



A Promising PrEP Navigation Intervention for Transgender Women and Men Who Have Sex with Men Experiencing Multiple Syndemic Health Disparities

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Abstract

Transgender women and MSM experience many stigma-related syndemic conditions that exacerbate HIV incidence and prevalence rates. While PrEP is an effective biomedical intervention to reduce HIV transmission, uptake and adherence of PrEP is low among transgender women and MSM experiencing multiple syndemic health disparities. This study tested the feasibility, acceptability and effectiveness of *A.S.K.-PrEP (Assistance Services Knowledge-PrEP)*, a five-session peer navigator program, designed to link transgender women and MSM to PrEP. From September 2016 to March 2018, 187 participants (transgender women = 58; MSM = 129) enrolled. Results demonstrated that approximately 90% of transgender women and MSM were linked to PrEP; MSM linked more quickly [KW $\chi^2(1) = 10.9, p < .001$]. Most transgender women (80%) and MSM (70%) reported they were still taking PrEP at the 90-day follow-up evaluation. Findings indicated that *A.S.K.-PrEP* is a promising intervention for PrEP linkage, uptake and preliminary adherence among transgender women and MSM.

Keywords PrEP · HIV prevention · Transgender · MSM · Health disparities

Transgender women (here after: trans women) and men who have sex with men (here after: MSM) are the two groups at highest risk of HIV infection in the U.S. Approximately 70% of new HIV diagnoses each year occur among MSM [1]. HIV prevalence rates among trans women are estimated to be between 22 and 28% nationally, higher than any other key population [2, 3]. A community-based sample of moderate- to high-risk trans women in Los Angeles County demonstrated an increase in self-reported HIV prevalence of nearly

60% over a 17-year period, from 22 in 1998–1999 to 35% in 2015–2016 [4].

Trans women are exposed to a range of syndemic environmental and socio-structural risks including stigma, discrimination, criminalization, violence, economic insecurity, and housing instability, which in turn mediate and moderate mental health and substance use comorbidities as well as sexual risk behaviors that lead to these high HIV incidence and prevalence rates [2, 4–6]. MSM substance users, particularly methamphetamine and other stimulant users, experience many similar syndemic risks that increase the likelihood of HIV transmission [7–12]. Among both trans women and MSM, rates of HIV prevalence are further elevated among racial/ethnic minority individuals, who experience more severe forms of marginalization and intersectional stigma [8, 13–15].

Pre-exposure prophylaxis (PrEP) of oral tenofovir disoproxil fumarate/emtricitabine (Truvada) is an effective HIV prevention method now recommended by the CDC for high-risk groups, including trans women and MSM [16, 17]. The iPrEx study, which demonstrated the efficacy of PrEP, forever changed the face of HIV prevention and established PrEP as the state-of-the-art, biomedical HIV prevention option [18]. Data from the iPrEx randomized controlled trial

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and open-label extension study of PrEP with trans women and MSM indicated that PrEP is up to 99% effective when taken daily [19, 20]. Furthermore, taking as few as four doses of PrEP per week provides roughly the same tenofovir level of protection against HIV transmission via anal sex as daily dosing [21, 22].

Of all early efficacy PrEP trials conducted, only iPrEx was confirmed to enroll transgender individuals, and subgroup efficacy analysis among trans women was not deemed feasible due to low enrollment and adherence [23–25]. A post hoc exploratory subanalysis with only the trans women in iPrEx ($n=339$) found that HIV incidence was no different in the treatment versus control group [26]. However, trans women assigned to PrEP who seroconverted during the trial had no drug detected in their blood, presumably due to low adherence. Furthermore, in the iPrEx open label extension study, no infections occurred among trans women or MSM with drug concentration levels indicating four or more doses taken per week. These clinical trial findings suggest that PrEP is effective for both trans women and MSM with adherence of a minimum of four doses per week [25–27].

Targeted interventions to increase PrEP linkage, uptake, and adherence among trans women and MSM are necessary to achieve optimal reach and effectiveness [28, 29]. More than 1.1 million adults in the U.S. could potentially benefit from PrEP based on CDC [30] estimates, yet fewer than 5% of eligible PrEP candidates have filled prescriptions. In addition, African American/Black and Hispanic/Latino MSM make up the majority of those who could potentially benefit from PrEP based on CDC guidelines, but only 1% of African American/Black and 3% of Hispanic/Latino individuals indicated for PrEP have received a prescription, including non-MSM individuals [30]. Rates of PrEP uptake among trans women have been even lower [16]. Although uptake has increased across the country, the population-level impact of PrEP is limited if the racial/ethnic and gender identity disparities in uptake are not addressed [13, 14].

In addition to limited uptake, low adherence, discontinuation, and loss to follow up have been common across PrEP demonstration projects in several cities including Los Angeles, Miami, San Francisco, Washington D.C., Chicago, New York City, and Atlanta [31]. Factors associated with low adherence and discontinuation include concerns about side effects, lack of insurance, cost of medication and medical care/testing, unstable housing, stigma and discrimination, race/ethnicity, and mental health and substance use disorders [29]. A growing body of evidence suggests that concerns about PrEP interactions with hormones might also be contributing to low adherence among trans women [32, 33].

To address the low rates of PrEP uptake, adherence, and persistence among trans women and MSM, navigation has emerged as a promising strategy to improve PrEP implementation. A systematic review on barriers to PrEP reported

that PrEP providers in several studies have emphasized the need for care coordination and peer-based groups to assist with patient navigation [34–40]. Preliminary findings from the NYC PrEP Cascade Program indicate that PrEP navigation significantly improved referral rates to PrEP providers among MSM [41]. Although acceptance of navigation was low overall, racial/ethnic minority MSM were more likely to accept navigation than Caucasian/White MSM.

This study tested the effect of a PrEP peer navigation program, *A.S.K.-PrEP (Assistance Services Knowledge-PrEP)* among trans women and MSM in Los Angeles County. The study examined PrEP linkage, uptake, and preliminary adherence at 90-day follow-up evaluation among a sample of highly impacted trans women and MSM, and tested the outcome differences between the two groups. The majority of participants in the *A.S.K.-PrEP* program were trans women and MSM of color who were experiencing multiple syndemic health disparities and structural vulnerabilities.

