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# Development and Evaluation of an Ecological Momentary Assessment–Based mHealth Platform for Monitoring HIV PrEP Adherence

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## Abstract

# Background

Ecological momentary assessment (EMA) enables real-time behavioral monitoring and may reduce recall bias associated with conventional retrospective questionnaires. However, few studies have validated EMA-based adherence monitoring against pharmacologic biomarkers. This study evaluated the accuracy of an EMA-enabled mHealth platform for assessing adherence to oral HIV pre-exposure prophylaxis (PrEP), using dried blood spot (DBS) drug concentrations as the gold standard and traditional questionnaires as a comparator.

# Method

A total of 342 real-world online PrEP users in China were enrolled in the Real-world E-consumers Cohort II of PrEP (RECOPE II) and followed at weeks 6, 12, and 18. The platform used event-triggered sampling for event-driven (ED) PrEP and fixed-interval sampling for daily PrEP to monitor medication adherence. Platform- and questionnaire-based adherence measures were compared with DBS drug concentrations by estimating sensitivity and specificity. Participants who never checked in on the platform, failed to return a DBS sample, or did not complete the corresponding questionnaire were excluded from the accuracy analysis.

# Result

Among the ED users, the prevalence of optimal adherence identified by the platform at week 6, 12, and 18 was 30.0%, 36.4%, and 28.0%, respectively, compared with 42.5%, 43.0%, and 43.2% identified by the questionnaire. Among the daily users, the platform-measured prevalence was 55.9%, 69.6%, and 68.3%, while the corresponding questionnaire-based measures were 84.3%, 81.5%, and 83.3%.When validated against the DBS results among ED users, the platform demonstrated consistently higher specificity than questionnaires at all time points (0.64 vs. 0.63, 0.66 vs. 0.61, and 0.77 vs. 0.63), but lower sensitivity (0.19 vs. 0.53, 0.40 vs. 0.50, and 0.38 vs. 0.58). Similarly, the platform demonstrated higher specificity (0.69 vs. 0.25, 0.59 vs. 0.11, and 0.50 vs. 0.21), but comparable sensitivity (0.65 vs. 0.79, 0.86 vs. 0.78, and 0.86 vs. 0.86) than the questionnaire among the daily users.

# Conclusion

The EMA-based mHealth platform demonstrated consistently higher specificity and comparable sensitivity for daily PrEP users than conventional questionnaires, supporting its validity for real-time adherence monitoring. These findings provide empirical evidence that EMA is a practical and scalable approach for monitoring medication adherence and may have broader applications in assessing health-related behaviors.

## 1. Introduction

The ecological momentary assessment (EMA) is an emerging and increasingly adopted method for real-time behavioral monitoring and just-in-time adaptive interventions. EMA involves repeated, real-time collection of data on individual behaviors and contextual factors in participants' natural environments, typically using smartphone-based technologies and employing sampling strategies such as event-triggered and fixed-interval assessments (Stone & Shiffman, 1994). Compared with conventional retrospective self-report, EMA reduces recall bias and captures behaviors as they occur in natural settings (Shiffman, Stone, & Hufford, 2008). Consequently, EMA has been increasingly applied to behavioral and medication adherence research(Czyz et al., 2023; Kianersi, Parker, Ludema, Agley, & Rosenberg, 2024; Shacham et al., 2019).

Despite its widespread adoption, whether EMA accurately measures real-world behaviors remains largely unknown. Establishing the measurement validity of EMA is essential because inaccurate behavioral measurements may compromise downstream behavioral surveillance, predictive analytics, and just-in-time adaptive interventions. Existing studies have primarily evaluated feasibility, acceptability, or predictive utility rather than measurement validity (Czyz et al., 2023; Gillespie et al., 2022; Shacham et al., 2019; Wray, Kahler, & Monti, 2016). Formal validation studies comparing EMA data with objective reference standards are rare. The existing validation research have been conducted primarily in limited settings such as monitoring sedentary behaviors (using the accelerometry as the gold standard) or alcohol consumption (taking the breathalyzers as the gold standard), where diagnostic performance indicators (e.g. sensitivity and specificity) of the EMA-based technologies have been reported (Bruening et al., 2016; Kianersi et al., 2024; Romanzini et al., 2019). In particular, studies using biomarkers to quantify the diagnostic accuracy of EMA-based tools in assessing medication adherence are scarce, although these tools have already been used in monitoring some medication behaviors (e.g. HIV antiretroviral treatment) (Shacham et al., 2019). Whether EMA can accurately quantify medication adherence therefore remains an unresolved methodological question.

