HPTN HIV Prevention Trials Network

THE NEGATIVE DIRECT EFFECT OF DEPRESSIVE SYMPTOMS ON PREP ADHERENCE AMONG HIGH-RISK SOUTH AFRICAN WOMEN IN HPTN 067

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BACKGROUND

- Daily oral pre-exposure prophylaxis (PrEP) is a highly efficacious HIV prevention strategy when taken regularly
- There remains a need to identify modifiable factors to improve PrEP adherence particularly for women at high risk of HIV
- Depression affects 30-50% of women in sub-Saharan Africa, and is a known barrier to healthcare engagement and daily medication adherence (e.g., contraceptives, ART)
  - May affect PrEP use through other psychosocial factors including anticipated stigma around PrEP, social support to use PrEP, and optimism about PrEP's effectiveness

OBJECTIVE

- Examine whether depression is linked to low PrEP adherence among women in Cape Town, South Africa
- Explore whether a relationship between depression and PrEP adherence is mediated by stigma, social support, or optimism about PrEP effectiveness

Figure 1. Directed acyclic graph depicting relationships between study variables

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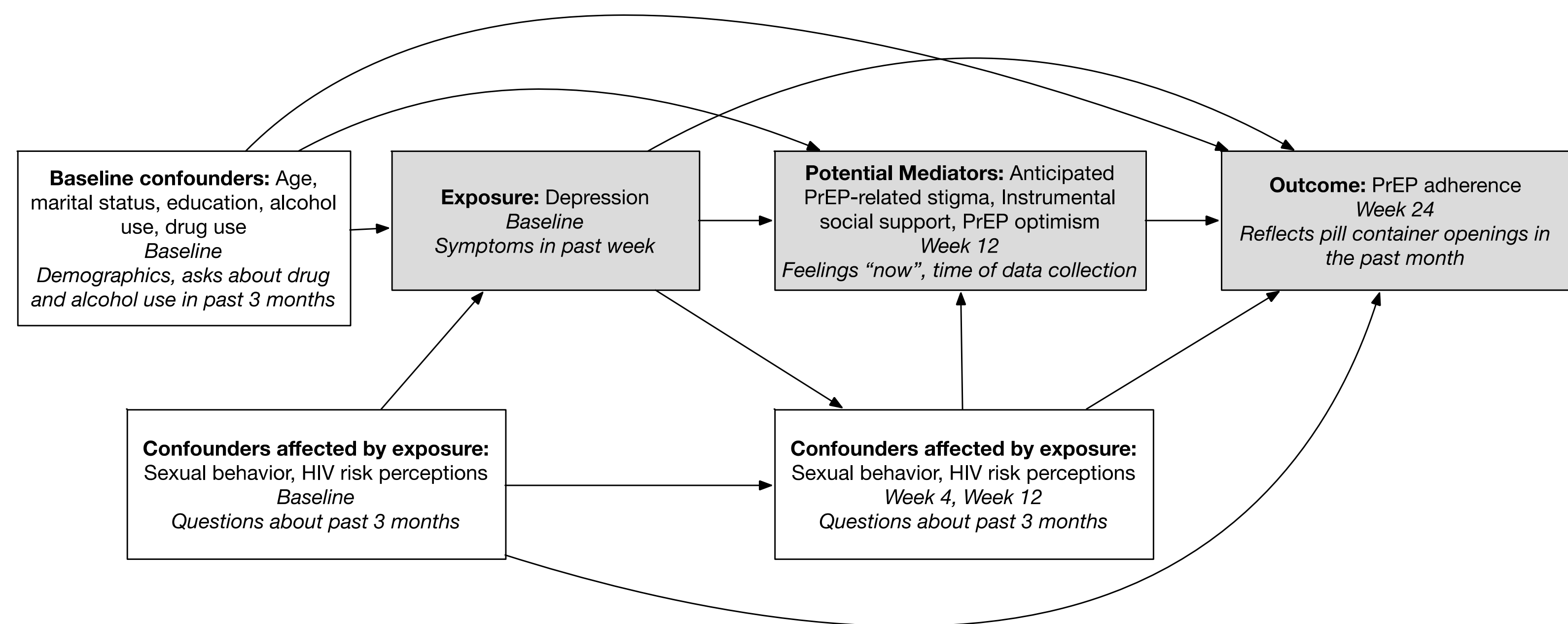
Depressive symptoms are a barrier to PrEP adherence for women and there was no evidence of mediation by stigma, social support, or optimism about PrEP.