Methods

Populations Studied

The populations studied were urban trans women and MSM experiencing numerous syndemic health disparities. Table 1 compares trans women ($n=58$) and MSM ($n=129$) on sociodemographic variables. MSM were on average eight-and-a-half years older than trans women [43.3 vs. 34.9, $t(110)=4.5$, $p<.001$]. There was a significant difference in the distribution of racial/ethnic identities in the two groups [$\chi^2(3)=9.6$, $p=.022$]; about half of MSM (52.7%) and trans (44.8%) participants identified as African-American/Black, followed by Caucasian/White for MSM (24.0%) and Hispanic/Latin for trans women (27.6%). Trans women and MSM reported comparable levels of educational attainment, employment, and current housing instability.

Participants

Over an 18-month enrollment period, from September 2016 to March 2018, 187 participants enrolled in the program (MSM = 129; trans women = 58). Eligibility criterion was based on the CDC PrEP Risk Index, which our group modified for the *A.S.K.-PrEP* program to include trans women. The modified CDC PrEP Risk Index was comprised of six questions: (1) How old are you today?; (2) In the last 6 months, how many men and/or trans women have you had sex with?; (3) In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man and/or trans woman without a condom?; (4) In the last 6 months, how many of your male and/or trans women sex partners were HIV-positive?; (5) In the last 6 months, how

Table 1 Sociodemographic characteristics (N = 187)

	MSM (<i>n</i> = 129) <i>n</i> (%) or <i>M</i> (<i>SD</i>)	Trans women (<i>n</i> = 58) <i>n</i> (%) or <i>M</i> (<i>SD</i>)	Statistic	<i>p</i>
Age	43.3 (12.4)	34.9 (11.4)	<i>t</i> (110) = 4.5	< .001
Race/ethnicity				
African-American/Black	68 (52.7%)	26 (44.8%)	$\chi^2(3) = 9.6$.022
Caucasian/White	31 (24.0%)	6 (10.3%)		
Hispanic/Latin	16 (12.4%)	16 (27.6%)		
Multiracial/other	10 (7.8%)	8 (13.8%)		
Education				
< high school	18 (14.0%)	13 (22.4%)	$\chi^2(2) = 2.9$.237
High school	52 (40.3%)	24 (41.4%)		
> high school	56 (43.4%)	19 (32.8%)		
Employment				
Full time	7 (5.5%)	2 (3.5%)	FET	.328
Part time	12 (9.4%)	8 (14.0%)		
Unemployed	93 (72.7%)	32 (56.1%)		
Housing instability				
Yes	62 (48.1%)	32 (55.2%)	$\chi^2(1) = 0.8$.368
No	67 (51.9%)	26 (44.8%)		

FET Fisher's exact test

many times did you have insertive anal sex (you were the top) without a condom with a man and/or trans woman who was HIV-positive?; and, (6) In the last 6 months, have you used methamphetamine such as crystal or speed? Each question had a score value with the total score ranging from 0 to 45. Per CDC guidelines, if a participant's total score on the CDC PrEP Risk Index was ten or greater, they were eligible for *A.S.K.-PrEP* participation. Participants with a total CDC PrEP Risk Index score of nine or less were ineligible for *A.S.K.-PrEP* participation but were referred to non-biomedical HIV prevention services. Three participants screened eligible on the CDC PrEP Risk Index, enrolled in *A.S.K.-PrEP*, linked to PrEP care, but were then deemed ineligible for PrEP initiation by the PrEP medical provider due to unstable diabetes (*n* = 2) and inadequate renal functioning to contraindicate PrEP use (creatinine clearance < 60 mL/min; *n* = 1).

Procedures

Potential participants were recruited through: (1) street- and venue-based outreach; (2) in-reach through existing programs at the site including a HIV counseling and testing program; (3) the distribution of culturally appropriate flyers and postcard-sized cards; (4) participant-incentivized snowball sampling; and, (5) collaborations with community-based organizations. Potential participants met with a peer navigator in a private room and were screened for eligibility using the CDC PrEP Risk Index. Those eligible began the

informed consent process, completed the baseline behavioral assessment, and had their first PrEP navigation session. One follow-up evaluation was conducted 90-days following enrollment. Participants were compensated with a \$20 gift card for completing the baseline assessment and session one, and with additional \$20 gift cards for completing each of the successive four sessions. To encourage linkage to PrEP uptake and not penalize participants who linked early and, thereby, would not receive incentives for further sessions, each participant received the balance of the \$100 maximum, upon linkage. For example, if a participant linked to PrEP services after their second session, the participant received a \$20 gift card following session one, a \$20 gift card following session two, and then the remaining \$60 in gift cards upon linkage for the maximum incentives of \$100 in gift cards. Therefore, each participant received the maximum of \$100 in gift cards, regardless of whether that participant linked to PrEP care on their first or fifth session, or if the participant chose not to link to PrEP care but attended all five PrEP navigation sessions. Participants were compensated with a \$40 gift card for completing the 90-day follow-up evaluation. All program activities occurred at the community research center in the Hollywood area of Los Angeles County, California.

Intervention

A.S.K.-PrEP is a five-session peer navigator service program adapted from *ARTAS* (*Antiretroviral Treatment Access*

Study), the five-session CDC evidence-based intervention for linkage to HIV care. Just as *ARTAS* was designed to link HIV-positive participants to HIV care, *A.S.K.-PrEP* was designed (by the first author) to link HIV-negative participants to PrEP care. As with *ARTAS*, the five session *A.S.K.-PrEP* intervention was conducted over a 3 month intervention period. Session one began with the administration of a PrEP Knowledge Pre-test. The Pre-test assessed each participant's level of knowledge at baseline; these values were then compared with the same values from the PrEP Knowledge Post-test administered at the conclusion of the first session. Additionally, in session one, participants were assessed for PrEP readiness, structural and individual barriers to linkage and adherence, and participants' adherence goals. Based on an individualized client-centered philosophy, the peer navigator strategically worked to refer and link participants into a number of ancillary support services based on their needs, including substance abuse treatment, mental health services, care and counseling for intimate partner violence, housing, food insecurity, and hormone therapy. Each participant's unique structural and individual barrier(s) were considered when intervening with the ultimate goal of PrEP linkage, uptake, and persistent daily adherence.