Adherence to oral HIV pre-exposure prophylaxis (PrEP) represents an ideal behavioral model for evaluating EMA accuracy. Oral PrEP has demonstrated high efficacy in both clinical and implementation/promotion trials (Grant et al., 2010; McCormack et al., 2016; Molina et al., 2015). When taken as prescribed, oral PrEP regimens can reduce the risk of HIV acquisition though sexual contact by up to 99% (Fonner et al., 2016). Despite its strong biological efficacy, the effectiveness of PrEP in real-world settings depends heavily on medication adherence. Currently, two primary PrEP regimens are available, daily regimen (one pill per day) and event-driven (ED) regimen (taking two pills 2 to 24 hours before anticipated sexual activity, followed by one pill 24 hours after the initial dose, and another pill 48 hours after, also known as '2-1-1' regimen). Suboptimal adherence can result in insufficient protective drug levels and reduced prevention effectiveness, that for every 10% reduction in PrEP adherence, the effectiveness of PrEP would reduce by 13% (E et al., 2022; Hendrix, 2013). Maintaining optimal adherence can be challenging due to fluctuating sexual activity patterns, stigma, psychosocial stressors, and the complexity of medication schedules, particularly for ED regimen users who must time medication intake around sexual events (Franks et al., 2018; Laurent et al., 2023; Onwubiko et al., 2024). Therefore, accurate and timely assessment of medication adherence is essential for PrEP management and development of targeted interventions in real-world settings. In addition, since the dried blood spot (DBS) testing can provide objective evidence of cumulative drug exposure of PrEP in the past six to eight weeks, it can act as a biological reference standard for adherence assessment (Franks et al., 2018; Hebel et al., 2020). The significant public health importance of PrEP adherence, the presence of clearly defined medication-taking events (daily medication or event-trigged medication), and the availability of a

robust biological gold standard together make the PrEP adherence an ideal behavioral model for methodological studies evaluating the validity of EMA.

Furthermore, the potential value of EMA-based mobile health (mHealth) tools for monitoring PrEP adherence may be particularly relevant in some countries like China. Approximately 70% of PrEP users in China obtain medication through online platforms, where routine adherence monitoring is more challenging (Li et al., 2026). In addition, the majority of the PrEP clients in China chose the ED regimen which has a more complex medication schedule than the daily regimen. Existing adherence monitoring technologies, such as electronic pillboxes, are primarily designed for daily medication use and are less suitable for online PrEP services and event-driven dosing (Chu et al., 2025; Haberer et al., 2021; Liu et al., 2019; Songtaweesin et al., 2020). In contrast, the event-trigged sampling strategy of EMA may be particularly well suited for monitoring medication adherence of ED regimen users. To the best of our knowledge, no studies have developed EMA-based mHealth platforms to assess PrEP adherence among online PrEP consumers and ED PrEP users; none have validated EMA-reported adherence against DBS-derived drug concentrations as a biological reference standard; and none have examined whether EMA provides superior measurement accuracy compared with conventional questionnaires surveys.

To address these gaps, this study developed an EMA-based mHealth platform (PLP, an abbreviation of PuLePu, which is a Chinese phonetic adaptation of the term PrEP) to monitor medication adherence among e-consumers of PrEP in China. The platform incorporates regimen-specific monitoring modules, including event-triggered and fixed-interval sampling for ED users and fixed-interval sampling for daily users (Fig. 1). Using DBS drug concentration as the reference standard, this study further evaluated the diagnostic performance of the platform, compared with traditional questionnaire-based assessments.

