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Randomized Trial of Individualized Texting for Adherence Building (iTAB) Plus Motivational Interviewing for PrEP Adherence in Transgender Individuals: The iM-PrEPT Study

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Background: Transgender and nonbinary individuals at risk for HIV may benefit from adherence support for pre-exposure prophylaxis.

Methods: Between June 2017 and September 2020, 255 transgender and nonbinary individuals received daily oral tenofovir disoproxil fumarate/emtricitabine for 48 weeks randomized 1:1 to receive individualized Texting for Adherence Building (iTAB) or iTAB plus motivational interviewing (iTAB + MI) through phone for nonadherence. The primary end point was dried blood spot tenofovir diphosphate concentrations at weeks 12 and 48 (or last on-drug study visit) ≥1246 fmol/punch consistent with ≥7 doses/week (ie, near-perfect adherence). Secondary outcomes included dried blood spot tenofovir diphosphate concentrations ≥719 fmol/punch consistent with ≥4 doses/week (ie, adequate adherence) and self-reported adherence by daily text messages.

Results: Adherence for the outcome ≥1246 fmol/punch and ≥719 fmol/punch, respectively, was 49.1% and 57.9% for transgender men, 37.7% and 47.2% for nonbinary individuals, and 31.0% and 44.1% for transgender women. No difference was seen in iTAB + MI compared with iTAB alone by drug levels except where it approached significance in transgender women for the outcome of ≥719 fmol/punch in the iTAB + MI group compared with iTAB only (52% versus 35.7%, $P = 0.065$). There was a significant difference in self-reported daily dose adherence in the iTAB + MI group compared with iTAB alone (57.9% of days versus 46.4%, $P = 0.009$). In transgender women, the mean percentage of daily doses taken was 58.5% with iTAB + MI and 37.3% with iTAB alone ($P < 0.001$).

Conclusions: In addition to automated approaches to adherence promotion, phone-based MI triggered by repeatedly missing doses may improve pre-exposure prophylaxis adherence among transgender women.

Key Words: transgender, HIV prevention, text messaging, intervention, PrEP

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INTRODUCTION

Efficacy of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) as pre-exposure prophylaxis (PrEP) has been established and, together with tenofovir alafenamide fumarate/emtricitabine (TAF/FTC), is considered standard care for HIV prevention.[1] Transgender and nonbinary (TGNB) individuals are at high risk for HIV with transgender women having some of the highest rates of HIV infection.[2,3] Nonbinary individuals and transgender men are also at elevated risk for HIV, depending on their risk behavior.[4] However, TDF/FTC or TAF/FTC PrEP efficacy studies to date have lacked sufficient data on transgender individuals.[5,6] This study aimed to understand ways to improve adherence to PrEP in TGNB with an evidence-based intervention.

Previous studies with individualized Texting for Adherence Building (iTAB) were predominantly conducted in cisgender men who have sex with men (MSM) and demonstrated that personalized daily text reminders improved near-perfect adherence to TDF/FTC by erythrocyte tenofovir diphophate (TFV-DP) concentrations.[7] Other technology-based interventions such as a general weekly "check in" text combined with medication reminders and participant support[8] and mobile applications that allow for medications to be entered and for push notifications to be sent at specified medication times have also shown promise.[8,9] The iTAB intervention is a 2-way text messaging system derived from the theory of planned behavior that sends text messages at patient specified times and includes both health promotion messages and factoids to promote engagement. The iTAB intervention was adapted to support adherence in cisgender women with HIV risk with addition of drug-level monitoring and intensive counseling that could involve multiple sessions to work on nonadherence.[10] This amount of engagement was not achievable for most participants and raised the question whether counseling added benefit and with what intensity.

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iTAB would be a reasonable option for adherence support for transgender individuals, but it is unclear whether counseling adds to the automated intervention.

Motivational interviewing (MI) is a widely accepted technique to change health behaviors,[11,12] and it has been used among persons with HIV to promote adherence to antiretroviral therapy.[13,14] Adding real-time, brief, telephone-delivered, MI when nonadherence occurs may provide a personalized experience that could enhance adherence yet could be delivered efficiently and at a low burden to participants. This study aimed to test whether the addition of brief MI with iTAB for nonadherence could improve the adherence to PrEP among TGNB individuals.