In sessions two through five, participants were assessed for readiness for PrEP adherence and planning for adherence, removal of structural and individual barriers, access to documentation (identification cards that are required for PrEP initiation), and continued linkage, uptake and adherence support. Thus, PrEP readiness and structural and individual barriers to adherence were discussed throughout the five sessions. As the goal of *A.S.K.-PrEP* was PrEP linkage, similar to the goal of *ARTAS* which was HIV care linkage, once a participant linked to PrEP care, they could then opt-out of the remaining sessions.

In addition, throughout the duration of the 3 month intervention period, participants could opt-in/opt-out of theory-based adherence support text messages. Each text message was founded on one of three behavioral health theories: Social Support Theory (to provide informational, emotional or instrumental support such as, "Live a trans healthy life, take your PrEP") [42, 43], Health Belief Model (to identify or reduce threat such as, "Don't be a statistic, take PrEP. We need every trans woman we have") [44], or Social Cognitive Theory (to increase self-regulation skills and self-efficacy such as, "Plan ahead even when you PNP, order PrEP refills early") [45, 46].

Measures

A.S.K.-PrEP Program and Follow-up Assessments: Both the program assessment and the follow-up assessment were designed by the first author. The program assessment, is a brief 7-page assessment that records data on participants'

sociodemographic characteristics (gender identity, sexual identity, age, race/ethnicity, educational attainment, employment status, housing status), substance use history (injection and non-injection drug use and safe needle use protocol) and sexual risk behaviors (number and gender of sexual partners and partner type, i.e., exchange partner). The follow-up assessment is a brief 2-page assessment that records data on PrEP uptake and adherence (past 4 days and past 30 days). The program assessment was administered at baseline and at 90-day follow-up evaluation; the follow-up assessment was administered at the 90-day follow-up evaluation. All data was self-reported.

Data Analysis

Substance use was assessed by asking participants whether they used the following substances in the previous 6 months: alcohol, marijuana, methamphetamine, powder cocaine, crack cocaine, amphetamines, heroin, opioids, sedatives, barbiturates, ecstasy, hallucinogens, amyl nitrates, Special K, GHB. For the assessment of sexual risk behaviors in the previous 30 days, participants reported the number of male, female, and transgender partners they had vaginal or anal sex with (range 0–999); the frequency of receptive and insertive anal intercourse in exchange for money, drugs or something they needed, and with male, female, and transgender partners (range 0–999) and concomitant condom use (always, sometimes, never). Linkage to PrEP care was operationalized as attending the first PrEP care medical appointment, and "Days to linkage to PrEP" was measured as the time in days between the date of enrollment into the *A.S.K.-PrEP* program and the date of linkage to PrEP care. The follow-up assessment included participants' report on whether they were still on PrEP medication and, if so, on how many days they missed at least one dose of any of their PrEP medication in the previous four and 30 days, and whether there had been a time when they did not take their PrEP medication for four or more days in a row. "Housing instability" was coded as "Yes" if a participant described their current living situation as one of the following: temporarily staying or sleeping on a couch in someone else's house, condo, or apartment; a hotel; homeless, staying in a shelter or transitional housing where other services are provided; a rooming or boarding house or other temporary indoor situation without additional services; on the streets (abandoned building, vacant lot, park, abandoned car, etc.); homeless, but cannot or will not give more detail). "Housing instability" was coded as "No" if a participant indicated that they owned or rented a house/condo/apartment/room. Condomless anal intercourse (CAI) was coded as "Yes" if a participant reported that they had anal sex with any type of partner or in exchange for money, drugs or something they needed, and did not always use a condom, otherwise "No."

Descriptive statistics were compiled separately for trans women and MSM. The independent-samples *t* test was used to compare differences between group means. Associations between categorical variables were evaluated with the Chi square test or with Fisher's exact test (FET; two-tailed) if an expected cell count was less than five. The Kruskal–Wallis (KW) test was used to assess stochastic dominance between groups. The significance level for all statistical tests was set to $\alpha = .05$. All analyses were carried out using the R language and environment for statistical computing, version 3.5.0.

Results

Substance Use and Sexual Risk Behaviors

Substance use and sexual risk behaviors are summarized in Table 2. About half of the participants reported alcohol use (MSM: 59.7%; trans women: 48.3%) and marijuana use (MSM: 56.6%; trans women 55.2%) in the previous six months, but a greater proportion of MSM than trans women participants reported using methamphetamine [63.6% vs. 36.2%; $\chi^2(1) = 12.1, p < .001$] and crack cocaine (16.3% vs. 5.2%; FET, $p = .036$). In the previous 30 days, MSM had fewer male sexual partners [KW $\chi^2(1) = 5.3, p = .021$] but more female [KW $\chi^2(1) = 7.8, p = .005$] and transgender partners [KW $\chi^2(1) = 9.0, p = .003$] than trans women. There was a greater proportion of MSM participants than trans women (59.7% vs. 25.9%) who reported insertive CAI [$\chi^2(1) = 18.3, p < .001$]. MSM were less likely to engage in exchange sex than trans women [11.6% vs. 31.0%; $\chi^2(1) = 10.2, p = .001$].

Linkage to PrEP and Adherence

As indicated in Table 3, approximately 90% of both trans women and MSM (trans women: 89.7%; MSM: 91.5%) were successfully linked to PrEP care. However, the MSM participants were linked to PrEP care more quickly than the trans women participants [KW $\chi^2(1) = 10.9, p < .001$]; for MSM, the median number of days to linkage was 9 (IQR 4–15) and the median number of days to linkage for trans women was 14 (IQR 8–28). Ninety-day follow-up evaluations were completed with 48 (84.2%) trans women and 112 (88.2%) MSM. Similar proportions of trans women (79.6%) and MSM (69.6%) reported that they were still taking PrEP medication. PrEP adherence also did not differ significantly between trans women and MSM. Most participants (trans women: 87.2%; MSM: 83.3%) reported that they did not miss one PrEP dose in the previous 4 days, and just under half of the participants (MSM: 48.7%; trans women: 48.7%) reported that they did not miss one PrEP dose in

the previous 30 days. About twenty percent of participants (MSM: 19.2%; trans women: 23.1%) reported that they did not take a PrEP dose on four or more consecutive days in the previous 30 days.

