Factors associated with the uptake of and adherence to HIV pre-exposure prophylaxis in people who have injected drugs: an observational, open-label extension of the Bangkok Tenofovir Study

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Summary

Background—Results of the randomised, double-blind, placebo-controlled Bangkok Tenofovir Study (BTS) showed that taking tenofovir daily as pre-exposure prophylaxis (PrEP) can reduce the risk of HIV infection by 49% in people who inject drugs. In an extension to the trial, participants were offered 1 year of open-label tenofovir. We aimed to examine the demographic characteristics, drug use, and risk behaviours associated with participants' uptake of and adherence to PrEP.

Methods—In this observational, open-label extension of the BTS (NCT00119106), non-pregnant, non-breastfeeding, HIV-negative BTS participants, all of whom were current or previous injecting drug users at the time of enrolment in the BTS, were offered daily oral tenofovir (300 mg) for 1 year at 17 Bangkok Metropolitan Administration drug-treatment clinics. Participant demographics, drug use, and risk behaviours were assessed at baseline and every 3 months using an audio computer-assisted self-interview. HIV testing was done monthly and serum creatinine was assessed every 3 months. We used logistic regression to examine factors associated with the decision to take daily tenofovir as PrEP, the decision to return for at least one PrEP follow-up visit, and greater than 90% adherence to PrEP.

Findings—Between Aug 1, 2013, and Aug 31, 2014, 1348 (58%) of the 2306 surviving BTS participants returned to the clinics, 33 of whom were excluded because they had HIV (n=27) or grade 2–4 creatinine results (n=6). 798 (61%) of the 1315 eligible participants chose to start open-label PrEP and were followed up for a median of 335 days (IQR 0–364). 339 (42%) participants completed 12 months of follow-up; 220 (28%) did not return for any follow-up visits. Participants who were 30 years or older (odds ratio [OR] 1·8, 95% CI 1·4–2·2; p<0·0001), injected heroin (OR 1·5, 1·1–2·1; p=0·007), or had been in prison (OR 1·7, 1·3–2·1; p<0·0001) during the randomised

trial were more likely to choose PrEP than were those without these characteristics. Participants who reported injecting heroin or being in prison during the 3 months before open-label enrolment were more likely to return for at least one open-label follow-up visit than those who did not report injecting heroin (OR 3·0, 95 % CI 1·3–7·3; p=0·01) or being in prison (OR 2·3, 1·4–3·7; p=0·0007). Participants who injected midazolam or were in prison during open-label follow-up were more likely to be greater than 90% adherent than were those who did not inject midazolam (OR 2·2, 95% CI 1·2–4·3; p=0·02) or were not in prison (OR 4·7, 3·1–7·2; p<0·0001). One participant tested positive for HIV, yielding an HIV incidence of 2·1 (95% CI 0·05–11·7) per 1000 person-years. No serious adverse events related to tenofovir use were reported.

Interpretation—More than 60% of returning, eligible BTS participants started PrEP, which indicates that a substantial proportion of PWID who are knowledgeable about PrEP might be interested in taking it. Participants who had injected heroin or been in prison were more likely to choose to take PrEP, suggesting that participants based their decision to take PrEP, at least in part, on their perceived risk of incident HIV infection.

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Introduction

One in ten of the 2 million new HIV infections in 2014[1] was probably caused by injection drug use, and more than 80% of all HIV infections in some countries of eastern Europe and central Asia are related to drug use.[2]

The Bangkok Tenofovir Study (BTS) was a randomised, double-blind, placebo-controlled, HIV pre-exposure prophylaxis (PrEP) trial, assessed in people who inject drugs (PWID) in Bangkok during 2005–12.[3] The trial showed that taking tenofovir disoproxil fumarate (tenofovir) daily can reduce the risk of HIV infection by 49% (95% CI 9·6–72·2) in PWID. On the basis of results of BTS,[3] as well as PrEP trials in men who have sex with men[4] and heterosexual men and women,[5,6] the US Public Health Service,[7] WHO,[8] and the Thailand Ministry of Public Health[9] have published guidelines for the use of PrEP to prevent HIV infections.

Following the publication of the BTS randomised trial results,[3] and consistent with the study protocol, participants were offered 1 year of daily tenofovir for HIV PrEP, and were followed-up in an open-label extension to the trial. During the randomised, placebo-controlled trial, we told participants that we did not know whether they were taking tenofovir or placebo, and that even if they were taking tenofovir, we did not know whether it would prevent HIV infection. During the open-label follow-up, we told participants that tenofovir, if taken daily in combination with other HIV prevention strategies, could reduce their risk of HIV infection.

