

Cohort effects on sexual behavior and risk of acquisition of sexually transmitted infections and HIV in a South African HIV prevention trial

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Abstract

Introduction: As we approach the fourth decade with human immunodeficiency virus (HIV), a plethora of prevention interventions have been tried; however, prevention of new infections among women remain poorly understood and current behavioral change interventions are simply not working.

Material and methods: We investigate whether women's sexual behavior risks vary by age cohort, and the effect of this on HIV and sexually transmitted infections (STI) incidence of women enrolled in the South African Carraguard HIV prevention trial, using Cox proportional hazard models.

Results: Relative to women born in the 1960s or earlier, HIV incidence was approximately twice as high compared to women born in the 1970s (adjusted hazard rate [aHR]: 1.91; 95% confidence interval [CI]: 1.04-3.48; $p < 0.001$). Women in the youngest 1980s cohort had the highest risk of HIV infection (aHR: 3.77; 95% CI: 2.25-6.32; $p < 0.001$). Similarly, women in the 1980s relative to the oldest (\leq 1960s) cohort had significantly higher hazards of acquiring STIs (aHR: 1.51; 95% CI: 1.16-1.96; $p = 0.002$), had a higher frequency of partner changes, higher coital frequency, higher proportion having had sex for money, to have an older partner, and less likely to have a circumcised partner.

Conclusions: Our findings show HIV and STIs incidence remains highest amongst younger compared to older age cohorts, despite decades of STI/HIV risk-reduction interventions. Research is urgently needed to understand why after so many decades of socio-behavioral interventions little appears to have changed in the behavior of young women; instead, there appears to even be a glamorization of risky behaviors such as having older male sexual partners commonly called 'blessers'.

HIV AIDS Rev 2018; 17, 3: 181-188
DOI: <https://doi.org/10.5114/hivar.2018.78490>

Key words: South Africa, human immunodeficiency virus (HIV), sexual behavior, birth cohorts.

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Article history:
Received: 20.09.2017
Received in revised form: 13.02.2018
Accepted: 13.02.2018
Available online: 15.08.2018

International Journal
of HIV-Related Problems
**HIV & AIDS
Review**

Introduction

High human immunodeficiency virus (HIV) transmission rates persist as a global challenge [1] and women remain more vulnerable than men to acquire HIV infection [2]. Women's increased vulnerability to HIV infection is multifactorial and encompasses biological, structural, and behavioral factors like being in sexual partnerships with high-risk older men [3], concurrent relationships [4, 5], and low condom use due to inability to negotiate safer sex [6, 7]. Structural factors like gender-based violence [8] and poor income [9] also contribute to women's increased risk of HIV. This is compounded by lack of effective woman-controlled biomedical HIV prevention tools [10-14]. Since discovery of HIV in the 1980s, great strides have been made to increase understanding of transmission and treatment. As we approach the fourth decade with HIV, a plethora of prevention interventions have been tried. The persistently high-rate of HIV infections in particular age groups like adolescents [2, 15-17], however, suggests prevention of new infections among women remains poorly understood and current interventions are simply not working.

While it is important to examine and design interventions targeting individual-level factors of risky sexual behavior, it may not be adequate to bring about the needed large-scale socio-behavioral change for a significant STI and HIV infection decline. Literature suggests population-level cohort or time-periods social norms may be more important determinants of socio-behavioural change than period or age effect norms [18-21]. Unfortunately, cohort effects are usually not part of many recommendations and interventions suggested to date to combat high HIV/STIs rates in younger women [12, 22-31]. Most of these recommendations or interventions reinforce targeting young women before coital debut and emphasize sexual health education for young people for prevention [28, 32]. It is imperative to ascertain differences in risky behavior patterns in different birth cohorts as it is likely to impact the effectiveness of proposed preventative interventions, which presently tend to emphasize individual-level and not cohort effects.