Text Message Adherence Support and PrEP Adherence

At the time of enrollment, approximately half of MSM (46.5%) and trans women (51.7%) participants elected to receive the adherence support text message component. Table 4 demonstrates that at 90-day follow-up evaluation, participants who received adherence support text messages were more likely to report that they still took PrEP medication than participants who did not receive the text messages [85.7% vs. 61.4%; $\chi^2(1) = 12.0, p < .001$]. The association between text message support and PrEP adherence was significant for both MSM (81.1% vs. 59.3%; FET, $p = .014$) and trans women (95.8% vs. 66.7%; FET, $p = .022$) participants.

Discussion

A.S.K.-PrEP, a five-session PrEP navigation intervention, targeted urban trans women and MSM experiencing numerous syndemic health disparities including housing instability, unemployment, substance use, and engagement in multiple HIV sexual risk behaviors including exchange sex. Trans women and MSM had similarly highly impacted sociodemographic and risk profiles, with higher proportions of MSM reporting methamphetamine and crack cocaine use as well as insertive CAI, and a higher proportion of trans women reporting exchange sex. Despite the vulnerable nature of this sample, *A.S.K.-PrEP* demonstrated feasibility, acceptability, and preliminary effectiveness in successfully linking a large majority of the sample to PrEP (~90%) and maintaining high levels (~70–80%) of reported PrEP adherence at 90-day follow up evaluations.

A critical innovation of *A.S.K.-PrEP* was the integration of peer navigation sessions designed specifically to target structural PrEP uptake barriers faced by marginalized trans women and MSM. Prior studies with trans women and MSM have highlighted that desired structural supports to increase PrEP acceptability include support in accessing legal identification, health insurance, housing, and gender confirming care (i.e., hormones) for trans women [33, 47, 48]. *A.S.K.-PrEP* incorporated up to five peer navigation sessions that were specifically tailored to each participant's needs including removal of structural barriers to PrEP linkage. However, even after addressing these multiple structural barriers to PrEP, the number of days to successfully link to PrEP was significantly higher among trans women (Med = 14) than among MSM

Table 2 Substance use (previous 6 months) and sexual risk behaviors (previous 3 months; N = 187)

	MSM (<i>n</i> = 129) <i>n</i> (%) or <i>med</i> (range)	Trans women (<i>n</i> = 58) <i>n</i> (%) or <i>med</i> (range)	Statistic	<i>p</i>
Alcohol				
Yes	77 (59.7%)	28 (48.3%)	$\chi^2(1) = 2.1$.146
No	52 (40.3%)	30 (51.7%)		
Marijuana				
Yes	73 (56.6%)	32 (55.2%)	$\chi^2(1) = 0.0$.857
No	56 (43.4%)	26 (44.8%)		
Methamphetamine				
Yes	82 (63.6%)	21 (36.2%)	$\chi^2(1) = 12.1$	<.001
No	47 (36.4%)	37 (63.8%)		
Crack cocaine				
Yes	21 (16.3%)	3 (5.2%)	FET	.036
No	108 (83.7%)	55 (94.8%)		
Powder cocaine				
Yes	17 (13.2%)	4 (6.9%)	FET	.779
No	112 (86.8%)	54 (93.1%)		
Opioids				
Yes	17 (13.2%)	3 (5.2%)	FET	.128
No	112 (86.8%)	55 (94.8%)		
Amyl nitrites				
Yes	11 (8.5%)	3 (5.2%)	FET	.555
No	118 (91.5%)	55 (94.8%)		
Number of sexual partners				
Male	2 (0–30)	3 (0–60)	KW $\chi^2(1) = 5.3$.021
Female	0 (0–30)	0 (0–5)	KW $\chi^2(1) = 7.8$.005
Transgender	0 (0–18)	0 (0–5)	KW $\chi^2(1) = 9.0$.003
CAI				
Receptive or insertive				
Yes	85 (65.9%)	31 (53.4%)	$\chi^2(1) = 2.6$.105
No	44 (34.1%)	27 (46.6%)		
Receptive				
Yes	50 (38.8%)	28 (48.3%)	$\chi^2(1) = 1.5$.222
No	79 (61.2%)	30 (51.7%)		
Insertive				
Yes	77 (59.7%)	15 (25.9%)	$\chi^2(1) = 18.3$	<.001
No	52 (40.3%)	43 (74.1%)		
Exchange sex^a				
Yes	15 (11.6%)	18 (31.0%)	$\chi^2(1) = 10.2$.001
No	113 (87.6%)	40 (69.0%)		

Results are reported for all substances that were used by at least 5% of participants

FET Fisher's exact test, KW Kruskal–Wallis, CAI condomless anal intercourse

^a*n* = 128

(Med = 9). This disparity was likely explained by the disproportionate structural barriers to PrEP linkage faced by trans women compared to MSM including ID documentation issues due to legal name and gender marker [49] and difficulties accessing clinician-prescribed hormones [50]. The significantly longer time to link trans women to PrEP compared to MSM highlights that interventions targeting

trans women should be prepared to incorporate key program components designed to remove trans-specific structural barriers to PrEP access.