# 2. Methods

## 2.1 Study design, setting, and participants

A diagnostic accuracy study based on an 18-week prospective screening cohort of real-world e-consumers of PrEP was conducted in China. The inclusion criteria of the participants included: (i) being aged 18 years old or above; (ii) having purchased PrEP via e-commerce platforms and having taken PrEP in the past 3 months; (iii) planing to continue to take PrEP for the next 6 months; and (iv) being HIV negative. The participants were recruited from the *HeHealth* (formerly known as *BluedHealth*), one of the largest online PrEP sale platforms. The potentially interested PrEP users were referred by the *HeHealth* staff to the research team via WeChat (the most widely used messaging/social media app in China). Detailed information and informed consent form of the study were then sent to the participants. After each participant provided the electronic informed consent, a unique study ID and the baseline e-questionnaire survey link (www.wjx.com) was sent to him. The participant recruitment and baseline assessment of the cohort were conducted in Janunary, 2025.

## 2.2 Data collection

*PLP monitoring*:

The monitoring functions of the PLP were developed to capture ED and daily PrEP users' medication behavior on a real-time basis, using the event-triggered and/or fixed-interval sampling strategy of the EMA method. For daily users, fixed-interval sampling were adopted to prompt daily medication reporting. The participants would receive a SMS reminder of checking-in on the platform every 24 hours at their chosen time. The check-in questions contained information on their sexual behaviors (number of sexual activities in the past 24 hours and condom use) and whether they have taken a pill in the past 24 hours.

For ED users, fixed-interval sampling was adopted by sending SMS reminder every 72 hours to participants at their chosen time to check-in on the platform. The check-in questions contained their sexual behaviors in the past 72 hours and whether they have taken PrEP correctly at all three time points (the '2-1-1' schedule) for each sexual encounter they reported. Furthermore, the event-triggered sampling method was also used to capture their sexual encounters, that the ED users were encouraged by the research team at the beginning of the study to actively record their medication behavior each time they encountered sexual activities (Fig. 1). The reminder function of PLP was designed to prompt participants to log in to the platform and complete EMA-based adherence reporting. It did not provide reminders to take PrEP medication or directly promote medication-taking behavior.

All the participants were asked to continuously check-in on the platform for 18 weeks. A *HeHealth* voucher up to 50 CNY (approximately 7 USD) which could be redeemed for HIV prevention products and services was sent to the participants based on their participation (check-in) rate on the platform, as a compensation for their time and effort.

*Questionnaire surveys*:

In addition to the baseline survey (Supplementary File 1), a follow-up e-questionnaire was sent to the participants on the 6th, 12th, and 18th week after baseline completion (Supplementary File 2). Survey links were sent to the participants through WeChat, and the participants could access the survey using their unique study ID as the passcode. Each baseline/follow-up survey took approximately 5–10 minutes to complete. Participants who did not respond in one survey wave remained eligible for subsequent follow-up surveys. To ensure data quality, three attention-check questions were embedded in each survey, and the participants who correctly answered at least two of them were retained for questionnaire-based analyses. Each participant would receive a *HeHealth* voucher valued 30 CNY for their time and effort.

*DBS test*:

At week 6, 12, and 18, a dried blood spot testing kit was directly mailed to the address provided by each participant. An information card which contained a QR code for the instruction video and return address was included in the package. Each DBS collection kit contained a Whatman 903 card, a single-use safety-locked Press Plus lancet, a sharps disposal container, a biosafety specimen transport bag, an adhesive bandage, a 75% alcohol swab, desiccants, and a size-7 sealing bag. The DBS samples were collected using the Whatman 903 Protein Saver Cards, which feature 14-mm diameter collection circles. After collecting blood from a fingertip according to standardized instructions provided by the study team, the blood spot was allowed to dry for more than 4 hours at a room temperature and be stored in refrigerator at -20 Celsius degree. Following sample collection and adequate drying, the participants were asked to package and mail their DBS cards with

desiccants in sealed bags for transportation under biosafe conditions at their earliest convenience. Quantification of tenofovir-diphosphate (TFV-DP) drug concentration was performed by a pre-designated qualified biomedical lab. The lab used the Waters ACQUITY UPLC Xevo TQS system, following established procedures for high-performance liquid chromatography coupled with tandem mass spectrometry. The lower limit quantification of the drug concentration was 70 fmol/punch. The results of the DBS-measured drug concentration level were finally provided to both the research team and the participants. Participants who have returned their DBS kit would receive a *HeHealth* voucher of 50 CNY each time.