Limited studies have investigated the effect of an era that one was born in on the incidence of HIV or sexually transmitted infections (STIs) in South African women. To help close this gap, we investigate in this study whether sexual behavior risks of women vary by time period defined by date of birth, and the effect of this on HIV and STI incidence of women enrolled in a South African HIV prevention trial. We hypothesize that there are cohort effects in sexual behavior patterns and HIV risk among women in South Africa.

Material and methods

Study participants and procedures

Data for this analysis came from a randomized, placebo-controlled, double-blinded clinical trial designed to

assess the efficacy of a microbicide gel in preventing HIV infection among women [33]. The Population Council, Carraguard™ trial was conducted at three locations in South Africa: Isipingo (Durban), Soshanguve (Pretoria), and Gugulethu (Cape Town). In brief, Carraguard enrolled sexually-active, HIV-negative, 16 years and older women. Participants completed an interviewer-administered questionnaire on demographics and sexual behavior. Women were seen at the study clinic at screening, enrolment, month 1, month 3, and every 3 months thereafter for 9-24 months. Women had pre-test, an HIV test, and post-test counselling at all visits (except enrolment). At screening and every 3 months, or when clinically indicated, women were tested for STIs (*Chlamydia trachomatis*, *Neisseria gonorrhoeae*, syphilis, and *Trichomonas vaginalis*). Throughout the study, all women both in the experimental and placebo arms received risk-reduction counselling and use of male condoms, which were provided. The study took place between March 2004 and March 2007. All protocols and informed consent forms were approved by the Biomedical Research Ethics Committee at the University of KwaZulu-Natal, and the various study-specific Institutional Review Boards.

Statistical analyses

Here, we analyze data collected from 1,456 ($n = 730$ experimental, $n = 726$ placebo) women at the Durban research site. Participants were grouped into four birth-cohorts: (1) before 1960, (2) 1960-1969, (3) 1970-1979, and (4) 1980-1989. In the survival analyses, participants in the first two cohorts were combined into one cohort (1960s or earlier) given the small numbers born before 1960. We first present descriptive statistics to explore socio-demographic and behavioral characteristics of women in each birth cohort. We then used survival analyses and Cox proportional hazards models to calculate hazard ratios and 95% confidence intervals for incidence of HIV and STIs across the four birth cohorts, adjusted for socio-demographic, and behavioral factors and interaction terms.

Control variables

Socio-demographic

Marital status: Marital status was categorized into married (0) or never married (1). The former included the very negligible proportion of separated, divorced, or widowed women.

Steady sexual partner: As per study protocol, all participants had to have a sexual partner. This was categorized as either a steady partner (1) or non-steady partner (0), where a steady sexual partner was anyone the participant had sex with on a regular basis in the last three months. We further included whether steady partner was circumcised (1) or not (0), condom use (1) or not (0) with steady partner, number of sexual partners in the last 3 months (1, 2 or ≥ 3 partners), and change of partners during the study (yes/no).