METHODS

Study Setting

The California Collaborative Treatment Group enrolled participants from June 2017 to September 2019 at 5 Southern California sites (University of California, San Diego; Family Health Centers of San Diego; University of Southern California; Harbor-University of California Los Angeles; and Los Angeles LGBT Center). Participants had follow-up visits every 12 weeks up to 48 weeks. The last patient visit was completed in September 2020. All participants provided written informed consent to participate in this IRB-approved study at all participating sites.

Eligible participants were English-speaking or Spanish-speaking HIV-negative TGNB individuals who were 18 years or older. HIV status was confirmed by a negative fourth-generation antigen–antibody assay or a third-generation antibody assay plus HIV nucleic acid amplification test. Elevated risk of HIV infection was determined by one or more of the following at screening: (1) at least 1 HIV-positive partner for a sexual relationship lasting 4 weeks or more in the past year, (2) anticipated condomless anal or vaginal sex with a assigned male at birth partner in the next 3 months, or (3) any assigned male at birth partners in the past 12 months AND at least one of the following: (1) any condomless anal or vaginal sex in the past 12 months; (2) any sexually transmitted infection in the past 12 months; (3) exchange of money, gifts, shelter, or drugs for sex; or (4) postexposure prophylaxis use in the past 12 months.

Exclusion criteria included active hepatitis B, calculated creatinine clearance of <60 mL/min by the Cockcroft–Gault formula, proteinuria 2+ or greater, pregnancy, or substantial condition that would put participants at risk or complicate interpretation of study outcome data. Methods used to recruit participants included: (1) the formation of the UCSD Trans Community Advisory Board; (2) hosting various events such as "trans health and wellness day," National Transgender HIV Testing day, and safe space clothing swaps at local community centers; (3) creation of a study-specific website and social media accounts, (4) "tabling" at local transcentered events; (5) engagement with local transfocused community organizations; (6) referrals from transfocused health providers; and (7) word of mouth.

Study and Intervention Design

Participants were randomized 1:1 to iTAB intervention with or without brief MI for suboptimal adherence for 48 weeks. Randomization was stratified by site, sex assigned at birth, and history of PrEP use. All participants received TDF/FTC 200/300 mg once daily plus the iTAB text intervention to support and monitor adherence to PrEP. This study provided a cellular phone for participants who did not have unlimited text messaging or phone service.

Three focus groups were conducted from late 2016 to early 2017 to tailor the content of iTAB for TGNB individuals. Based on feedback, the previous version of iTAB[7,10] was updated to include additional "factoid" domains of information about PrEP, TGNB Health Facts, and TGNB History. Participants had to select at least 5 domains. Otherwise, the core iTAB messaging system was retained and used as previously reported. Daily text message reminders included a personalized lead-in health promotion or "factoid" message, eg, "You are an important person to the people around you, please take your [dose]," followed by "did you take your [dose] today?"[15] One letter text responses included (Y) yes, (N) no, or (P) postpone. If postpone was selected, participants would receive a follow-up text message 1 hour later. Participants could choose what they wanted to call their medication and when they received their texts. After a response, participants would receive an automated response reinforcing their medication taking (eg, "Good job!") or a response encouraging adherence (eg, Please take your PrEP ASAP). A nonresponse or "no" was counted as a self-reported missed dose of study medication for that day. Messages were also available in Spanish.

In the iTAB + MI arm, participants with nonresponses and/or "no" responses for 3 consecutive days were contacted through telephone. Brief MI was delivered by a centralized research coordinator (to ensure fidelity of MI across sites) who had received a 16-hour training in targeted MI from an MI specialized psychologist. The MI staff member had a script that was used across participants with core MI components to be covered. The research coordinator who conducted the MI varied depending on staff availability and turnover. Topics covered in MI phone calls included a brief discussion of barriers and facilitators to adherence and adherence techniques. Individual site coordinators made participants aware of the centralized MI support person in advance. A nondisclosing voicemail message was left for participants who did not answer the MI phone calls.

