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## Limited risk compensation among women who inject drugs: Results from the Project SHE PrEP Demonstration Study in Philadelphia

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### Abstract

The impact of pre-exposure prophylaxis (PrEP) uptake on sexual and injection-related behaviors among women who inject drugs (WWID) is poorly understood. Over 24-weeks, PrEP uptake among WWID was associated with increased sharing of injection equipment but not syringes and no changes in condomless sex, providing limited evidence of risk compensation in this vulnerable population.

### SUMMARY

Among women who inject drugs, sexual and injection-related risk behaviors were prevalent at baseline, but we found limited evidence of risk compensation with PrEP uptake over follow-up.

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**CONFLICT OF INTERESTS**

The authors do not have any competing interests to declare.

## Keywords

pre-exposure prophylaxis; injection-related behavior; sexual behavior; women who inject drugs; risk compensation; HIV prevention

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## Introduction

Women who inject drugs (WWID), especially those engaging in sex work, could benefit from pre-exposure prophylaxis (PrEP), a discrete, user-driven medication that is efficacious for HIV prevention among cisgender women<sup>1</sup> and people who inject drugs.<sup>2</sup> Although PrEP has considerable promise for HIV prevention in these populations, there is concern that its use could lead to an increase in risk-taking behaviors (e.g., condomless sex, sharing of syringes or other injection equipment), which could inadvertently lead to adverse health outcomes. The prevailing explanation for behavioral changes following the adoption of a new prevention strategy is known as risk compensation.<sup>3</sup> According to this theory, PrEP use may reduce individuals' perceived HIV risk, leading them to reduce their use of condoms, sterile syringes, or other injection equipment, potentially resulting in increased exposure to sexually transmitted infections (STI), Hepatitis C, skin and soft tissue infections, or unintended pregnancy.<sup>4</sup>

Most research on risk compensation to date has focused on sexual minority men (SMM) in high-income settings. Evidence from these studies has been inconclusive: some but not all studies suggest that PrEP uptake is associated with increased condomless sex and STI incidence among SMM.<sup>5-7</sup> Research with serodiscordant couples<sup>8,9</sup> and women engaged in sex work<sup>10</sup> in PrEP demonstration projects have not provided evidence of risk compensation. While potentially informative, data on PrEP use and sexual behaviors from these samples may not generalize to WWID, who experience uniquely intersectional and gendered sexual and injection-related exposures to HIV.<sup>4,11,12</sup> Thus, it is critical to examine whether PrEP uptake is associated with changes in HIV-related risk to inform prevention messaging and programming for WWID.

## METHODS

Data from this study are from Project Sexual Health Equity (SHE), the first PrEP demonstration project for WWID conducted in Philadelphia, Pennsylvania.<sup>13</sup> Women were recruited from the largest syringe services program in the mid-Atlantic region of the United States, Prevention Point Philadelphia, from April 2018 – June 2019. All study activities, including recruitment, occurred on a weekly “ladies only” event that provides women a drop-in space to access food, showers, clean clothing, harm reduction kits including syringes, and condoms with additional support/educational services (e.g., self-defense training or free haircuts) being offered on a regular basis. Eligible participants were cisgender women who were HIV-negative, 18 years old, reported injecting drugs in the past 30 days in combination with at least one CDC-recommended clinical indication for PrEP at the time of enrollment (including being in an ongoing serodiscordant partnership or reporting past-six-month sharing of syringes, inconsistent condom use with men injecting drugs or having sex with other men, or receiving a bacterial STI diagnosis).<sup>14</sup> As part of the

enrollment visit, participants viewed a brief educational video about PrEP.<sup>15</sup> At each of three visits (baseline, week 12, and week 24), participants underwent PrEP relevant screenings (e.g., creatinine, HIV, STI) and received pre/post-test counseling that included a thorough assessment of sexual history and a conversation about risk reduction. Participants could also decide to initiate, renew, or terminate their PrEP prescriptions at each visit. Participants received \$90 as compensation for completing all study-related visit. Drexel University's Institutional Review Board and Prevention Point Philadelphia's Executive Board approved all study protocols.

We summarized key socio-demographic factors and calculated the percentage of PrEP uptake as well as the following sexual and injection-related behaviors (i.e., risk compensation outcomes) at each time point: transactional sex; inconsistent condom use (overall, with casual partners, with a main HIV+/unknown status partner, or with transactional sex partners); backloading (dividing drugs or drug solution using a syringe); sharing syringes and/or other injection equipment (cotton, rinse water, and cookers). PrEP uptake and all behavioral outcomes were dichotomized as yes/no. In addition, we considered self-perceived HIV risk based on the following question, "*What is your gut feeling about how likely you are to get infected with HIV?*" (responses: somewhat/very/extremely likely vs. extremely/very unlikely).