The *A.S.K.-PrEP* intervention was also successful in providing participants with ongoing adherence support through an opt-in/opt-out weekly text message component. This mobile support component demonstrated feasibility

Table 3 Linkage to PrEP and adherence (N = 187)

	MSM (<i>n</i> = 129) <i>n</i> (%) or <i>med</i> (range)	Trans women (<i>n</i> = 58) <i>n</i> (%) or <i>med</i> (range)	Statistic	<i>p</i>
Linked to PrEP				
Yes	118 (91.5%)	52 (89.7%)	$\chi^2(1)=0.2$.689
No	11 (8.5%)	6 (10.3%)		
Days to linkage to PrEP	9 (0–121)	14 (2–120)	KW $\chi^2(1)=10.9$	<.001
90-day follow-up				
	(<i>n</i> = 112)	(<i>n</i> = 48)		
Currently on PrEP	78 (69.6%)	39 (81.3%)	$\chi^2(1)=2.3$.129
Days with ≥ 1 dose missed				
Previous 4 days				
0	65 (83.3%) ^a	34 (87.2%) ^b	$\chi^2(1)=0.3$.587
1–4	13 (16.7%) ^a	5 (12.8%) ^b		
Previous 30 days				
0	38 (48.7%) ^a	19 (48.7%) ^b	$\chi^2(2)=0.0$.989
1–3	27 (34.6%) ^a	13 (33.3%) ^b		
≥ 4	13 (16.7%) ^a	6 (15.4%) ^b		
No PrEP ≥ 4 days in a row				
Previous 30 days				
Yes	15 (19.2%) ^a	9 (23.1%) ^b	$\chi^2(1)=0.3$.576
No	61 (78.2%) ^a	29 (74.4%) ^b		

KW Kruskal–Wallis

^a*n* = 78^b*n* = 39**Table 4** Text message adherence support and PrEP adherence at 90-day follow-up evaluation (*n* = 160)

Currently taking PrEP	Text message support		Statistic	<i>p</i>
	Yes <i>n</i> (%)	No <i>n</i> (%)		
All participants (<i>n</i> = 160)				
Yes	66 (85.7%)	51 (61.4%)	$\chi^2(1)=12.0$	<.001
No	11 (14.3%)	32 (38.6%)		
MSM (<i>n</i> = 112)				
Yes	43 (81.1%)	35 (59.3%)	FET	.014
No	10 (18.9%)	24 (40.7%)		
Trans women (<i>n</i> = 48)				
Yes	23 (95.8%)	16 (66.7%)	FET	.022
No	1 (4.2%)	8 (33.3%)		

FET Fisher's exact test

and preliminary effectiveness with 51.7% of trans women and 46.5% of MSM participants opting-into receive weekly text messages. Participants who opted-into receive text messages were significantly more likely to be adherent to PrEP at the 90-day follow-up evaluation than those who opted-out. The results were particularly striking for trans women as over 95% of trans women who opted-into receive adherence

support text messages were PrEP adherent at the 90-day follow-up evaluation compared to approximately 67% of those who opted-out. Text messages were culturally tailored and theoretically informed by one of three behavioral health theories (i.e., Social Support Theory, Health Belief Model, Social Cognitive Theory). Our group has successfully developed, implemented and evaluated theory-based text message HIV interventions for trans women and MSM facing syndemic health disparities [51–54]. Adherence support text messages might be particularly beneficial for trans women and MSM experiencing numerous syndemic health disparities, as both groups report low levels of social support [55–58] and often have chaotic lives that might require ongoing reminders for PrEP adherence [32, 47]. Future randomized controlled trials are necessary to test the efficacy of weekly adherence support text messaging to improve PrEP adherence among trans women and MSM.

The A.S.K.-PrEP program was staffed with two indigenous peer navigators, one of whom identified as a trans woman and one of whom identified as a MSM, both self-disclosed being HIV negative and one (the trans woman) self-disclosed long-term PrEP adherence and persistence. A critical review of over 100 papers focused on PrEP implementation models from 2012 to 2017 stressed the

effectiveness of PrEP peer navigators in assisting PrEP candidates with both navigating complicated health insurance issues and providing ongoing PrEP adherence support, especially with socially marginalized and low-income patients [59]. Interventions that are focused on linkage to HIV primary care and PrEP among trans women and MSM have also highlighted the importance of using peer navigators who have similar life experiences to the populations they serve [60–62]. Beyond practical assistance with health insurance, peer navigators might help to reduce patient reluctance to link to care and concerns over healthcare stigmatization, a primary issue faced by racial/ethnic minority trans women and MSM [47, 48, 63–65]. Given that over 80% of the sample were trans women and MSM of color, the integration of peer navigators to assuage patient concerns over linkage to PrEP care was likely instrumental to the success of *A.S.K.-PrEP*.

At the 90-day follow-up evaluation, approximately 20% of the full sample reported missing at least four consecutive doses of PrEP in the previous 30 days. Seroconversion in the iPrEx trial was due to low adherence [26], and studies have shown that a minimum of four PrEP pills per week are required for protective tenofovir levels [22]. Findings from *A.S.K.-PrEP* indicated that, in the previous 30 days from their 90-day follow-up evaluation, one in five participants most likely had had suboptimal tenofovir levels for HIV protection. This finding demonstrates that ongoing PrEP adherence support is likely required for many trans women and MSM experiencing multiple health disparities. While *A.S.K.-PrEP* did offer an opt-in/opt-out weekly adherence support text message component that was associated with increased PrEP adherence at 90-day follow-up among those who opted-in, future interventions might test the efficacy of daily text message reminders, which have been shown to be effective in increasing adherence to HIV antiretroviral medication [66–68].

Limitations and Conclusions

The results from *A.S.K.-PrEP* must be interpreted in light of several limitations. Enrollment into *A.S.K.-PrEP* was self-selective; thus, the high rates of PrEP linkage and adherence may be partially due to self-selection biases as participants enrolled in the program specifically because they were interested in learning more about and possibly initiating PrEP. Additionally, there could be sampling bias among those who self-selected to opt-into the adherence support text message component, as those who expected to adhere to PrEP could have been more likely to opt-in, whereas those who did not want to adhere to PrEP might

also not want to receive text messages. All data was self-reported and, as such, were vulnerable to reporting bias, social desirability, and recall errors. Furthermore, due to the self-reported nature of the data, tenofovir levels measured through TFV-DP dried blood spot analysis were not collected to test for actual levels of adherence. Additionally, given the nature of the community service program as opposed to a clinical trial, there was only one follow-up evaluation time point at 90-days post-enrollment. Consequently, distal follow-up time points for PrEP adherence and persistence, which requires a minimum of six months, were not available. *A.S.K.-PrEP* was a non-randomized service program, without a control group, limiting the ability to demonstrate the causal effectiveness of the intervention. However, the demonstrated effectiveness of this non-randomized intervention calls for a future clinical trial to determine efficacy. Finally, the sociodemographic profile of the sample demonstrated that the sample was highly impacted by numerous syndemic health disparities that are less common among other populations; therefore, results may not be generalizable.