The objectives of this open-label extension to the trial were to examine demographic characteristics, drug use, and risk behaviours of BTS participants who chose to take daily open-label tenofovir to identify factors associated with the decision to take daily tenofovir as

PrEP, the decision to return for at least one open-label PrEP follow-up visit, and greater than 90% adherence to open-label PrEP.

Methods

Study design and participants

The randomised, double-blind, placebo-controlled trial (BTS) and the observational, open-label 1-year extension were done in HIV-negative people who were aged 20–60 years at BTS enrolment and who had injected drugs in the year preceding BTS enrolment, at 17 Bangkok Metropolitan Administration (BMA) drug-treatment clinics in densely populated urban communities of Bangkok. At the end of the randomised BTS, study drug (placebo or tenofovir) was stopped while the data were analysed. Study staff attempted to contact BTS participants with information provided by participants at least once every 3 months after the randomised trial was completed to tell them about study progress, when results were expected, and to update contact information. After the publication of the BTS results in 2013,[3] staff contacted participants and asked them to return to the clinic to hear about the results and to be told whether they had received tenofovir or placebo during the trial. All non-pregnant, non-breastfeeding, HIV-uninfected BTS participants who did not have grade 2, 3, or 4 creatinine results during the randomised trial were offered daily oral tenofovir (300 mg) for 1 year, free of charge, at the 17 BMA drug-treatment clinics. Tenofovir was also provided to imprisoned participants within prisons. Study staff met with officials from the Thailand Department of Correction before initiation of the randomised trial and open-label extension to discuss the study and request permission and assistance to offer imprisoned participants the study drug during the randomised trial and daily tenofovir during the open-label extension. Study staff worked with prison medical staff to identify a private space in the prison medical clinic for participants to complete study activities. At study visits during the open-label extension staff asked participants whether they would like to continue to receive PrEP or to stop. Participants took tenofovir in the clinics or the prisons; tenofovir was not given to participants to take at home.

Ethical review committees of the BMA and the Thailand Ministry of Public Health and the US Centers for Disease Control and Prevention (CDC) Institutional Review Board approved the BTS protocol, including the open-label extension. Volunteers meeting all eligibility criteria could enrol after providing written informed consent.

Procedures

At open-label enrolment and monthly visits (we defined months as 28 days) over a period of up to 1 year, we assessed participants for adverse events, provided individualised adherence and risk-reduction counselling, tested participants' oral fluid for HIV antibodies (OraSure Technologies Inc, Bethlehem, PA, USA), and female participants had urine pregnancy tests (ULTI Med Products, Ahrensburg, Germany). Participants signed a tenofovir adherence diary on the days that they came to the clinic to take tenofovir; clinic staff marked the days that participants did not return. These data were used to assess adherence and follow-up. Participants completed a risk behaviour assessment of injection drug use, sexual activity, and incarceration in an audio computer-assisted self-interview, every 3 months. We tested

participant blood samples for HIV (enzyme-immunoassay [EIA], Bio-Rad Laboratories, Redmond, WA, USA), and kidney and liver function every 3 months. Participants received 350 baht (about US$9·20) compensation for their time and travel at the 3 month visits. Participants with reactive HIV test results discontinued tenofovir, and infection was confirmed with EIA and western blot (Bio-Rad). Newly infected individuals were referred for care according to national guidelines.[9]

Statistical analyses

We used logistic regression to determine whether participant demographic characteristics, drug use, or risk behaviours reported during the randomised trial were associated with the decision to take daily tenofovir as PrEP during the open-label extension, whether risks during the 3 months before the PrEP open-label enrolment visit were associated with returning for at least one PrEP open-label follow-up visit, and whether risks reported during PrEP open-label follow-up were associated with greater than 90% adherence.[10] Variables with a p value of less than 0·15 in the bivariable analysis were assessed in a multivariable model. We assessed the fit of the logistic models with the Hosmer-Lemeshow goodness-of-fit test. We defined adherence as the number of days, recorded in the tenofovir adherence diary, that the participant took tenofovir divided by the number of days that the participant was followed up, expressed as a percentage. We chose 90% adherence because data from PrEP trials suggest a high level of adherence is associated with protection from HIV infection.[3,4,6,11,12] HIV incidence and exact 95% Poisson CIs were calculated per 1000 person-years of HIV-negative observation. Spearman's correlation coefficient was used to assess the association between adherence to study drug in the randomised trial and adherence to tenofovir in the open-label follow-up.[10] We used generalised estimating equations logistic regression to model trends in participant reports of injecting drugs, sharing needles, incarceration, and sexual activity.[13]

We used SAS version 9.3 for statistical analyses. The BTS is registered with ClinicalTrials.gov, number NCT0011910G.