# 2.3 Measurement

*PrEP adherence*

**PLP-based adherence**

Regarding the PLP platform, for daily users, each check-in entry recorded whether the participant had taken a pill in the past 24 hours. A binary outcome named “optimal adherence” was calculated. Those who achieved an adherence rate of 100% on the days they have checked in on the PLP in the past 6 weeks (number of days reporting taking the pill / number of days having checked in) were classified as “optimal adherence”. The missed 24-hour check-in records were treated as missing data and excluded from the calculation of prevalence of optimal adherence among daily users, as it was hard to document or assume the reasons for non-check-in in the real-world context.

For ED PrEP users, each PLP check-in record would capture sexual behaviors and PrEP use occurring within the reporting interval (defined as the time since the previous check-in, up to a maximum of 72 hours). The adherence was assessed based on the reported sexual encounters and their related medication uptake (whether followed the standard ‘2-1-1’ dosing schedule). A reported sexual encounter was classified as adherent if the participant reported he had taken two PrEP pills 2 to 24 hours before sex, one pill 24 hours after the initial dose, and one additional pill 48 hours after the initial dose. The ED users would be classified as having optimal adherence if all the reported sexual encounters in the past 6 weeks met the dosing requirements; otherwise, they would be classified as having suboptimal adherence. This definition was selected as the primary outcome because it represents complete adherence to the recommended ED dosing protocol and provides a conservative assessment of agreement between self-reported adherence and DBS-derived adherence. The missed 72-hour check-in records were treated excluded from the calculation of prevalence of optimal adherence among ED users, as it was hard to document or assume the reasons for non-check-in in the real-world context.

**Questionnaire-based adherence**: In questionnaire surveys, adherence to ED regimen was assessed by four items. First, the participants were asked whether they had engaged in sexual activity in the past 6 weeks. Those who reported no sexual activity were censored from the analysis. Those who answered “yes” were then asked if they had taken PrEP for each sexual encounter in the past 6 weeks. Following that, the participants who had used PrEP would be asked about whether they have taken PrEP as instructed in each time point according to ‘2-1-1’ PrEP guideline. The participants who reported to take PrEP for each sexual encounter and took PrEP as instructed at all three timepoints were classified as “optimal adherence”. Adherence to daily PrEP regimen was assessed with a single item in the questionnaire: “In the past 6 weeks, have you ever failed

to take PrEP on time and in a correct dosage? (yes/no)". Participants who answered "no" were classified as "optimal adherence" and those who chose "yes" were categorized as "non-optimal adherent" and subsequently asked to report how many PrEP pills they had missed in the past 6 weeks.

**DBS-based adherence**

The adherence was classified using the established pharmacological thresholds from DBS testing. For ED PrEP users, an assay result of ≥ 700 fmol/punch (assuming an average of 1 sexual encounter with 4 PrEP pills taken each week) was classified as " optimal adherence", indicating full adherence for each sexual encounter in the past 6 weeks (Grant et al., 2014; Jongen et al., 2021). For daily users, a threshold of ≥ 1250 fmol/punch was required for the "optimal adherence" classification, corresponding to an average of 7 pills taken per week in the past 6 weeks (Grant et al., 2014).

*Other variables*

In the questionnaire surveys, the participants were asked about their sociodemographic characteristics, including age, sex assigned at birth, ethnicity, employment status, education level, marital status, and monthly income, as well as their PrEP regimen type in the past 6 weeks (daily, ED, or switch).