Log-binomial GEE models with an independence correlation matrix were used to assess whether PrEP uptake was associated with sexual and injection-related behaviors that increase HIV risk over 24 weeks of follow-up. Models were adjusted for age and baseline SSP access given evidence from our prior work that these covariates may have influenced retention in our sample.<sup>13</sup> In addition, we lagged our exposure by one follow-up visit to assess the association of PrEP uptake at  $t_i - 1$  and each risk compensation outcome at  $t_i$ . All analyses were conducted in R version 4.0.2.

## RESULTS

The analysis included 95 WWID with a mean age of 38, the majority of whom identified as non-Hispanic white (68%), considered themselves homeless (63%), and experienced physical or sexual violence (44%) within the preceding six months. At baseline, PrEP uptake (69/95; 73%) and engagement in sexual and injection-related behaviors associated with HIV risk were high; over 70% engaged in transactional sex and any inconsistent condom use, 61% engaged in backloading, and 43% shared syringes and injection equipment (Figure 1). However, less than half (46%) perceived themselves at risk for HIV.

Over 24 weeks of follow-up, 59 (62%) returned at week 12 and 42 (44%) at week 24. Among those returning for follow-up visits, PrEP uptake remained high, including 48/59 (81%) at week 12 and 25/42 (60%) at week 24. WWID accepting PrEP had the same or lower risk of transactional sex, backloading, as well as sharing both syringes and injection equipment over follow-up compared to those who did not accept PrEP. However, those accepting PrEP had an elevated risk of inconsistent condom use and sharing injection equipment (but not syringes) over time (Figure 1). In models adjusted for age and baseline SSP access, PrEP uptake was not associated with transactional sex (risk ratio [RR] = 0.92;

95% confidence interval [CI]: 0.72, 1.18), inconsistent condom use (RR = 1.28; 95% CI: 1.00, 1.63), backloading (RR = 0.91; 0.64, 1.28), sharing syringes and injection equipment (RR = 0.80, 95% CI: 0.50, 1.28), or sharing injection equipment but not syringes (RR = 1.51; 95% CI: 0.85, 2.63). In time-lagged models, these results were consistent, with PrEP uptake not being significantly associated with subsequent sexual or injection-related behaviors.

## DISCUSSION

We found that sexual and injection-related risk behaviors were common and co-occurring in this sample of WWID. Engagement in most HIV-related risk behaviors remained the same or decreased over time, providing little empirical evidence of risk compensation in this population. However, it is critical to note that inconsistent condom use, transactional sex, and sharing injection equipment were reported by at least one in four women at all visits, regardless of PrEP acceptance. Few of these behaviors are directly controlled by women, highlighting the potential of PrEP as an important HIV prevention tool for this population. However, the proportion of participants accepting PrEP waned over time, suggesting that ongoing adherence support and risk reduction counseling should accompany PrEP services for WWID.

A novel contribution of our study was the ability to tease apart sexual and injection-related behaviors in a population where both are meaningful for HIV transmission. Although not statistically significant, the increase in sharing injection equipment detected over 24 weeks was moderately high. Increasing injection frequency attributed to fentanyl and psychostimulant use has been implicated in the recent HIV outbreaks among people who inject drugs.<sup>16</sup> While sharing injection equipment may be a less efficient mechanism for transmitting HIV than sharing syringes and drugs via backloading, this finding is of concern due to recent studies documenting the link between sharing injection equipment and transmission of Hepatitis C, often considered a precursor to HIV outbreaks.<sup>17</sup> These results underscore the importance of promoting sufficient access to harm reduction supplies, including syringes and sterile cookers, cottons, and rinse water. Further, this suggests that bio-behavioral interventions to support and enhance PrEP adherence and persistence may be useful for reducing HIV-related risk and should include messaging tailored to women's specific behavioral risk profiles (e.g., those reporting sexual risk, sharing injection equipment, or both).

Caution is needed when interpreting our results, especially given the small sample size. It is possible that individuals who elected to participate in our study differ from those who did not participate in terms of health risk perceptions, motivations, and behaviors. In addition, interacting with the study team may have led to underreporting of risk behaviors due to social desirability bias. Furthermore, prior work suggests that women's HIV risk is cyclical,<sup>18</sup> thus, it is uncertain whether the trends we documented here would continue over longer follow-up periods. Larger longitudinal studies are needed to observe whether changes in risk behaviors are stable, and biomarkers of PrEP adherence and disease acquisition would help assess relationships between behaviors and morbidity in this group.

In conclusion, we found limited evidence of sexual or injection-related risk compensation among WWID accepting PrEP. However, we detected high rates of behaviors associated with STI and Hepatitis C transmission over time. Given that these infections may be precursors to HIV, it is critical to provide WWID with sufficient harm reduction supplies and encouragement to continue using them even in the context of PrEP use. Interventions are also needed to promote the importance of PrEP adherence and retention in PrEP-related care, which could help monitor for STI and Hepatitis C acquisition while ensuring that women receive supported referrals to services that help address underlying structural vulnerabilities (e.g., homelessness, gender-based violence) that exacerbate sexual and injection-related risks.