Role of the funding source

Staff from the CDC participated in study design, data collection, data analysis, data interpretation, and writing of the report. The corresponding author had full access to all the data in the study and final responsibility for the decision to submit for publication.

Results

Follow-up of BTS participants in the randomised trial was completed on June 8, 2012, and trial results were announced on June 13, 2013. From Aug 1, 2013, to Aug 31, 2014, 1348 (58%) of the 230G surviving BTS participants returned to the clinics to discuss BTS results with staff and decided whether or not to take daily tenofovir as HIV PrEP in the open-label extension. Participants who returned were older (526 [51%] of 1033 aged <30 years *vs* 822 [60%] of 1380 aged 30 years; p<0·0001), more likely to have injected drugs (723 [52%] of 1399 who did not inject *vs* 625 [62%] of 1014 who injected; p<0·0001), and more likely to have been imprisoned (699 [49%] of 1420 who were not imprisoned *vs* G49 [G5%] of 993

who were imprisoned; p<0·0001) during the randomised trial than were participants who did not return. Of the 1348 participants who returned, 27 (2%) had tested positive for HIV and six (<1%) had grade 2, 3, or 4 creatinine results during the randomised trial and were not eligible for the open-label tenofovir extension. Of the 1315 eligible BTS participants, 798 (61%) chose to start taking open-label tenofovir. The median age of participants who started PrEP in the open-label extension was 39 years (IQR 35–47) and 640 (80%) were men. In multivariable analysis, older participants (odds ratio [OR] 1·8; 95% CI 1·4–2·2), those who had injected heroin during the randomised trial, and those who had been in prison during the randomised trial were more likely to choose PrEP than those who did not share these characteristics (table 1).

Of the 798 BTS participants who chose to start open-label PrEP, five (1%) tested positive for HIV and were referred for care. On the basis of the date of the final HIV test in the randomised trial, HIV incidence was estimated to be 3·6 (95% CI 1·2–8·3) per 1000 person-years in the 798 participants re-tested for HIV at the start of open-label extension.

The 793 HIV-negative BTS participants who chose to start open-label tenofovir were followed up for a median of 335 days (IQR 0–364). 220 (28%) participants did not return for any of the follow-up visits. In the multivariable analysis, participants who reported injecting heroin or being in prison during the 3 months before open-label enrolment were more likely to return for at least one follow-up visit than those who did not report injecting heroin or being in prison (table 2).

The 573 participants who returned for at least one open-label follow-up visit contributed 474 person-years of follow-up; 67 (12%) completed 3 months of follow-up, 38 (7%) completed 3–6 months, 37 (6%) completed 6–9 months, and 431 (75%) completed 9–12 months (figure). Adherence data from three participants was missing. On the basis of adherence diaries of the remaining 570 participants, participants took tenofovir for a mean of 38·5% (SD 41·3) of the days that they were followed up. 267 (47%) of 570 participants took tenofovir for 10% or less of the days in follow-up, and 143 (25%) took tenofovir for greater than 90% of the days in follow-up; these two groups accounted for 72% (410 of 570) of the participants in follow-up who returned for at least one visit. In the multivariable analysis, tenofovir adherence on more than 90% of the days in follow-up was more likely in male versus female participants, those who injected midazolam versus those who did not, and those who had been (or were) in prison versus those who had (or were) not (table 3). Participants who reported sex with a casual partner were less likely to take tenofovir on more than 90% of follow-up days than those who did not report sex with casual partners (table 3). We did not find a correlation between adherence to study drug during the randomised trial and adherence to tenofovir during the open-label follow-up (Spearman correlation coefficient r=0·03; data not shown).

Drug use and risk behaviour data were available for 780 (98%) of the 793 HIV-negative participants who chose to start open-label tenofovir, 153 (20%) of whom reported injecting drugs during the 3 months before open-label extension enrolment (91 [59%] injected midazolam, 62 [41%] injected heroin, and 47 [31%] injected methamphetamine); 16 (10%) of these 153 participants reported sharing needles. Of the 339 participants (43%) who

completed the 12 month open-label visit, the number of participants injecting drugs and sharing needles did not change significantly during follow-up (table 4). The proportion of participants who were incarcerated (ie, in jail or in prison) during follow-up significantly declined, as did the proportion who injected methamphetamine, and the proportion reporting sexual activity with more than one sexual partner or sex with a casual partner (table 4).