# 2.4 Statistical analysis:

First, descriptive analyses were performed to summarize the distributions of all the collected data. The participants who self-reported a switch of regimens in the questionnaire surveys during the follow-up period were excluded from the subsequent analysis due to difficulties in defining cutoffs of optimal adherence of the DBS drug concentration level. Those who never checked in on the PLP platform were also excluded. Then, the distributions of background variables at baseline of the analytic sample were summarized and presented. Moreover, baseline characteristics were compared between participants included and excluded from the analytic sample using independent-sample t-tests for continuous variables and chi-square tests for categorical variables. Statistical significance was defined as a two-sided P value < 0.05.

Regarding the accuracy evaluation, only the participants who both reported adherence data via the PLP platforms/questionnaires and returned their DBS samples during the corresponding follow-up periods were included in the analysis. First, the prevalence of optimal adherence by regimen types, measurement types, and follow-up time points were calculated, respectively. Then, the DBS-based adherence was treated as the biochemical gold standard to calculate the sensitivity (SE), specificity (SP), positive predictive value (PPV), and negative predictive value (NPV) of the PLP platform and questionnaire surveys by regimen types at each time point. Specifically, when calculating the SE, SP, PPV, and NPV of the PLP platform for ED and daily users at week 6, 12, and 18, the DBS-based adherence data were first matched with PLP-based adherence; the participants were excluded from the calculation if they failed to return a DBS sample or did not record any medication intake on the PLP during the corresponding assessment period; then, the SE/SP/PPV/NPV were calculated based on the standard formulars using the remaining analytic sample. Similarly, accuracy analyses of the traditional questionnaire survey were conducted among the participants who both completed the questionnaire survey and returned a DBS sample in the corresponding follow-up period.

As a sensitivity analysis, the robustness of the diagnostic accuracy estimates was assessed using an alternative definition of PrEP adherence for daily users. The primary analysis defined optimal adherence based on a DBS TFV-DP concentration threshold of ≥ 1250 fmol/punch and self-reported use of 7 pills per week for daily users. In the sensitivity analysis, adherence was redefined as self-reported PrEP use of ≥ 4 pills per week, corresponding to a DBS TFV-DP concentration threshold of ≥ 700 fmol/punch. Diagnostic accuracy measures, including sensitivity, specificity, positive predictive value, and negative predictive value, were recalculated based on this alternative adherence definition. R version 4.3.1 was used for the analyses.

## 3. Result

## 3.1 Participant Enrollment, Follow-up Completion, and Platform Utilization

A total of 342 participants were enrolled in the study and followed for 18 weeks. There were 12 participants who self-reported a switch of regimens during the follow-up period, and were excluded from the analysis due to difficulties in defining cutoffs of optimal adherence of the DBS drug concentration level; another 24 participants were excluded as they never checked in on the PLP platform throughout the follow-up period. At week 6, 12, and 18, 305 (231 ED and 74 daily), 207 (148 ED and 59 daily), and 184 (131 ED and 53 daily) participants had at least one check-in record on the PLP platform in the past 6 weeks, respectively. For the ED regimen participants, the average participation rate of PLP check-in (i.e. the actual number of check-in entries divided by expected number of check-in entries [number of total follow-up days/3 days]) was 68.1%, 73.1%, and 80.9%, respectively; for the daily users, the average participation rate (i.e. the actual number of check-in entries divided by number of total follow-up days) was 80.2%, 82.2%, and 91.2%, respectively (Fig. 2).

For the questionnaire survey, the response rate was 89.5%, 84.2% and 81.6% at week 6, 12 and 18, respectively. The number of participants who provided a valid mailing address and were sent a DBS collection kit was 296, 300, and 294, at week 6, 12, and 18; and the percentage of returned DBS kit was 81.8%, 65.7%, and 56.8% (Fig. 2).

Among the analyzed 306 participants who had not switched regimens and had at least one check-in record on the PLP, the mean age was 31.6 years old (SD = 6.9); all were men who have sex with men (MSM); and 94.1% were Han ethnicity. The majority of the participants were employed (86.3%), having obtained a college degree or above (95.8%), unmarried/divorced/separated/widowed (83.3%), and having a monthly income over 7000 CNY (≈ 980 USD, 65.4%) (Table 1). Baseline characteristics between participants included and excluded from the analytic sample showed no significant differences (Table S1).