Table 1. Socio-demographic characteristics and study product use by birth cohort

Variable, n (%)	≤ 1959	1960-1969	1970-1979	1980+	p-value
	122 (100)	318 (100)	401 (100)	615 (100)	
Never married	42 (34.43)	160 (50.31)	285 (71.07)	587 (95.45)	< 0.001
Has steady partner	122 (100)	317 (99.69)	400 (99.75)	611 (99.35)	0.639
Condom used with steady partner at last sex act	19 (15.57)	78 (24.53)	125 (31.17)	208 (33.82)	< 0.001
Changed partner(s) during study	7 (5.74)	21 (6.6)	45 (11.22)	76 (12.36)	0.014
Coital frequency in last 2 week before screening: 3+	40 (32.79)	131 (41.19)	178 (44.39)	190 (30.89)	< 0.001
Ever had forced sex	20 (16.39)	61 (19.18)	51 (12.72)	63 (10.24)	0.001
Ever had sex for cash	2 (1.64)	11 (3.46)	11 (2.74)	16 (2.6)	0.750
Partner circumcised	31 (25.41)	87 (27.36)	107 (26.68)	120 (19.51)	0.015
Number of sexual partners in last 3 months at screening					
1	115 (94.26)	289 (90.88)	378 (94.26)	567 (92.2)	0.155
2	6 (4.92)	17 (5.35)	19 (4.74)	37 (6.02)	
3+	1 (0.82)	12 (3.77)	4 (1)	11 (1.79)	
Age difference with steady partner					
Younger	23 (19.0)	56 (17.2)	32 (8.0)	9 (1.5)	< 0.001
Peer (0-4 years)	62 (51.2)	130 (41.1)	208 (52.0)	339 (55.5)	
Older (≥ 5 years)	36 (29.8)	130 (41.1)	160 (40.0)	263 (43.0)	
Contraception used as screening					
Male condom	13 (10.66)	29 (9.12)	49 (12.22)	106 (17.24)	< 0.001
Long term (injectable)	4 (3.28)	68 (21.38)	182 (45.39)	304 (49.43)	
Female sterilization	40 (32.79)	96 (30.19)	35 (8.73)	4 (0.65)	
Oral pills	1 (0.82)	16 (5.03)	30 (7.48)	32 (5.2)	
None	64 (52.46)	109 (34.28)	105 (26.18)	169 (27.48)	
% visits unprotected anal sex (≥ 10%)	6 (4.92)	13 (4.09)	26 (6.48)	26 (4.23)	0.359
% visits unprotected oral sex (≥ 10%)	9 (7.38)	22 (6.92)	64 (15.96)	107 (17.4)	< 0.001
Condom use at baseline	44 (30.77)	45 (30.77)	46 (30.77)	47 (30.77)	< 0.001
% visits condom used post enrolment					
≥ 50%	71 (58.2)	183 (57.55)	253 (63.09)	413 (67.15)	0.020
100%	29 (23.77)	89 (27.99)	129 (32.17)	204 (33.17)	0.114
% visits condom and gel post enrolment					
≥ 50%	70 (57.38)	178 (55.97)	243 (60.6)	397 (64.55)	0.062
100%	22 (18.03)	74 (23.27)	108 (26.93)	171 (27.8)	0.091

Contraceptive use: We included contraceptive method used at screening: male/female condoms (1), long-term injectables (2), oral pills (3), sterilization (4), and none (5).

Sexual behavior

Coital frequency in last two weeks: This was categorized as: 1, 2, or ≥ 3. It was later dichotomized as ≥ 3 (1) or < 3 (0).

Sexual violence: We included women who had ever been abused (yes/no) or ever been forced to have sex (yes/no). We also included whether the woman had ever had sex for money (yes/no).

Sexual practices: Sexual expressions over the generations are likely to have gone through some major transformation.

To test for this, we included frequency of reporting anal or oral sex among study participants. The cut-point of ≥ 10% of visits with unprotected anal or oral sex was considered as risky sexual behavior. We further considered the frequency and consistency of condom use post enrolment. This was categorized as condom use reported in ≥ 50% or in 100% of post-enrolment visits.

Outcome variables

STIs and HIV incidence: Incidence of STIs and HIV were main outcomes. Since some STIs could be recurrent events, time to first positive was considered for any of the STIs (*Chlamydia trachomatis*, *Neisseria gonorrhoeae*,

Table 2. Unadjusted and adjusted hazard ratios of acquiring human immunodeficiency virus (HIV) and sexually transmitted infections (STI) infections by birth cohort

Birth cohorts	HIV unadjusted hazard ratio (95% CI)	p-value	HIV adjusted* hazard ratio (95% CI)	p-value
≤ 1969	1.00		1.00	
1970-1979	1.85 (1.02-3.37)	0.043	1.91 (1.04-3.48)	0.035
1980s	3.62 (2.18-6.01)	< 0.001	3.77 (2.25-6.32)	< 0.001
Birth cohorts	STI** unadjusted hazard ratio (95% CI)	p-value	STI** adjusted hazard ratio (95% CI)	p-value
≤ 1969	1.00		1.00	
1970-1979	0.86 (0.64-1.18)	0.335	0.85 (0.63-1.15)	0.291
1980s	1.56 (1.20-2.01)	0.001	1.51 (1.16-1.96)	0.002

*Adjusted for having a steady partner, partner circumcised, number of partners in last 3 months, coital frequency, frequency and consistency of condom use, ever been forced sex, ever been abused.