Study Procedures and Measures

Study visits occurred at screening, baseline, a week 2 telephone check-in call, and week 12, 24, 36, and 48. Study visits aligned with CDC guidance to complete HIV testing every 3 months in those taking PrEP.[16] In addition to HIV testing, participants had creatinine measurements, medical monitoring, and completed a computer-assisted survey instrument. Sexually transmitted infection (STI) testing included RPR or syphilis EIA and 3-site (urine, rectal, and pharyngeal) *Chlamydia trachomatis* and *Neisseria gonorrhoeae* (CT/NG) nucleic acid amplification testing; these were completed at

baseline, week 24, and week 48. Additional HIV and STI testing could be requested for symptoms or recent exposures at any time.

Dried blood spots (DBSs) analyzed by the University of Colorado measured intracellular RBC TFV-DP levels.[17] Adequate adherence was categorized as ≥4 doses/wk of PrEP and near-perfect adherence as ≥7 doses/wk at ≥719 and ≥1246 fmol/punch, respectively.

Statistical Measures

Descriptive analyses were performed to compare baseline characteristics between the 2 arms. Categorical variables were evaluated using the Fisher exact test. Continuous variables were analyzed with the Wilcoxon rank-sum test.

The primary adherence outcome was a composite outcome of DBS TFV-DP concentrations ≥ 1246 fmol/punch at week 12 and, if continued on PrEP past week 12, the last DBS visit at week 24, 36, or 48, representing near-perfect adherence during the study period. Participants who were lost to follow-up before week 12 were considered nonadherent. This study was powered to compare the primary adherence rate between the 2 study arms using a 2-sample, 2-sided proportion test. Assuming the adherence rate of the transgender iTAB alone group will be the same as our previous MSM trial (33%), this study was planned to have 77% power to detect a difference of 16% between the iTAB + MI group and the iTAB alone group, with 150 subjects per group.

A secondary TFV-DP adherence outcome was defined with a cut off of ≥719 fmol/punch, representing adequate adherence. Self-reported daily iTAB adherence was defined as the percentage of "yes, I took the dose" responses over the total number of days a text reminder was sent. Missing responses were counted as "no dose taken." The Fisher exact test was used to compare the composite DBS TFV-DP adherence outcomes between the study arms; The Wilcoxon rank-sum test was used to compare the self-reported iTAB text messaging adherence outcome between the study arms. Subgroup analyses were further conducted separately for transgender men, transgender women, and nonbinary individuals. Multivariable logistic regression models were also conducted to assess the association of baseline factors including demographics and inclusion criteria with TFV-DP adherence. P values < 0.05 were considered statistically significant. All statistical analyses were performed using the R software version 3.6.1 (http://www.r-project.org).

RESULTS

Study Flow

Of 277 individuals who completed a screening visit, 256 participants were enrolled; a total of 255 individuals completed a baseline visit and were randomized (Fig. 1). There were 127 participants randomized to the iTAB arm and 128 randomized to the iTAB + MI arm. Of the 21 screen failures (Fig. 1), 1 participant was HIV+ at screening, 1 participant had chronic hepatitis B, 1 participant did not meet risk criteria, 3 participants had proteinuria of 2+ or greater, and 15 failed to complete their baseline visit or withdrew consent before their baseline visit. One person was enrolled at their baseline visit but was never randomized and did not continue on study.

Early termination occurred for 84 participants [32.9% overall; n = 42 (33.1%) in iTAB versus n = 42 (32.8%) in iTAB + MI] with no difference by study arm ($P > 0.99$). Reasons for early termination were 2 HIV infections, 60 lost to follow-up before week 48, 22 did not attend the week 48 visit, 21 subject requests to withdraw, and 1 participant was unable to attend visits for an "other" reason which was due to enrollment at a 24-hour rehabilitation facility (Fig. 1). In total, 149 (58.4%) participants completed the final study visit with no difference between iTAB and iTAB + MI arms (57.0% versus 59.8%, $P = 0.70$).

Participants and Demographics

Baseline characteristics were balanced between arms including age, race, ethnicity, sex identity, education, primary language, relationship status, housing situation, and baseline STIs (Table 1). At baseline, there were 13 STIs (10.2%) in the iTAB arm and 18 (14.1%) in the iTAB + MI arm. The mean age of participants was 30.7 years (SD = 9.4, range of 18–78 years). Sex identity included transgender women (145, 56.9%), transgender men (57, 22.4%), and nonbinary individuals (51, 20%). Participants included 37.3% identifying as Hispanic and 18.0% as Black or as part of their multiple racial identities.