METHODS

STUDY SAMPLE

- South African women participating in HPTN 067/ADAPT randomized trial of intermittent and daily PrEP
  - Data collection and follow-up concluded in 2014
  - Study visits at weeks 0, 4, 12, and 24 post randomization
- PrEP adherence: ≥80% expected doses in the month prior to week 24 study visit measured via Wisepill™
  - Wisepill™ data adjusted via weekly interviews to assess whether participant took a pill corresponding with the device opening and whether they took other PrEP doses (Bekker et al., *Lancet HIV*, 2018)
- Likely depression exposure: CES-D score ≥16 measured by CASI at baseline study visit
- Potential mediators of relationship between likely depression and PrEP adherence: PrEP stigma, social support, optimism about PrEP effectiveness measured via scales and categorized into binary variables

PRIMARY STATISTICAL ANALYSES

- Marginal structural model to estimate *total effect of depression on PrEP adherence*
  - Inverse probability weights estimated with logistic regression with age, marital status, education, alcohol and drug use (baseline confounders) and HIV risk perception and condomless sex (mediator-outcome confounders affected by the exposure)
  - Models fit with a log link, binomial distribution, and robust standard errors
- Marginal structural models to quantify the magnitude of association between depression and PrEP adherence that remains after removing downstream influence of each mediator (*controlled direct effect of depression on PrEP adherence*)
  - Separate weights for exposure and mediator, multiplied together to calculate total weight
- Fit interaction terms for exposure and mediators to examine moderated-mediation

RESULTS

SAMPLE CHARACTERISTICS

- 174 women included in analysis sample (>90% visit attendance)
  - 57 (32.8%) in daily PrEP arm; 58 (33.3%) were in time-driven dosing arm; 59 (33.9%) were in event-driven arm
- 79 (45.4%) had CES-D scores ≥16 at baseline
- 87 (50.0%) ≤25 years old
- 60 (34.5%) completed secondary education
- 16 (9.2%) reported transactional sex
- 76 (43.7%) reported high or unknown chance of HIV infection
- CES-D score ≥16 was associated with older age, less education, fewer vaginal or anal sex acts in the 3 months prior to enrollment, greater report of transactional sex, greater report of drug and alcohol use, and higher HIV risk perceptions at baseline (p<0.05 for all)

TABLE 1. Total effect of association between depression and PrEP adherence

	Visits with high PrEP adherence[1] (N=87; 53.0%)	Relative scale[2]	
		aRR (95% CI)	p-value
Depressive symptoms	35 (44.3%)	0.79 (0.63, 0.99)	0.05
No symptoms	52 (54.7%)	REF	REF

aRR= adjusted relative risk; 95% CI= 95% confidence interval
[1]Participants were considered adherent to PrEP if their adjusted Wisepill data indicated that they had taken ≥80% of expected pills at the Week 24 study visit
[2]Stabilized inverse probability weights account for confounding by the sets of baseline (age, marital status, education, alcohol and drug use) and longitudinal confounders (any unprotected sex, HIV risk perceptions; weight mean=0.99; range=0.47-2.38)

TABLE 2. Controlled direct effect estimates for the association[1] for each mediator

Exposure	Mediator	Outcome	Relative scale[2]	
			aRR (95% CI)	p-value
Depression	Stigma	Adherence	0.74 (0.51, 0.97)	0.02
Depression	Social support	Adherence	0.77 (0.57, 1.03)	0.07
Depression	PrEP optimism	Adherence	0.75 (0.55, 0.99)	0.05

aRR= adjusted relative risk; 95% CI= 95% confidence interval
[1]Participants were considered adherent to PrEP if their adjusted Wisepill data indicated that they had taken ≥80% of expected pills at the Week 24 study visit
[2]Stabilized inverse probability weights account for confounders (same set of baseline and longitudinal confounders included for Table 1) and mediators

DISCUSSION

- In this open-label randomized evaluation of PrEP dosing regimens in South Africa, depression was highly prevalent and women with depression were less adherent to PrEP
  - Anticipated stigma, instrumental social support, and optimism about PrEP were not mediators of this association
  - Similar finding to other recent analyses showing negative influence of depression on PrEP adherence for women
- Mechanism for the relationship between depression and PrEP adherence is not well understood:
  - Lower healthcare engagement and reduced motivation to take PrEP?
  - Changes in sexual behavior?
- Need for future interventions to build mental health screening platforms and treatment approaches integrated with PrEP service delivery for women
  - Potential to improve mental health and maximize public health impact of PrEP for women
- Additional research needed on mechanisms for relationship between depression and PrEP adherence

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