One participant tested positive for HIV (at the 4 month visit) during open-label follow-up, yielding an HIV incidence of 2·1 (95% CI 0·05–11·7) per 1000 person-years among the 793 participants. The participant took tenofovir for 30 (23%) of 129 days that they were followed up and had not taken tenofovir during the G0 days before the reactive HIV test.

Six participants died during the open-label extension study: three from respiratory and circulatory failure, one from drug overdose, one from a femoral artery haemorrhage, and one from a skull fracture caused by an assault. Eleven participants were admitted to hospital: four for gastrointestinal issues, two for drug-use related causes, and one each for assault-related injuries, cataract replacement, fatigue, a hernia, and an infection. No serious adverse events related to tenofovir use were reported, and there were no reports of renal or hepatic injury or grade 3 or 4 creatinine results.

Discussion

We offered daily tenofovir as PrEP to participants of the randomised, placebo-controlled BTS[3] at drug-treatment clinics and prisons for 1 year after the trial was completed. 798 BTS participants, 35% of all surviving participants and 61% of those who returned and were eligible, chose to start taking daily PrEP. Older participants and participants who had injected heroin or been in prison during BTS were more likely to choose to take PrEP than were younger participants or those who did not report heroin use or incarceration in prison. Similarly, participants who reported injecting heroin or had been in prison during the 3 months before open-label enrolment were more likely to return for at least one open-label follow-up visit than those who did not report heroin use or incarceration in prison. Both injecting drugs and incarceration have been associated with HIV infection in PWID in Bangkok,[14–16] suggesting that participants based their decision to take or not take PrEP, at least in part, on their perceived risk of incident HIV infection. Of participants who returned for at least one follow-up visit, 25% were more than 90% adherent to PrEP.

Participants who returned for at least one follow-up visit who reported injecting midazolam during open-label follow-up were more likely to be greater than 90% adherent than those who did not inject midazolam. Why people who injected midazolam would be more adherent than those who did not is unclear. Participants who injected midazolam in the BTS were not more likely to become infected with HIV than those who did not,[15] but they were more likely to die.[17] Perhaps participants recognised their risk-taking behaviours and chose to take PrEP to prevent HIV infection. Participants who were imprisoned during open-label follow-up were more likely to be more than 90% adherent than those who were not imprisoned. These participants might have perceived themselves to be at risk of HIV and decided to take daily PrEP. Additionally, tenofovir was made available in prison clinics, easing access, which might have encouraged adherence.

Participants who reported sex with casual partners were less adherent than those who did not report casual sex. Reporting sex with a live-in or a casual partner was not associated with HIV infection during the randomised trial,[15] and a previous study in PWID in the same clinics as those used in the BTS found that participants who reported having sex were less likely to become HIV infected than those who did not have sex.[14] Participants who reported casual sex might have perceived their risk of HIV infection as low; however, PrEP reduces sexual HIV transmission[4–6] and HIV prevention counselling to inform PWID of sexual HIV risks, in addition to injecting and needle sharing risks, might be useful.

Overall, daily adherence to tenofovir in this open-label extension of the BTS, even in the 570 participants who returned for at least one follow-up visit and for whom we had adherence data, was low (participants took tenofovir an average of 38·5% of the days that they were followed up) and lower than that observed in the randomised trial that preceded it (ie, based on study drug diaries, participants took the study drug [either tenofovir or placebo] an average of 83·8% of days in the randomised trial). This difference in adherence might be related to compensation that participants received for study visits: participants received 70 baht (US$2) for each day they came to clinic and 350 baht (US$10) for each monthly visit in the randomised trial, and only 350 baht for each 3-monthly visit in the open-label follow-up. Adherence might also have been related to participants' self-assessed risk of HIV infection. Reports of injecting and sharing needles declined substantially during the randomised trial; 63% of participants reported injecting drugs during the 3 months before enrolment in the randomised trial compared with 17·5% at the end of the study (month 72); 18% reported sharing needles at enrolment compared with 1% at month 72.[15] In BTS participants who chose to take tenofovir in the open-label extension (who completed the 12-month open-label visit), reports of injecting drugs and sharing needles did not increase during follow-up; the proportion who were injecting drugs (ranging from 20% at month 12 to 23% at enrolment) and sharing needles (ranging from <1% at month 6 to 2% at month 12) was similar to the proportion injecting and sharing at the end of the randomised trial (ie, at 72 months).[15] Of the 570 participants who returned for at least one follow-up visit, the 267 (47%) participants who took tenofovir on 10% or less of the days that they were followed up might have correctly determined that they were not at risk of HIV infection, and the 160 (28%) participants who took daily tenofovir on 11–90% of the days they they were followed up might have opted to stop taking tenofovir during periods when they were not at risk for HIV infection.