Despite these limitations, *A.S.K.-PrEP* is a promising peer navigation intervention that demonstrated feasibility, acceptability, and effectiveness in PrEP linkage, uptake and preliminary adherence among a sample of trans women and MSM experiencing multiple syndemic health disparities. Critical to the intervention's success was the specific focus on removing structural barriers to PrEP linkage and the staffing of indigenous peer navigators. Racial/ethnic minority status trans women and MSM represent the two groups in the U.S. with the highest need for PrEP, but the lowest access [30]. By tailoring a PrEP peer navigation intervention to the specific needs of marginalized trans women and MSM, the *A.S.K.-PrEP* program demonstrated that even the most vulnerable groups can successfully link and adhere to PrEP. The *A.S.K.-PrEP* program provided a strong foundation from which to adapt the intervention to other urban, highly impacted populations of trans women and MSM across the U.S. Findings from the service program will be gleaned as larger clinical trials are developed and implemented to evaluate sustained PrEP adherence and persistence through biomarkers of tenofovir levels, intervention efficacy, cost effectiveness and sustainability.

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Compliance with Ethical Standards

Conflict of interest No potential conflict of interest was reported by the authors.

References

- Centers for Disease Control and Prevention. (2017). *Fact sheet: HIV among gay and bisexual men*. Atlanta, GA: Centers for Disease Control and Prevention. Retrieved from <https://www.cdc.gov/hiv/group/msm/index.html>.
- Baral, S. D., Poteat, T., Strömdahl, S., Wirtz, A. L., Guadamuz, T. E., & Beyrer, C. (2013). Worldwide burden of HIV in transgender women: A systematic review and meta-analysis. *The Lancet Infectious Diseases*, *13*(3), 214–222.
- Centers for Disease Control and Prevention. (2017). *Fact sheet: HIV among transgender people*. Atlanta, GA: Centers for Disease Control and Prevention. Retrieved from <https://www.cdc.gov/hiv/group/gender/transgender/index.html>.
- Reback, C. J., Clark, K., Holloway, I. W., & Fletcher, J. B. (2018). Health disparities, risk behaviors and healthcare utilization among transgender women in Los Angeles County: A comparison from 1998–1999 to 2015–2016. *AIDS and Behavior*, *22*(8), 2524–2533.
- Brennan, J., Kuhns, L. M., Johnson, A. K., et al. (2012). Syndemic theory and HIV-related risk among young transgender women: The role of multiple, co-occurring health problems and social marginalization. *American Journal of Public Health*, *102*(9), 1751–1757.
- Reback, C. J., & Fletcher, J. B. (2014). HIV prevalence, substance use, and sexual risk behaviors among transgender women recruited through outreach. *AIDS and Behavior*, *18*(7), 1359–1367.
- Beyrer, C., Sullivan, P., Sanchez, J., et al. (2013). The increase in global HIV epidemics in MSM. *Aids*, *27*(17), 2665–2678.
- Fletcher, J. B., & Reback, C. J. (2017). Mental health disorders among homeless, substance-dependent men who have sex with men. *Drug and Alcohol Review*, *36*(4), 555–559.
- Reback, C. J., & Fletcher, J. B. (2017). Outcomes from a home-grown HIV prevention program for extremely high-risk, substance-using men who have sex with men with multiple health disparities. *Journal of Gay & Lesbian Social Services*, *29*(2), 167–181.
- Santos, G. M., Wilson, E. C., Rapues, J., Macias, O., Packer, T., & Raymond, H. F. (2014). HIV treatment cascade among transgender women in a San Francisco respondent driven sampling study. *Sexually Transmitted Infections*, *90*(5), 430–433.
- Shoptaw, S., & Reback, C. J. (2007). Methamphetamine use and infectious disease-related behaviors in men who have sex with men: Implications for interventions. *Addiction*, *102*, 130–135.
- Stall, R., Mills, T. C., Williamson, J., et al. (2003). Association of co-occurring psychosocial health problems and increased vulnerability to HIV/AIDS among urban men who have sex with men. *American Journal of Public Health*, *93*(6), 939–942.
- Chapin-Bardales, J., Rosenberg, E. S., & Sullivan, P. S. (2017). Trends in racial/ethnic disparities of new AIDS diagnoses in the United States, 1984–2013. *Annals of Epidemiology*, *27*(5), 329–334.