Motivational Interviewing

Within the iTAB + MI arm, there were 552 instances when a MI contact/attempt was made. Of the 128 in the iTAB + MI arm, 93 participants had at least 1 contact or contact attempt. There was no difference in the percentage of participants by sex identity that triggered a phone call. Of the 552 contacts/attempts, 128 (23%) were a phone MI session, 9

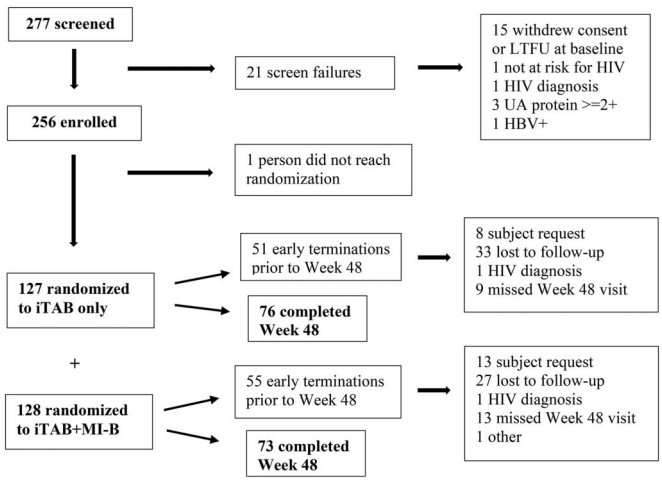

FIGURE 1. Study flow. HBV, hepatitis B virus; LTFU, lost to follow-up; MI-B, brief motivational interviewing; UA, urinalysis.

TABLE 1. Baseline Characteristics

	iTAB Alone	iTAB + Motivational Interviewing
	N (%) of 127	N (%) of 128
Mean age (SD, range)	30.4 (9.1, 19–53)	30.9 (9.7, 18–78)
Sex assigned at birth		
Male	85 (66.9)	85 (66.4)
Female	41 (32.3)	43 (33.6)
Sex identity		
Transgender man	27 (21.3)	30 (23.4)
Transgender woman	70 (55.1)	75 (58.6)
Nonbinary/sex nonconforming	30 (23.6)	23 (18.0)
Race/ethnicity		
Hispanic only	33 (26.0)	39 (30.5)
White	42 (33.1)	38 (29.7)
Black	20 (15.8)	18 (14.1)
Asian	12 (9.5)	16 (12.5)
Other (NA/NH/Other/multiracial/DK)	20 (15.7)	17 (13.3)
Any Black race	25 (19.7)	21 (16.4)
Hispanic/Latinx	47 (37.0)	48 (37.5)
Proficient Spanish speaker	89 (70.1)	83 (64.8)
Maximum level of education		
HS or less	30 (23.6)	39 (30.5)
Some college	71 (55.9)	57 (44.5)
Bachelors or higher	23 (18.1)	30 (23.4)
Current housing		
Own/rent home or apartment	71 (55.9)	66 (51.6)
Live in someone else's place	29 (22.8)	37 (28.9)
In temporary housing	18 (14.2)	11 (8.6)
On street	8 (6.3)	8 (6.3)
Institutional	0 (0)	5 (3.9)
Current relationship status		
Single	83 (65.4)	78 (60.9)
Monogamous	11 (8.7)	19 (14.8)
Open	15 (11.8)	17 (13.3)
Married	6 (4.7)	4 (3.1)
Separated/divorced/widowed	1 (0.8)	3 (2.3)
Other	10 (7.9)	5 (3.9)

DK, does not know; NA, Native American/Alaska Native; NH, Native Hawaiian/Pacific Islander.

(2%) answered the call but deferred the MI until a later date, 137 (25%) were contacted unsuccessfully because of problems leaving a voicemail because of "mailbox full" or phone not in service, and 278 (50%) received a voicemail. The median number of MI sessions per participant ranged from 0 to 7. MI sessions were received by 63 participants with 31 receiving 1 session and 32 receiving more than 1 session. There was no difference by sex identity for the proportion who have received MI.