One participant who opted to take tenofovir in this open-label extension became infected with HIV, yielding an HIV incidence of 2·1 (95% CI 0·05–11·7) per 1000 person-years, similar to the incidence in tenofovir recipients during the randomised trial (3·5 per 1000 person-years).[3] The participant who became infected had not taken a dose of tenofovir for 2 months before testing positive for HIV. An open-label extension study that included participants from the iPrEx study, a PrEP trial in men who have sex with men, also found a low HIV incidence in adherent participants: 5·6 (95% CI 0·0–25·0) per 1000 person-years if drug concentrations were consistent with use of two to three tablets a week, and 0·0 (95% CI 0·0–6·1) per 1000 person-years with four or more tablets per week.[18]

This study has several limitations. Our assessment of factors associated with PrEP use was limited to factors included in the BTS risk behaviour questionnaire. A more detailed assessment of factors motivating PrEP use and adherence would require additional research. Participants might have under-reported stigmatised and illegal behaviours such as injecting drugs.[19] However, the illegality and stigma associated with these activities did not change during follow-up, so rates of under-reporting should have remained constant. Participants were followed up in drug-treatment clinics and prisons and were required to come to the clinics if they wanted to receive tenofovir; a supply of tenofivir was not given to the participants to take home. Adherence might differ if other distribution methods are used. Adherence might also differ if more or less compensation is provided.

Four large randomised, placebo-controlled trials have shown that a daily dose of tenofovir or tenofovir–emtricitabine (ie, HIV PrEP) can reduce sexual and parenteral HIV transmission,[3–6] and reports suggest that interest in and use of PrEP might be increasing.[20,21] Adherence is a key factor for PrEP effectiveness.[12,22] These trials, and our experience with this open-label extension study in PWID, highlight the need for tools to help people using PrEP achieve effective levels of adherence.[23–25] Additional work is also needed to understand the appropriate place for PrEP in a package of services to reduce HIV transmission and other harms in PWID.[26–28]

In this observational, open-label follow-up to a randomised trial, we offered daily oral HIV PrEP with tenofovir to PWID in drug-treatment clinics and prisons in Bangkok. Although overall adherence was low, 25% of participants who returned for at least one open-label follow-up visit were more than 90% adherent and 59% returned for the 12-month visit. The US Centers for Disease Control and Prevention[7] and WHO[8] recommend PrEP for people at substantial risk of acquiring HIV. Our results suggest that PWID can assess their risk of HIV infection and appropriately decide whether or not to take PrEP. PrEP should be offered to people who inject drugs as an important part of an HIV prevention package.

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Research in context

Evidence before this study

On May 1, 2016, we searched PubMed for studies assessing HIV pre-exposure prophylaxis (PrEP) in people who inject drugs (PWID). We used the search terms "pre-exposure prophylaxis HIV" and "people who inject drugs". We did not apply any language restrictions. The Bangkok Tenofovir Study report was the only randomised clinical trial published and we did not find any open-label or implementation science PrEP studies in PWID. The Bangkok Tenofovir Study, a randomised, double-blind, placebo-controlled trial in PWID during 2005–12, showed that taking tenofovir disoproxil fumarate (tenofovir) daily can reduce the risk of HIV infection by 49%.

Added value of this study

To our knowledge, this is the first assessment of the open-label use of HIV PrEP in PWID. More than 60% of eligible participants who returned to the clinics to discuss the trial results chose to start open-label PrEP. Participants who had injected heroin or been in prison were more likely to choose to take PrEP than those who had not, suggesting that participants based their decision, at least in part, on their perceived risk of incident HIV infection. No HIV infections occurred in participants adherent to daily tenofovir.