**At least one positive test for *Neisseria gonorrhoea*, *syphilis*, and/or *Trichomonas vaginalis*.

syphilis, and *Trichomonas vaginalis*). As previously done [33], time to HIV seroconversion in days and then woman-years was calculated as time from one plus enrolment date to an estimated seroconversion date, where the seroconversion date was taken to be the midpoint between first positive and last negative dates (regardless of missed visits). For right-censored, woman-years of exposure were calculated as time from enrolment date plus one to last visit date.

Results

Socio-demographic and behavioral characteristics by birth cohort

A total of 1,456 predominantly Black South African women born between 1939 and 1989 were included in this analysis. As shown in Table 1, $n = 122$ (8.4%) were categorized into the < 1,960 cohort; $n = 318$ (21.8%) 1960-1969 cohort; $n = 401$ (27.5%) 1970-1979 cohort, and the majority $n = 615$ (42.2%) into the 1980-1989 cohort. There were statistically significant differences in marital status by birth cohorts. Nearly everyone in the 1980-1989 cohort was never married, whereas only a third of the < 1960 cohort were never married. However, despite such differences in marital status, more than 99% of all participants had a steady sexual partner. The levels of steady partner changes and use of condoms with steady partner at last sex were statistically significantly higher among the younger cohorts (1970-1979 and 1980-1989) compared to the older cohorts (< 1960 and 1960-1969). Nevertheless, the proportion of women to have ever experienced forced sex from a steady partner was nearly twice as high in the older, compared with the younger cohorts. Women in the older birth cohorts were in addition more likely to report having a circumcised steady partner. There were also interesting patterns in age differences between the women and their regular partners in the different cohorts. Majority of young women in the 1980s cohort either had a partner within 0-4 years (peer) (68.7%) or an older partner (29.8%), but majority in the oldest cohort (≤ 1960s) had a peer partner (51.3%) or an older partner (30.7%). Crucially though, approximately 1 in 5 of women in the oldest cohort

(19.0%) had a younger sexual partner; previous studies have tended to present having younger partners as a problem of older men (Table 1).

With regard to other sexual behavior patterns at screening and post-enrolment, a higher proportion of women in the two middle birth cohorts relative to those in the oldest and the youngest birth cohorts reported a higher frequency of 3 or more coital acts in the two weeks prior to screening. Only a small proportion of participants reported anal sex acts, with no significant differences by birth cohort. However, oral sex acts were significantly more frequently reported among the younger (1970-1979 and 1980-1989) than among the older cohorts (< 1960 and 1960-1969).

Risk of HIV infection by birth cohort

As shown in Figure 1, there was a linear trend in the incidence rates of HIV among women by birth cohort in this study. The HIV incidence rate in the 1980s cohort was nearly 4-times as high as in the ≤ 1960s cohort. Table 2 presents the unadjusted and adjusted hazard ratios for risk of HIV acquisition by birth cohort: adjusted for having a steady partner, coital frequency, ever been forced sex, ever been abused, number of partners in last 3 months, partner being circumcised, and condom use at last sex activity.

Relative to women born in the ≤ 1960s, unadjusted hazard ratios of HIV infection increased for each successive birth cohort. This remained the case even after adjusting for socio-demographic and behavioral factors. Women born in the 1970s had nearly two-fold increased odds of HIV acquisition compared to women in the ≤ 1960s ($p = 0.035$). Whereas being born in the 1980s was associated with an approximately four-fold increased hazards of HIV infection compared to the ≤ 1960s ($p < 0.001$).