Primary and Secondary Adherence End points

There was no significant difference between the iTAB only and the iTAB + MI arms [44 (34.7%) versus 49 (38.3%), respectively; $P = 0.60$] for the primary composite outcome of DBS TFV-DP concentrations ≥ 1246 fmol/punch (Table 2) or for the secondary composite outcome of ≥719 fmol/punch (≥4 doses in the past week) [55 (43.3%) compared with 67 (52.3%), $P = 0.17$]. The secondary analysis of self-reported daily iTAB adherence included 251 participants who received text adherence reminders. Four participants never received iTAB: 1 discontinued immediately after baseline and 3 reported their phones did not receive messages. The iTAB + MI arm was superior to the iTAB only arm in the percentage of "yes" responses for having taken their daily doses with a mean of 57.9% compared with 46.4% ($P = 0.009$).

Stratified Analyses by Sex

Adherence for the composite outcomes of ≥1246 fmol/punch and ≥719 fmol/punch, respectively, was 31.0% and 44.1% for transgender women, 49.1% and 57.9% for transgender men, and 37.7% and 47.2% for nonbinary individuals. Among transgender men and nonbinary individuals, there was no MI intervention effect for either the ≥1246 or the ≥719 fmol/punch composite outcomes. However, transgender women in the iTAB + MI arm compared with the iTAB arm had a statistically nonsignificant higher rate for the composite outcome for ≥1246 fmol/punch (near-perfect adherence with 36.0% versus 25.7%; $P = 0.211$) and approached significance for a higher rate of the composite outcome for ≥719 fmol/punch (adequate adherence) with 52.0% versus 35.7% ($P = 0.065$). For self-reported adherence, transgender men and nonbinary individuals in the iTAB + MI arm did not report higher adherence than those that received iTAB alone (Table 2). Transgender women had higher mean percentage of self-reported "yes" responses in the iTAB + MI arm compared with iTAB alone (58.5% versus 37.3%, $P < 0.001$).

Association of Baseline Factors With TFV-DP Adherence End points

Some baseline factors of demographic and inclusion criteria were associated with the main TFV-DP end points (Tables 3 and 4). Individuals with a history of STIs in the past year (adjusted odds ratio [AOR] = 0.38, 95% CI: 0.16 to 0.90, $P = 0.027$) and those who reported exchange sex in the past year (AOR = 0.40, 95% CI: 0.18 to 0.91, $P = 0.029$) were less likely to achieve near-perfect adherence (TFV-DP ≥ 1246 fmol/punch) during this study. Non-Hispanic Black (AOR = 0.30, 95% CI: 0.12 to 0.79, $P = 0.049$) and those who reported exchange sex in the past year (AOR = 0.49, 95% CI: 0.24 to 0.999, $P = 0.05$) were also less likely to achieve adequate adherence (TFV-DP ≥ 719 fmol/punch) during this study.

Safety Analysis

Participants were queried for any adverse events at each study visit beginning at baseline. There were 17 adverse events with a grade 3 severity or higher per the DAIDS

TABLE 2. Adherence Outcomes in the iM-PrEPT Study

	iTAB	iTAB + MI-B	
	N (%)	N (%)	*P*
≥1246 fmol/punch at week 12 and the last DBS visit at week 24, 36, or 48 (near-perfect adherence)			
Entire cohort (N = 255, N1 = 127, N2 = 128)	44 (34.7)	49 (38.3)	0.603
Transgender man (N = 57, N1 = 27, N2 = 30)	14 (51.9)	14 (46.7)	0.793
Transgender woman (N = 145, N1 = 70, N2 = 75)	18 (25.7)	27 (36.0)	0.211
Nonbinary (N = 53, N1 = 30, N2 = 23)	12 (40.0)	8 (34.8)	0.779
≥719 fmol/punch at week 12 and the last DBS visit at week 24, 36, or 48 (adequate adherence)			
Entire cohort (N = 255, N1 = 127, N2 = 128)	55 (43.3)	67 (52.3)	0.169
Transgender man (N = 57, N1 = 27, N2 = 30)	16 (59.3)	17 (56.7)	>0.999
Transgender woman (N = 145, N1 = 70, N2 = 75)	25 (35.7)	39 (52.0)	0.065
Nonbinary (N = 53, N1 = 30, N2 = 23)	14 (46.7)	11 (47.8)	>0.999
Mean (SD) percentage of "yes" responses received out of text received			
All receiving iTAB (N = 251, N1 = 124, N2 = 127)	46.4 (33.6)	57.9 (32.3)	0.009
Transgender man (N = 56, N1 = 26, N2 = 30)	62.0 (29.1)	60.7 (34.1)	0.895
Transgender woman (N = 144, N1 = 69, N2 = 75)	37.3 (34.1)	58.5 (32.0)	<0.001
Nonbinary (N = 51, N1 = 29, N2 = 22)	54.0 (29.7)	52.0 (31.4)	0.742