Implications of all the available evidence

Our results suggest that PWID can assess their risk of HIV infection and appropriately decide whether or not to take PrEP. PrEP should be offered to PWID as an important part of an HIV prevention package.
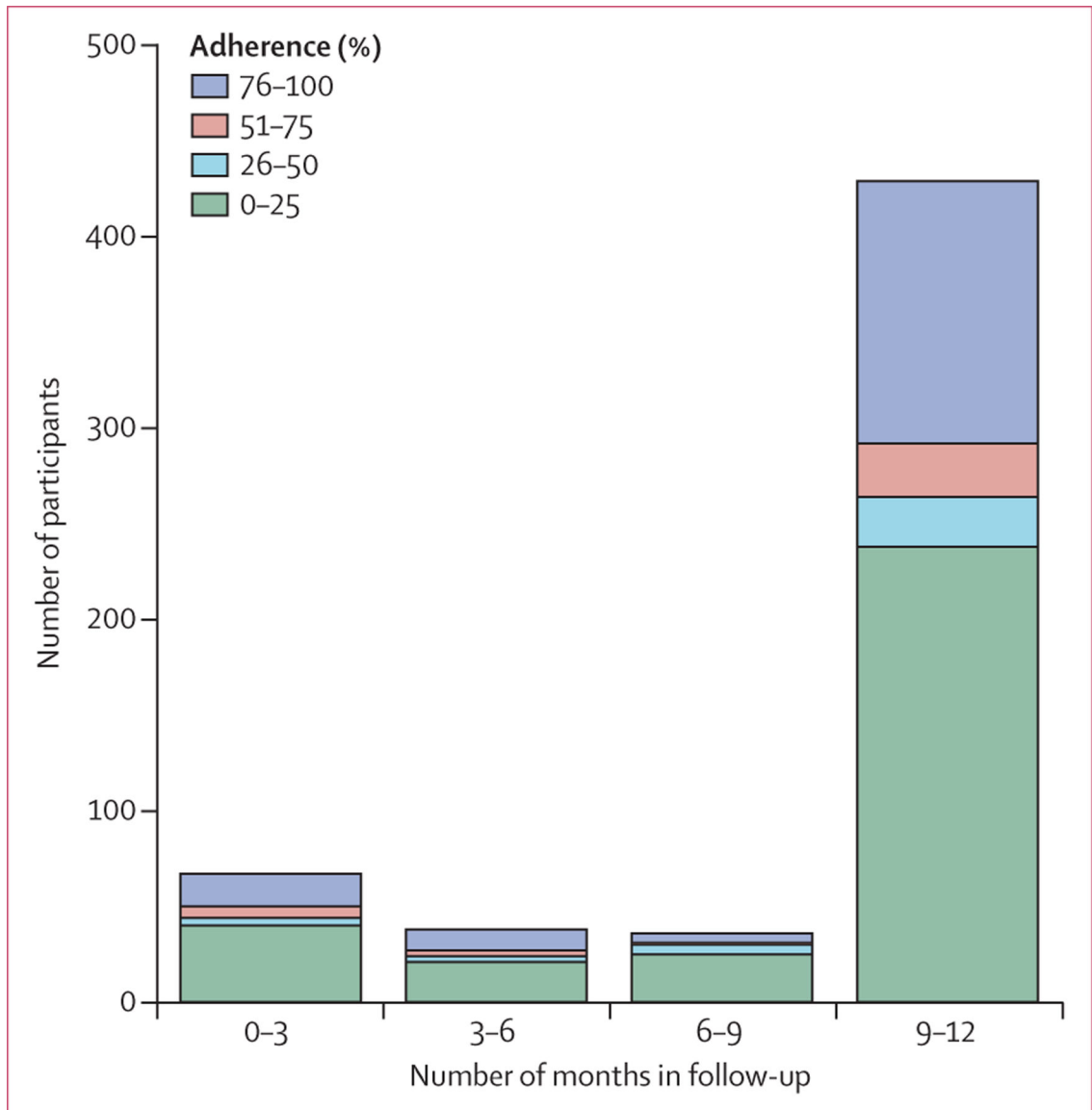
Figure: Length of follow-up in participants in the open-label extension of the Bangkok Tenofovir Study who returned for at least one visit (n=570)*, according to adherence to open-label tenofovir

Adherence is number of days participant took open-label tenofovir divided by number of days participant was followed up. *Excludes three patients for whom adherence data were missing.