- Clark, H., Babu, A. S., Wiewel, E. W., Opoku, J., & Crepez, N. (2017). Diagnosed HIV infection in transgender adults and adolescents: Results from the National HIV Surveillance System, 2009–2014. *AIDS and Behavior*, *21*(9), 2774–2783.
- Maulsby, C., Millett, G., Lindsey, K., et al. (2014). HIV among black men who have sex with men (MSM) in the United States: A review of the literature. *AIDS and Behavior*, *18*(1), 10–25.
- Grant, R. M., Anderson, P. L., McMahan, V., et al. (2014). Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: A cohort study. *The Lancet Infectious Diseases*, *14*(9), 820–829.
- Huang, X., Hou, J., Song, A., et al. (2018). Efficacy and safety of oral TDF-based pre-exposure prophylaxis for men who have sex with men: A systematic review and meta-analysis. *Frontiers in pharmacology*, *9*(799), 1–11.
- Grant, R. M., Lama, J. R., Anderson, P. L., et al. (2010). Pre-exposure chemoprophylaxis for HIV prevention in men who have sex with men. *New England Journal of Medicine*, *363*(27), 2587–2599.
- Buchbinder, S. P. (2018). Maximizing the benefits of HIV pre-exposure prophylaxis. *Topics in Antiviral Medicine*, *25*(4), 138.
- Spinner, C. D., Boesecke, C., Zink, A., et al. (2016). HIV pre-exposure prophylaxis (PrEP): A review of current knowledge of oral systemic HIV PrEP in humans. *Infection*, *44*(2), 151–158.
- Anderson, P. L., Glidden, D. V., Liu, A., et al. (2012). Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. *Science Translational Medicine*, *4*(151), 151ra125–151ra125.
- Baxi, S. M., Vittinghoff, E., Bacchetti, P., et al. (2018). Comparing pharmacologic measures of tenofovir exposure in a US pre-exposure prophylaxis randomized trial. *PLoS ONE*, *13*(1), e0190118.
- Escudero, D. J., Kerr, T., Operario, D., Socías, M. E., Sued, O., & Marshall, B. D. (2015). Inclusion of trans women in pre-exposure prophylaxis trials: A review. *AIDS Care*, *27*(5), 637–641.
- Grant, R. M., Sevelius, J. M., Guanira, J. V., Aguilar, J. V., Charneyalertsak, S., & Deutsch, M. B. (2016). Transgender women in clinical trials of pre-exposure prophylaxis. *Journal of Acquired Immune Deficiency Syndromes*, *72*(Suppl 3), S226.
- Sevelius, J. M., Deutsch, M. B., & Grant, R. (2016). The future of PrEP among transgender women: The critical role of gender affirmation in research and clinical practices. *Journal of the International AIDS Society*, *19*, 21105.
- Deutsch, M. B., Glidden, D. V., Sevelius, J., et al. (2015). HIV pre-exposure prophylaxis in transgender women: A subgroup analysis of the iPrEx trial. *The Lancet HIV*, *2*(12), e512–e519.
- Marshall, B. D., & Mimiaga, M. J. (2015). Uptake and effectiveness of PrEP for transgender women. *The Lancet HIV*, *2*(12), e502–e503.
- Baeten, J. M. (2018). Amplifying the population health benefits of PrEP for HIV prevention. *Journal of Infectious Diseases*, *217*(10), 1509–1511.
- Pasipanodya, E. C., Jain, S., Sun, X., et al. (2018). Trajectories and predictors of longitudinal PrEP adherence among men who have sex with men. *The Journal of Infectious Diseases*, *218*, 1551–1559.
- Centers for Disease Control and Prevention. (2018). *HIV prevention pill not reaching most Americans who could benefit: Especially people of color*. Press release. National center for HIV/AIDS, viral Hepatitis, STD, and TB prevention. Atlanta, GA: Centers for Disease Control and Prevention. Retrieved from <https://www.cdc.gov/nchhstp/newsroom/2018/croi-2018-PrEP-press-release.html>.
- Conference on Retroviruses and Opportunistic Infections (CROI). (2018). *PrEP at CROI 2018 report 2: Uptake, HIV incidence, barriers/challenges*. Report from Conference on Retroviruses and Opportunistic Infections (CROI), Boston, MA.
- Rael, C. T., Martinez, M., Giguere, R., et al. (2018). Barriers and facilitators to oral PrEP use among transgender women in New York city. *AIDS and Behavior*, *22*, 3627–3636.
- Sevelius, J. M., Keatley, J., Calma, N., & Arnold, E. (2016). ‘I am not a man’: Trans-specific barriers and facilitators to PrEP acceptability among transgender women. *Global Public Health*, *11*(7–8), 1060–1075.