MI-B, brief motivational interviewing; N, overall sample size; N1, iTAB sample size; N2, iTAB + MI-B sample size.

grading criteria.[18] Six participants had suicidal ideation, 2 of whom were hospitalized for treatment. Other grade 3 or higher events included throat infection, major depression, surgical site infection, ankle fracture, postoperative wound infection, cannabinoid hyperemesis syndrome, thrombophlebitis, and chest pain. There were no differences of adverse events by study arm.

HIV and STI Incident Cases

Two HIV seroconversions occurred during this study, 1 in each arm, associated with poor adherence. Absolute CD4 count for the participants who seroconverted was 1056 cells/mm^3 and 620 cells/mm^3, and viral loads were 5840 copies/mL and 46,437 copies/mL. Both participants were transgender women who reported intermittent PrEP use with gaps in adherence between 10 and 14 days. One patient had M184V, and the other patient had M184V, K70E, and E138A detected by GenosureMG. New STI diagnoses were found in 22 of 127 (17.3%) in the iTAB arm and 18 of 128 (16.4%) in the iTAB + MI arm ($P = 0.44$).

TABLE 3. Multivariable Model for TFV-DP ≥ 1246 fmol/punch

	OR	OR Lower	OR Upper	χ^2	*P*
Age	1.018	0.988	1.048	1.31	0.253
Transgender man	1.650	0.803	3.388	1.86	0.394
Nonbinary/sex nonconforming	1.233	0.598	2.540		
Non-Hispanic Black	0.346	0.123	0.977	6.67	0.155
Non-Hispanic mixed race	0.878	0.289	2.660		
Race/Ethnicity Hispanic	0.721	0.365	1.426		
Race/Ethnicity Other	1.373	0.596	3.166		
STI Dx past 12 mo	0.384	0.164	0.899	4.86	0.027
Transactional sex past 12 mo	0.399	0.175	0.912	4.74	0.029
iTAB + MI-B Arm	1.095	0.636	1.885	0.11	0.743

MI-B, brief motivational interviewing; OR, odds ratio.

DISCUSSION

Adherence to HIV PrEP in transgender individuals was found to be low in the original iPrEx study resulting in no effect on HIV prevention in that study.[19] In this a demonstration project of PrEP in transgender individuals 63 of 185 (43%) were retained over 12 months and of those continuing on PrEP those maintaining effective adherence (TFV-DP DBS ≥ 700 fmol/punch) over that time varied by sex identity with 58% of retained transgender women staying adherent but as low as 34% for nonbinary individuals.[20] These results suggest that improvement in retention and adherence among transgender individuals is needed to maximize benefit for PrEP. There have been a number of platforms developed that use mHealth to improve adherence to PrEP.[21] These mHealth interventions have used a combination of components of social networking, diaries, education, gamification, and notifications with some showing adherence improvement in randomized controlled trials. With a multicomponent mHealth tool, 1 study found an increase of 15% to achieve adequate PrEP adherence at some point over 48 weeks.[8] In our 48-week, randomized, controlled trial, we enrolled a cohort of TGNB with HIV risk to assess whether telephone delivered brief MI

TABLE 4. Multivariable Model for TFV-DP ≥ 719 fmol/punch

	OR	OR Lower	OR Upper	χ^2	*P*
Age	1.010	0.981	1.039	0.45	0.503
Transgender man	1.396	0.688	2.834	0.94	0.624
Nonbinary/sex nonconforming	1.022	0.511	2.043		
Non-Hispanic Black	0.304	1.117	0.789	9.54	0.049
Non-Hispanic mixed race	0.668	0.229	1.950		
Race/Ethnicity Hispanic	0.715	0.370	1.380		
Race/Ethnicity Other	1.420	0.620	3.254		
STI Dx past 12 mo	0.626	0.307	1.274	1.67	0.196
Transactional sex past 12 mo	0.492	0.242	0.999	3.85	0.050
iTAB + MI-B Arm	1.380	0.823	2.315	1.49	0.222