Table 1:

Logistic regression analysis of behaviours during the BTS as predictors of starting open-label tenofovir in the extension study, in all participants eligible for the extension study

	Total (N=1315)	Chose to take tenofovir (n=798)*	Bivariable analysis		Multivariable analysis	
			Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
General characteristics						
Sex						
Female	274	158 (58%)	1	··	··	··
Male	1041	640 (61%)	1·2 (0·9–1·5)	0·25	Not included	NA
Age at BTS enrolment						
20–29 years	509	269 (53%)	1	··	1	··
30–59 years	806	529 (66%)	1·7 (1·4–2·1)	<0·0001	1·8 (1·4–2·2)	<0·0001
Education						
grade 6	648	401 (62%)	1	··	··	··
>grade 6	667	397 (60%)	0·9 (0·7–1·1)	0·38	Not included	NA
Behaviours during the BTS						
Injected any drugs						
No	711	399 (56%)	1	··	··	··
Yes	604	399 (66%)	1·5 (1·2–1·9)	0·0002	Not included [†]	NA
Injected heroin						
No	990	570 (58%)	1	··	1	··
Yes	325	228 (70%)	1·7 (1·3–2·3)	<0·0001	1·5 (1·1–2·1)	0·007
Injected methamphetamine						
No	924	539 (58%)	1	··	1	··
Yes	391	259 (66%)	1·4 (1·1–1·8)	0·007	1·1 (0·8–1·4)	0·72
Injected midazolam						
No	970	583 (60%)	1	··	··	··
Yes	345	215 (62%)	1·1 (0·9–1·4)	0·47	Not included	NA
Shared needles						
No	1140	677 (59%)	1	··	1	··
Yes	175	121 (69%)	1·5 (1·1–2·2)	0·01	1·0 (0·7–1·6)	0·83
In prison						
No	684	375 (55%)	1	··	1	··
Yes	631	423 (67%)	1·7 (1·3–2·1)	<0·0001	1·7 (1·3–2·1)	<0·0001
Sex with a casual partner						
No	452	259 (57%)	1	··	1	··
Yes	863	539 (62%)	1·2 (1·0–1·6)	0·07	1·2 (0·9–1·5)	0·16

BTS=Bangkok Tenofovir Study. NA=not applicable.

[*] Proportions in this column are out of the denominator listed in the Total column.

[†] Not included in the multivariable analysis because it correlated closely with the injection of heroin, methamphetamine, or midazolam.

Table 2:

Logistic regression analysis of behaviours during the 3 months before enrolment in the open-label extension study as predictors of returning for at least one follow-up visit, in HIV-negative participants who chose to start open-label tenofovir

	Total	Returned for at least one visit (n=573)[*]	Bivariable analysis		Multivariable analysis	
			Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
General characteristics (N=793)						
Sex						
Female	156	108 (69%)	1	··	··	··
Male	637	465 (73%)	1·2 (0·8–1·8)	0·35	Not included	NA
Age at BTS enrolment						
20–29 years	267	184 (69%)	1	··	1·0	··
30–59 years	526	389 (74%)	1·3 (0·9–1·8)	0·13	1·3 (0·9–1·8)	0·18
Education						
grade 6	397	286 (72%)	1	······		
>grade 6	396	287 (72%)	1·0 (0·8–1·4)	0·89	Not included	NA
Behaviours during the 3 months before open-label enrolment (N=780)[†]						
Injected any drugs						
No	627	439 (70%)	1	··	··	··
Yes	153	125 (82%)	1·9 (1·2–3·0)	0·004	Not included[‡]	NA
Injected heroin						
No	718	509 (71%)	1	··	1	··
Yes	62	55 (89%)	3·2 (1·5–7·2)	0·003	3·0 (1·3–7·3)	0·01
Injected methamphetamine						
No	733	524 (71%)	1	··	1	··
Yes	47	40 (85%)	2·3 (1·0–5·2)	0·04	1·7 (0·7–4·0)	0·24
Injected midazolam						
No	689	491 (71%)	1	··	1	··
Yes	91	73 (80%)	1·6 (1·0–2·8)	0·07	1·0 (0·6–1·9)	0·93
Shared needles						
No	764	549 (72%)	1	··	1	··
Yes	16	15 (94%)	5·9 (0·8–44·7)	0·05	3·2 (0·4–25·6)	0·27
In prison						
No	636	444 (70%)	1	··	1	··
Yes	144	120 (83%)	2·2 (1·4–3·5)	0·001	2·3 (1·4–3·7)	0·0007
Sex with a casual partner						
No	616	449 (73%)	1	··	··	··
Yes	164	115 (70%)	0·9 (0·6–1·3)	0·48	Not included	NA

BTS=Bangkok Tenofovir Study. NA=not applicable.

