence-related studies [e.g. Violence Against Women Scale (VAWS)] [21,29,30]. Self-administered and/or electronic-based tools may also help address human resource constraints and potential underreporting of social harms.

Although anticipated to be a source of social harms, community-based stigmatization social experiences were seldom reported in these trials. This may be reflective of a trend towards wider acceptance and knowledge of HIV in communities with significant research taking place. It may also reflect upon research groups' efforts to engage with Community Advisory Boards, and their sensitization activities in research catchment areas. Indeed, Volk *et al.* [17] reported the extensive community outreach they conducted prior to an HIV vaccine trial in South Africa may have reduced social harm in their study. A number of opinion papers and guideline documents, including those on Good Participatory Practice [31], have argued that introductory presentations to local communities will create a better understanding of their research perceptions, and have a positive impact on the uptake and acceptability of investigational products [2,32].

Tarimo *et al.* [20] argue it is vital to follow-up with participants after they have completed a trial because some will continue to suffer from social harm posttrial, and these harms may be different than those experienced during the study. To our knowledge, this has not been done and might offer important information for the research community. There is also increased recognition that investigation into social harm should be counter-balanced with measurement of social benefits, such as enhanced confidence, counseling support, or HIV prevention and health screening. This is being formalized in some protocols, like the MTN-025/HOPE Open Label Extension study of the dapivirine ring.

There are several limitations of this analysis. First, a systematic review was not feasible because of paucity of published social harm data, and the included studies represent the majority, but not all, recent microbicide trials, therefore results should not be considered comprehensive. These data were captured from trial participants who may be inherently different from other women in important ways, including their risk for social harm. Underreporting of social harm was likely to have occurred because of participant fear of being exited from these studies, because a social harm was not remembered, was perceived as 'normal' behavior, or for other measurement-related reasons, thus the true 'accuracy' of our estimates is not known. Although these data and approaches could inform future assessments of barriers to PrEP uptake in women, it is also unknown how the frequency and type of social harm reported in these studies will extend to real-world contexts and other HIV approaches.

In conclusion, measurement of and screening for social harms is an important component of conducting ethical research on novel HIV prevention methods. To date, social harm incidence reported in microbicide trials has been relatively low (<4% per 100 person-years), and the majority have been partner-related events, rather than experiences of stigma in the community. To gain a more comprehensive understanding of the context in which novel HIV prevention methods are integrated into women's lives, future research should screen more widely for social harms, social benefits and experiences of partner-related and nonpartner-related violence. Social harm events are important to capture and understand for the safety of women and the successful impact of prevention methods in real-world contexts.

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Conflicts of interest

There are no conflicts of interest.

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