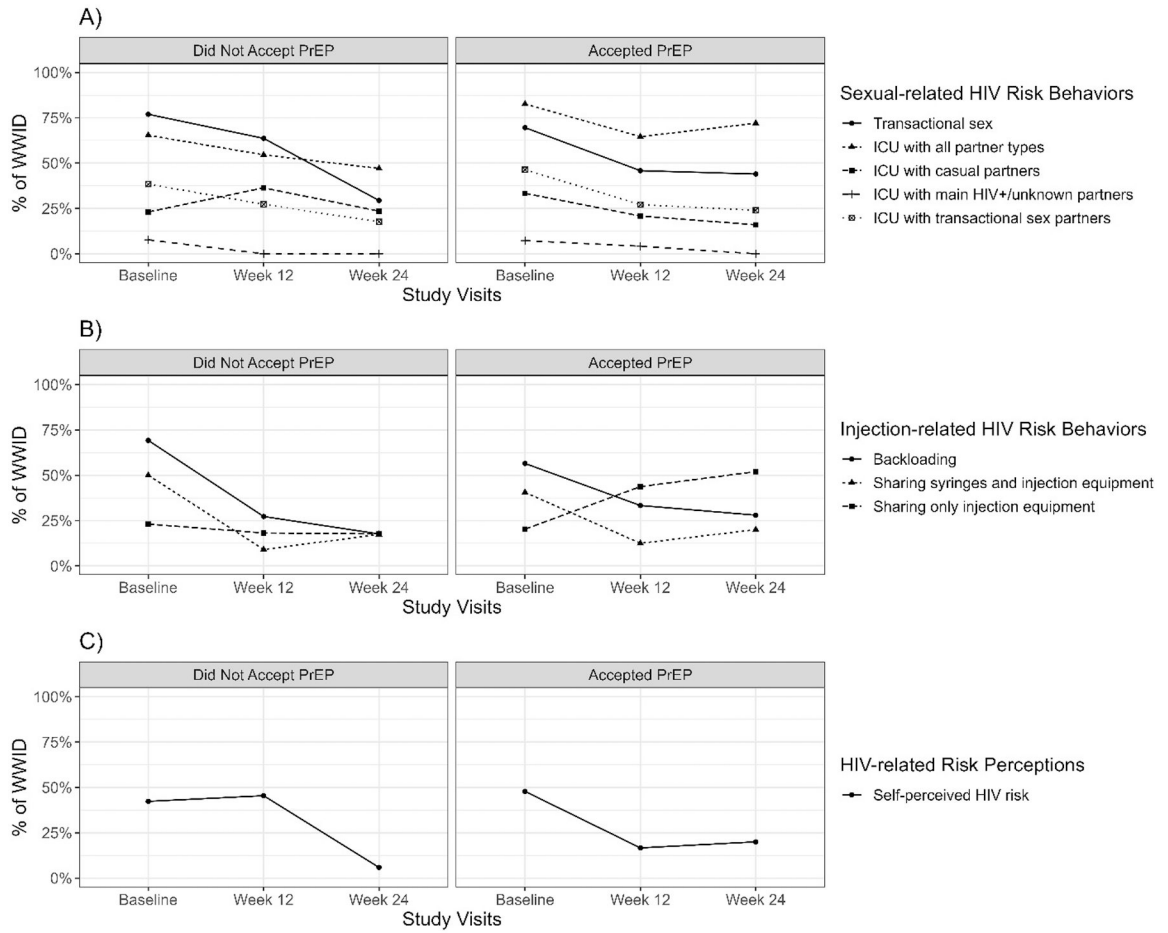
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**Figure 1.** Sexual behaviors (A), injection-related behaviors (B), and HIV-related risk perceptions (C) over time stratified by PrEP uptake among women who inject drugs participating in a PrEP demonstration project, Philadelphia, Pennsylvania, 2018 – 2019. ICU: inconsistent condom use; sharing other injection equipment includes cookers, cottons, or rinse water.

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**Table 1.**

Bivariable and multivariable GEE models of sexual and injection-related behaviors associated with PrEP uptake over 24 weeks of follow-up

	Adjusted Model <sup>c</sup>	Lagged Model <sup>c,d</sup>
	RR (95% CI)	RR (95% CI)
Transactional sex	0.92 (0.72, 1.18)	0.93 (0.55, 1.58)
Inconsistent condom use <sup>a</sup>	1.28 (1.00, 1.63)	1.18 (0.74, 1.90)
Backloading	0.91 (0.64, 1.28)	0.59 (0.29, 1.18)
Sharing syringes and injection equipment <sup>b</sup>	0.80 (0.50, 1.28)	0.75 (0.23, 2.40)
Sharing only injection equipment <sup>b</sup>	1.51 (0.85, 2.63)	1.62 (0.65, 4.02)

RR: risk ratio; CI: confidence interval;

<sup>a</sup> inconsistent condom use across all types of sexual partnerships;

<sup>b</sup> sharing injection equipment includes cookers, cottons, and rinse water;

<sup>c</sup> models were adjusted for age and baseline access to syringe service program;

<sup>d</sup> PrEP uptake was lagged by one follow-up visit