Risk of sexually transmitted infections by birth cohort

Figure 2 shows the hazards of acquiring various STIs including HIV for women born in the 1970s referent to

the \leq 1960s cohort, adjusted for socio-demographic, and behavioral factors. Women in the 1970s cohort were associated with approximately two-fold increased risk of acquiring the STI *Chlamydia trachomatis* ($p = 0.006$) and HIV ($p = 0.035$). Although women in the 1970s relative to the referent group were less likely to acquire *Neisseria gonorrhoeae* ($p = 0.601$), syphilis ($p = 0.090$), and *Trichomonas vaginalis* ($p = 0.559$), none of the risks were statistically significant.

In Figure 3, women belonging to the youngest (1980s) compared to the oldest cohort (\leq 1960s) were more likely to acquire *Chlamydia trachomatis* ($p < 0.001$) and *Neisseria gonorrhoeae* ($p < 0.001$). But the risks of acquiring syphilis were statistically significantly lower ($p = 0.004$) for women in the youngest compared to the \leq 1960s cohort. Overall, women in the youngest relative to the oldest cohort were more likely to acquire an STI ($p = 0.002$) and HIV ($p < 0.001$).

Discussion

In this study we hypothesized and showed that there are significant differences in sexual risk behavior patterns and risk for an STI and HIV infection by birth cohorts of women participating in an HIV prevention trial. We found that despite the majority being never married, younger women relative to older women had a higher frequency of partner changes, higher coital frequency, higher proportion of ever having had sex for money, and to practice unprotected oral sex – factors, which are all associated with increased risk of an STI and HIV infection [34]. Other factors that may have contributed to younger women having higher HIV/STI risks included lower proportion having a circumcised partner and higher likelihood to have an older sexual partner. Our findings are supported by other studies from South Africa that have found quite a young median age at first sex of between 15 and 18 years [24-26, 35], falling age at coital debut across age cohorts [22, 23] and that early coital debut is associated with other risky sexual behaviors such as having multiple partners [22], an older partner [24, 29], and inability to negotiate condom use [25, 26]. But this is not peculiar to South Africa. Even in America, successive birth cohorts are increasingly engaging in sexual activity early and having multiple sexual partners [32].

Women in the current study were exposed to intensive HIV and STI risk reduction counselling during their study visits [33], but this appears to have had little or no impact on behavior change to reduce their risk of STIs and HIV infection, particularly in young women. As shown in this and other studies, young women continue to experience early age at sexual debut, use condoms inconsistently, engage in transactional sex, and tend to have sexual partners that are several years older than themselves [29, 36, 37]. Risky sexual behavior and HIV incidence rates, particularly in young cohorts in high HIV endemic areas like Southern Africa, have remained virtually unchanged for decades since the start of the HIV pandemic [2, 38-40], prompting the question 'what else do we need to end HIV/AIDS?' [41], given that

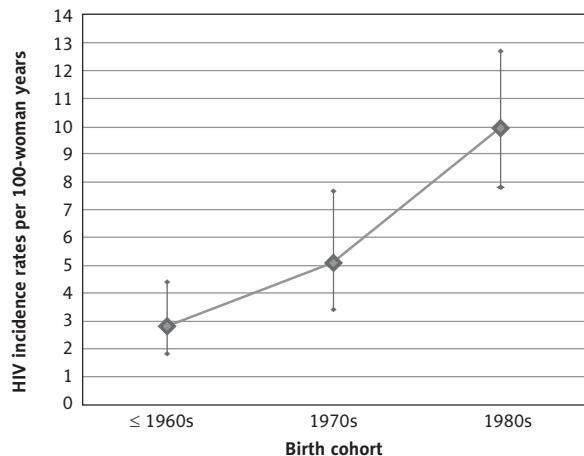


Fig. 1. Human immunodeficiency virus incidence rates per 100-woman years by birth cohort