34. Pinto, R. M., Berringer, K. R., Melendez, R., & Mmeje, O. (2018). Improving PrEP implementation through multilevel interventions: A synthesis of the literature. *AIDS and Behavior*, *22*(11), 3681–3691.
35. Arnold, E. A., Hazelton, P., Lane, T., Christopoulos, K. A., Galindo, G. R., Steward, W. T., et al. (2012). A qualitative study of provider thoughts on implementing pre-exposure prophylaxis (PrEP) in clinical settings to prevent HIV infection. *PLoS ONE*, *7*(7), e40603.
36. Burns, D. N., Grossman, C., Turpin, J., Elharrar, V., & Veronese, F. (2014). Role of oral pre-exposure prophylaxis (PrEP) in current and future HIV prevention strategies. *Current HIV/AIDS Reports*, *11*(4), 393–403.
37. Calabrese, S. K., Magnus, M., Mayer, K. H., et al. (2016). Putting PrEP into practice: Lessons learned from early-adopting US providers' firsthand experiences providing HIV pre-exposure prophylaxis and associated care. *PLoS ONE*, *11*(6), e0157324.
38. Hosek, S., Celum, C., Wilson, C. M., Kapogiannis, B., Delany-Moretlwe, S., & Bekker, L. G. (2016). Preventing HIV among adolescents with oral PrEP: Observations and challenges in the United States and South Africa. *Journal of the International AIDS Society*, *19*, 21107.
39. Underhill, K., Morrow, K. M., Colleran, C. M., et al. (2014). Access to healthcare, HIV/STI testing, and preferred pre-exposure prophylaxis providers among men who have sex with men and men who engage in street-based sex work in the US. *PLoS ONE*, *9*(11), e112425.
40. Wilton, J., Senn, H., Sharma, M., & Tan, D. H. (2015). Pre-exposure prophylaxis for sexually-acquired HIV risk management: A review. *HIV/AIDS*, *7*, 125.
41. Pathela, P., Jamison, K., Blank, S., et al. (2018). *The PREP cascade at NYC sexual health clinics: Navigation is the key to uptake*, in Presented at: Conference on Retroviruses and Opportunistic Infections (CROI), Boston, MA.
42. Turner, R. J., & Turner, J. B. (1999). Social integration and support. *Handbook of the sociology of mental health* (pp. 301–319). Boston, MA: Springer.
43. Veiel, H. O., & Baumann, U. (2014). *The meaning and measurement of support*. Abingdon: Taylor & Francis.
44. Janz, N. K., & Becker, M. H. (1984). The health belief model: A decade later. *Health Education Quarterly*, *11*(1), 1–47.
45. Bandura, A. (1991). Social cognitive theory of self-regulation. *Organizational Behavior and Human Decision Processes*, *50*(2), 248–287.
46. Bandura, A. (2001). Social cognitive theory: An agentic perspective. *Annual Review of Psychology*, *52*(1), 1–26.
47. Golub, S. A., Gamarel, K. E., Rendina, H. J., Surace, A., & Lelutiu-Weinberger, C. L. (2013). From efficacy to effectiveness: Facilitators and barriers to PrEP acceptability and motivations for adherence among MSM and transgender women in New York City. *AIDS Patient Care and STDs*, *27*(4), 248–254.
48. Levy, M. E., Wilton, L., Phillips, G., et al. (2014). Understanding structural barriers to accessing HIV testing and prevention services among black men who have sex with men (BMSM) in the United States. *AIDS and Behavior*, *18*(5), 972–996.
49. Hill, B. J., Crosby, R., Bouris, A., et al. (2018). Exploring transgender legal name change as a potential structural intervention for mitigating social determinants of health among transgender women of color. *Sexuality Research and Social Policy*, *15*(1), 25–33.
50. Clark, K., Fletcher, J. B., Holloway, I. W., & Reback, C. J. (2018). Structural inequities and social networks impact hormone use and misuse among transgender women in Los Angeles County. *Archives of Sexual Behavior*, *47*(4), 953–962.
51. Reback, C. J., Fletcher, J. B., Shoptaw, S., & Mansergh, G. (2015). Exposure to theory-driven text messages is associated with HIV risk reduction among methamphetamine-using men who have sex with men. *AIDS and Behavior*, *19*(2), 130–141.
52. Reback, C. J., Fletcher, J. B., Swendeman, D. A., & Metzner, M. (2019). Theory-based text-messaging to reduce methamphetamine use and HIV sexual risk behaviors among men who have sex with men: Automated unidirectional delivery outperforms bidirectional peer interactive delivery. *AIDS and Behavior*, *23*(1), 37–47.
53. Reback, C. J., Grant, D. L., Fletcher, J. B., Branson, C. M., Shoptaw, S., Bowers, J. R., et al. (2012). Text messaging reduces HIV risk behaviors among methamphetamine-using men who have sex with men. *AIDS and Behavior*, *16*(7), 1993–2002.
54. Reback, C. J., Ling, D., Shoptaw, S., & Rohde, J. (2010). Developing a text messaging risk reduction intervention for methamphetamine-using MSM: Research note. *The Open AIDS Journal*, *4*, 116.
55. Baams, L., Jonas, K. J., Utz, S., Bos, H. M., & Van Der Vuurst, L. (2011). Internet use and online social support among same sex attracted individuals of different ages. *Computers in Human Behavior*, *27*(5), 1820–1827.
56. Factor, R. J., & Rothblum, E. D. (2007). A study of transgender adults and their non-transgender siblings on demographic characteristics, social support, and experiences of violence. *Journal of LGBT Health Research*, *3*(3), 11–30.
57. Nemoto, T., Bödeker, B., & Iwamoto, M. (2011). Social support, exposure to violence and transphobia, and correlates of depression among male-to-female transgender women with a history of sex work. *American Journal of Public Health*, *101*(10), 1980–1988.
58. Puckett, J. A., Woodward, E. N., Mereish, E. H., & Pantalone, D. W. (2015). Parental rejection following sexual orientation disclosure: Impact on internalized homophobia, social support, and mental health. *LGBT Health*, *2*(3), 265–269.
59. Mayer, K. H., Chan, P. A., Patel, R., Flash, C. A., & Krakower, D. S. (2018). Evolving models and ongoing challenges for HIV pre-exposure prophylaxis implementation in the United States. *Journal of Acquired Immune Deficiency Syndromes*, *77*(2), 119.
60. Bauman, L. J., Braunstein, S., Calderon, Y., et al. (2013). Barriers and facilitators of linkage to HIV primary care in New York City. *Journal of Acquired Immune Deficiency Syndromes*, *64*(01), S20.
61. Garcia, J., Colson, P. W., Parker, C., & Hirsch, J. S. (2015). Passing the baton: Community-based ethnography to design a randomized clinical trial on the effectiveness of oral pre-exposure prophylaxis for HIV prevention among black men who have sex with men. *Contemporary Clinical Trials*, *45*, 244–251.
62. Parisi, D., Warren, B., Leung, S. J., et al. (2018). A multicomponent approach to evaluating a pre-exposure prophylaxis (PrEP) implementation program in five agencies in New York. *Journal of the Association of Nurses in AIDS Care*, *29*(1), 10–19.
63. Seelman, K. L., Colón-Díaz, M. J., LeCroix, R. H., Xavier-Brier, M., & Kattari, L. (2017). Transgender noninclusive healthcare and delaying care because of fear: Connections to general health and mental health among transgender adults. *Transgender Health*, *2*(1), 17–28.
64. White Hughto, J. M., Murchison, G. R., Clark, K., Pachankis, J. E., & Reisner, S. L. (2016). Geographic and individual differences in healthcare access for US transgender adults: A multi-level analysis. *LGBT Health*, *3*(6), 424–433.
65. Hughto, J. M. W., Reisner, S. L., & Pachankis, J. E. (2015). Transgender stigma and health: A critical review of stigma determinants, mechanisms, and interventions. *Social Science and Medicine*, *147*, 222–231.
66. Dowshen, N., Kuhns, L. M., Gray, C., Lee, S., & Garofalo, R. (2013). Feasibility of interactive text message response (ITR) as a novel, real-time measure of adherence to antiretroviral therapy for HIV + youth. *AIDS and Behavior*, *17*(6), 2237–2243.
67. Dowshen, N., Kuhns, L. M., Johnson, A., Holoyda, B. J., & Garofalo, R. (2012). Improving adherence to antiretroviral

therapy for youth living with HIV/AIDS: A pilot study using personalized, interactive, daily text message reminders. *Journal of Medical Internet Research*, 14(2), e51.

68. Reback, C. J., Ruenger, D., Fletcher, J., et al. (2019). *Text messaging to promote advancement along the HIV care continuum among young transgender women living with HIV*, in Presented at: National HIV Prevention Conference, Atlanta, GA.

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