MI-B, brief motivational interviewing; OR, odds ratio.

with personalized daily text messaging (iTAB + MI) improved PrEP adherence to TDF/FTC over iTAB only. Using a composite end point, iTAB + MI did not significantly improve rates of near-perfect adherence or adequate adherence by TFV-DP levels; however, iTAB + MI did improve a secondary outcome of self-reported adherence of daily text reporting by around 10% when including the entire cohort and 20% specifically for transgender women. Most, if not all, of the effect of improved self-reported adherence were among transgender women. There was also a 16% increase in the composite outcome of adequate adherence only among transgender women, but statistical significance was not reached. This may have reached significance if the sample size for transgender women had been greater, but no predetermined sample for any specific sex group had been planned to maximize inclusivity. These findings, while not definitive, may have implications on methods to improve adherence to oral PrEP in transgender women using mHealth tools. It is important to also note even with this intervention that there were still disparities in adherence related to key risk factors for HIV including race (non-Hispanic Black), substance use, and history of STIs. These individuals may need additional mHealth features to bring adherence to the levels of their transgender peers.

A strength of this study was that it was specifically designed for TGNB individuals and includes not only transgender women but also transgender men and nonbinary individuals. Most other studies have combined transgender women with MSM as 1 cohort. Similarly, few interventions are adapted for transgender individuals as was performed in this study. Our data suggest that further refinement of research and interventions for TGNB individuals is needed. Our qualitative work found that barriers to PrEP in transgender individuals are multifactorial and include competing health conditions (mental health and substance use), social conditions (housing insecurity and transportation), concerns over interactions with hormones, stigma of taking PrEP, negative health care experiences, and mistrust of providers.[22,23]

It is unclear why the intervention was effective for transgender women but not transgender men or nonbinary individuals. Among sex identities, transgender women had the lowest adequate adherence within the iTAB control arm, suggesting they were less adherent than transgender men and nonbinary individuals to begin with. Of note, directly observed dosing studies found higher TFV-DP levels in transgender men compared with transgender women due in part to renal function.[24] This could partly explain the higher proportions of transgender men who met the adherence thresholds. The increase in adequate adherence that was achieved with the addition of MI brought adherence rates for transgender women closer to the other cohorts on this study. However, which component of the MI helped to improve adherence among transgender women is yet to be determined. A telephone contact from another person alone may be important enough to motivate dose taking among transgender women because many did not actually complete the MI interaction. Although there was no difference in MI session attendance by sex identity, there could be a difference in how individuals reacted to a telephone contact or MI session resulting in changes in adherence behaviors. Further research is needed to understand what components of this intervention were most influential.

Limitations of this study include that we were intentionally inclusive, which led to potential heterogeneity between sex identities for their perceived and actual HIV risk. Compared with our previous studies with MSM, the baseline HIV prevalence and STI rates were lower, suggesting a lower overall HIV risk of this cohort. Our previous work has found that those with higher HIV risk behaviors have better adherence.[25] This could account for some of the somewhat lower adherence seen in this study, but there may be many other contributing factors for transgender individuals to adherence that need to be further analyzed. The MI intervention was delivered through phone by 1 coordinator to all study sites to be cost-effective and to ensure fidelity. However, this meant that there may have been less of a personal connection than if each site had a local MI provider and the low uptake of completed MI sessions. Although our MI was low intensity, additional studies of personnel burden are needed to determine the overall cost benefit if MI was to be integrated into an mHealth approach for PrEP adherence. There was also some heterogeneity of study sites by how engaged they were in transgender care. Some sites were primary providers of transgender affirming care. Other study sites were not providers of transgender affirming care but did employ transgender individuals as study coordinators, which was vital for success in enrollment and creating trust within the community. Finally, there was considerable drop out in this study where 41.6% of participants did not complete week 48. However, this retention rate is on par or better than in a similar study where 57% did not complete a year on study.[8]

In summary, iTAB daily texting with brief MI compared with iTAB alone improved self-reported adherence and helped transgender women achieve adequate adherence to TFV/FTC through 48 weeks of follow-up. Transgender women may benefit from targeted adherence support where there is person-to-person contact in addition to automated methods such as texting or mobile applications.

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