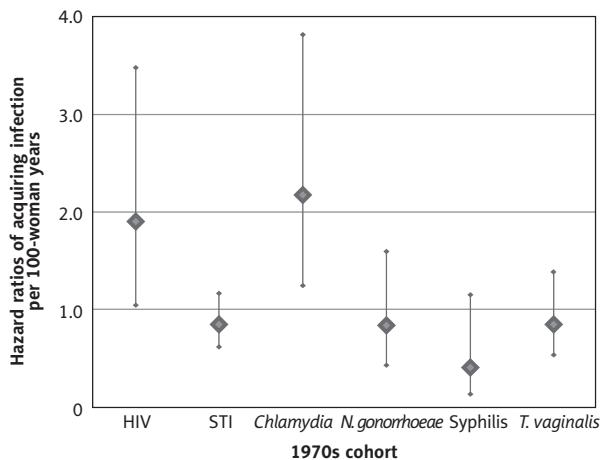


Fig. 2. Adjusted risks of acquiring human immunodeficiency virus or sexually transmitted infections by birth cohorts

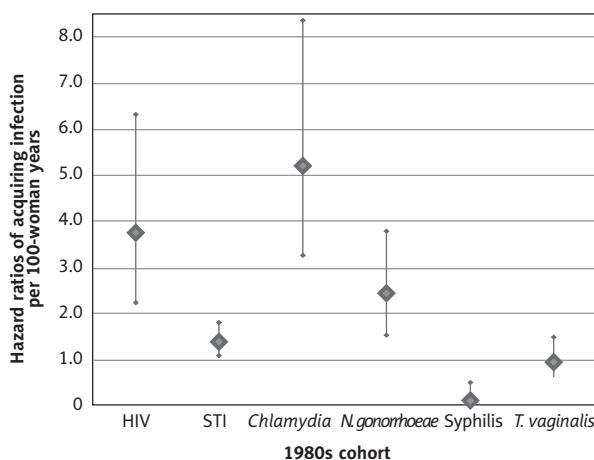


Fig. 3. Adjusted risks of acquiring human immunodeficiency virus or sexually transmitted infections by birth cohorts. Notes: Adjusted for having a steady partner, partner circumcised, number of partners in last 3 months, coital frequency, frequency, and consistency of condom use, ever forced sex, ever been abused. Referent category is \leq 1960s cohort

numerous structured risk reduction interventions have been implemented for many years [42-50].

Some of these risk reduction programmes in well controlled research settings have demonstrated efficacy in reducing risky sexual behavior [43-45] as revealed in a meta-analysis of sexual risk reduction interventions in South African young people, where a delay in coital activity and an increase in condom use was achieved [47]. In another systematic review of behavior change interventions to prevent HIV in adolescents, peer education was singled out as being the most effective in HIV risk reduction interventions [46]. Other intervention programs have however not been as successful [46, 50, 51]. The need for huge financial resources to sustain these interventions long-term and the disregard of the influence of cohort effects in many of these behaviors change interventions are the major shortcoming. Using a mathematical model of heterosexual spread of HIV, Hallett *et al.* [30] demonstrated how sexual behavior changes at an individual level such as delaying sexual debut or narrowing the age gap with sexual partners, has only a limited effect on preventing HIV spread at the population level; greater population-level declines are more likely to be achieved with cohort-wide changes in sexual attitudes and practices.