[*] Returned for at least one of 13 follow-up visits during the open-label extension; proportions in this column are out of the denominator listed in the Total column.

†Behaviour data missing for 13 participants.

‡Not included in the multivariable analysis because it correlated closely with the injection of heroin, methamphetamine, or midazolam.

Table 3:

Logistic regression analysis of behaviours during open-label extension as predictors of >90% adherence to open-label tenofovir, in participants who returned for at least one open-label follow-up visit

	Total	(N=573)	Adherence >90% (n=143)[*]		Bivariable analysis	
			Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
General characteristics						
Sex						
Female	108	15 (14%)	1	··	1	··
Male	465	128 (28%)	2·4 (1·3–4·2)	0·003	1·9 (1·0–3·6)	0·04
Age at BTS enrolment						
20–29 years	184	46 (25%)	1	··	··	··
30–59 years	389	97 (25%)	1·0 (0·7–1·5)	0·99	Not included	NA
Education						
<grade 6	286	64 (22%)	1	··	··	··
>grade 6	287	79 (28%)	1·3 (0·9–1·9)	0·16	Not included NA	
Behaviours during open-label extension						
Injected any drugs						
No	422	104 (25%)	1	··	··	··
Yes	151	39 (26%)	1·1 (0·7–1·6)	0·77	Not included [†]	NA
Injected heroin						
No	491	117 (24%)	1	··	1	··
Yes	82	26 (32%)	1·5 (0·9–2·5)	0·13	1·2 (0·6–2·5)	0·56
Injected methamphetamine						
No	514	133 (26%)	1	··	1	··
Yes	59	10 (17%)	0·6 (0·3–1·2)	0·13	0·5 (0·2–1·0)	0·06
Injected midazolam						
No	480	112 (23%)	1	··	1	··
Yes	93	31 (33%)	1·6 (1·0–2·7)	0·04	2·2 (1·2–4·3)	0·02
Shared needles						
No	543	137 (25%)	1	··	··	··
Yes	30	6 (20%)	0·7 (0·3–1·9)	0.52	Not included	NA
In prison						
No	417	70 (17%)	1	····	1	··
Yes	156	73 (47%)	4·4 (2·9–6·5)	<0·0001	4·7 (3·1–7·2)	<0·0001
Sex with a casual partner						
No	401	116 (29%)	1	··	1	··
Yes	172	27 (16%)	0·5 (0·3–0·7)	0·0008	0·5 (0·3–0·8)	0·002

BTS=Bangkok Tenofovir Study. NA=not applicable.

[*] Proportions in this column are out of the denominator listed in the Total column.

[†] Not included in the multivariable analysis because it correlated closely with the injection of heroin, methamphetamine, or midazolam.

Table 4:

Behaviours reported by participants in the open-label extension of the Bangkok Tenofovir Study, in participants who completed the 12-month open-label visit

	Open-label extension study visit					p value
	Enrolment (n=336)	Month 3 (n=290)	Month 6 (n=287)	Month 9 (n=286)	Month 12 (n=339)	
Injected drugs in previous 3 months						
Injected drugs	78 (23%)	64 (22%)	62 (22%)	64 (22%)	68 (20%)	0·16
Shared needles	7 (2%)	3 (1%)	1 (<1%)	3 (1%)	8 (2%)	0·79
Injected daily	24 (7%)	22 (8%)	20 (7%)	21 (7%)	27 (8%)	0·67
Drugs injected in previous 3 months						
Heroin	34 (10%)	25 (9%)	28 (10%)	34 (12%)	33 (10%)	0·51
Methamphetamine	24 (7%)	15 (5%)	19 (7%)	13 (5%)	15 (4%)	0·03
Midazolam	49 (15%)	34 (12%)	34 (12%)	39 (14%)	37 (11%)	0·10
Incarceration in previous 3 months						
In jail	60 (18%)	33 (11%)	26 (9%)	22 (8%)	20 (6%)	<0·0001
In prison	70 (21%)	54 (19%)	41 (14%)	50 (17%)	40 (12%)	<0·0001
Sexual activity in previous 3 months						
More than one sexual partner	35 (10%)	26 (9%)	20 (7%)	21 (7%)	19 (6%)	0·006
Sex with casual partner	67 (20%)	40 (14%)	42 (15%)	35 (12%)	43 (13%)	0·002
Men reporting sex with male partner	5/274 (2%)	2/241 (1%)	3/238 (1%)	2/237 (1%)	3/276 (1%)	0·57

Months were defined as 28 days.