The failure of behavior changes interventions [46] to bring about greater population declines in HIV infection rates has prompted researchers and policy makers to turn to biomedical strategies [39, 41]. One such strategy is treatment as prevention [52], where mathematical models have postulated regular HIV testing, and universal uptake of antiretroviral treatment could lead to massive population-wide reductions in HIV transmission rates [53]. Sadly, a recent phase 4 unblinded cluster randomised study that tested the efficacy of a universal test and treat intervention in 22 rural South African communities showed disappointing results with no significant difference in HIV incidence rates between the experimental and control groups, despite offering treatment to all in the experimental group and risk reduction counselling to all participants [54]. Similarly, other biomedical HIV prevention interventions in Sub-Saharan Africa have hitherto had disappointing or less than expected effect on HIV prevention [13, 14]. Unfortunately, persons in the young age cohorts who stand to benefit the most from such HIV prevention biomedical interventions, tend to also have a lower uptake of the interventions as recently shown in a phase 3 placebo-controlled and double-blind randomized trial that tested the safety and efficacy of a dapivirine vaginal ring in 18-45-year-old women [14]. Baeten *et al.* [14] found a 56% (95% CI: 31-71, $p < 0.001$) protection from HIV infection in women over 21 years but a possible increased risk to HIV infection (-27%, 95% CI: -133-31; $p = 0.045$) in young women 21 years or below. What these results point to is that while biomedical interventions such as treatment as prevention or tools like a vaginal ring are entirely in the hands of a woman, they offer a lot of promise in population-level reductions in HIV and STI infection rates [55], no matter the efficaciousness of such interventions, they will remain of little effect in

the real world in the absence of effective behavioral change interventions across birth cohorts, because the choices exercised by individuals are often a result of their individual life experiences and their environment [56].

Although this is not an exhaustive treatise of the social norms towards sex and sexuality in different birth cohorts or time periods, we discuss about cohort effects associated with each time period that contribute to differences in sexual risk behavior and risk of acquisition of STIs including HIV [57]. Furthermore, behaviour change approaches are not enough to tame the tide against STIs and HIV infections given the resilience to change for behaviours patterned into norms across birth cohorts [58, 59]. Since socio-behavioral change interventions alone have so far been unable to bring about the desired sexual behavior change, especially in young cohorts, a combination of behavior changes such as not having multiple partners or age-disparate relationships, and biomedical interventions like treatment as prevention, an HIV prevention vaginal ring, or an HIV vaccine currently offers the best promise for addressing the high HIV risk in South Africa.

There are limitations to this study to be noted. Volunteers in this study were not drawn from a random sample of the general population. Generalization of findings of this study can therefore only be made to non-pregnant HIV-uninfected women in similar study settings. Participants in this study were born between 1939 and 1989 and were a small population relative to the general population resulting in limited cohort variation. In addition, since this was a once-off study with no repeat follow-up or recruitment of similar cohorts over time, we had limited ability to separate out period from cohort effects. However, there is little evidence of bias in our findings as the direction and magnitude of sexual risk behavior in the different cohorts were consistent with historical sexual behavior patterns associated with respective birth cohorts [60, 61]. For example, younger women born in the 1980s cohort are increasingly having multiple sexual partners, pre-marital sex, easy access to pornography [60, 62], and appear (unlike the Victorian era women) to desire sex for pleasure not just for procreation [61, 63]. Our conclusions are further supported by the available empirical evidence that period effects affect behavior to a lesser degree than cohort effects [18, 19].

Conclusions

We have shown that societal views on sexual risk taking have changed over the decades, but these generalized views appear to predominate in a manner that risk reduction interventions have had little effect on reducing HIV infection rates, particularly in young people. While a proven effective biomedical intervention is years away from being available on South Africa, women in younger birth cohorts should continue to be encouraged to adopt less risky sexual behavior practices. Research is urgently needed to understand why after so many decades of living with the HIV pandemic little appears to have changed in the behavior of

young age cohorts; instead, there appears to even be a glamorization of risky behavior such as having an older sexual partner as recently seen in main stream and social media regarding a 'blessing' (an old male partner who provides material and monetary resources to young women) or 'blessed' (woman who are prepared to trade sex and their bodies in exchange for the material possessions and money). Currently, there is no literature on this risky behavior phenomena). Finally, there is a need for multilevel combination prevention approaches that combine biomedical tools with an understanding of psycho-socio and structural facilitators of HIV transmission for greater population-level declines in HIV infection across birth cohorts. Further research for a nuanced understanding of cohort effects on sexual behavior and risk of HIV/STI infections in South Africa is needed.

Conflict of interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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