Table 1
Background characteristics of the analytic participants at baseline (N = 306).

| Characteristics | N(%)/Mean ± SD |
|---|---|
| **Age** | 31.6 ± 6.9 |
| 18–29 | 121 (39.5) |
| 30–39 | 150 (49.0) |
| ≥ 40 | 35 (11.4) |
| **Designated Sex at Birth** | |
| Male | 306 (100.0) |
| Female | 0 (0.0) |
| **Ethnicity** | |
| Han | 288 (94.1) |
| Others | 18 (5.9) |
| **Employment** | |
| Students/Unemployed | 42 (13.7) |
| Employed | 264 (86.3) |
| **Education Level** | |
| High school and below | 13 (4.2) |
| College and above | 293 (95.8) |
| **Marital Status** | |
| Married or living with a partner | 51 (16.7) |
| Unmarried/divorced/separated/widowed | 255 (83.3) |
| **Monthly income** (CNY) [a] | |
| ≤ 3000 | 24 (7.8) |
| 3001–5000 | 36 (11.8) |
| 5001–7000 | 46 (15.0) |
| 7001–10000 | 53 (17.3) |
| 10001–15000 | 73 (23.9) |
| 15001–20000 | 46 (15.0) |
| *CNY, Chinese Yuan (1 CNY = 0.14 USD) | |

| Characteristics | N(%)/Mean ± SD |
|---|---|
| > 20000 | 28 (9.2) |
| **PrEP regimen** | |
| Daily | 74 (24.3) |
| Event-driven | 232 (75.7) |
| *CNY, Chinese Yuan (1 CNY = 0.14 USD) | |

## 3.2 PrEP Adherence Measured by PLP, Questionnaire, and DBS

The participants were then included in the accuracy analyses if they both reported adherence via the PLP or questionnaires and returned their DBS samples during the corresponding follow-up periods. At week 6, 199 (140 ED, 59 daily) and 197 (146 ED, 51 daily) participants were included in the accuracy analyses of the PLP and questionnaires, respectively. At week 12, the corresponding numbers were 134 (88 ED, 46 daily) and 161 (107 ED, 54 daily); and at week 18, they were 116 (75 ED, 41 daily) and 136 (88 ED, 48 daily), respectively.

Among the ED users, the prevalence of optimal adherence at week 6, 12, and 18 recorded by the PLP platform was 30.0% (42/140), 36.4% (32/88), and 28.0% (21/75), respectively, while that measured by the questionnaire was 42.5% (62/146), 43.0% (46/107), and 43.2% (38/88). The DBS-confirmed adherence in the PLP sample was 37.1% (52/140), 39.8% (35/88), and 32.0% (24/75), while the DBS-confirmed adherence among the questionnaire respondents was 33.6% (49/146), 35.5% (38/107), and 29.5% (26/88) at the three time points, respectively (Fig. 3).

Among the daily users, the PLP-recorded prevalence of optimal adherence was 55.9% (33/59), 69.6%, (32/46) and 68.3% (28/41) at week 6, 12, and 18, respectively, while the questionnaire-reported adherence was 78.4% (40/51), 81.5% (44/54), and 83.3% (40/48), respectively. The DBS-confirmed adherence in the PLP sample was 72.9% (43/59), 63.0% (29/46), and 51.2% (21/41), while that among the questionnaire respondents was 84.3% (43/51), 66.7% (36/54), and 60.4% (29/48) at weeks 6, 12, and 18 (Fig. 3).

## 3.3 Specificity, sensitivity, PPV, and NPV in the screening test

Among the ED users, the PLP platform showed a specificity of 0.64, 0.66, and 0.77, and a sensitivity of 0.19, 0.40, and 0.38 across the three visits, respectively. The corresponding positive predictive value (PPV) was 0.24, 0.44, and 0.43; and the negative predictive value (NPV) was 0.57, 0.63, and 0.72, respectively. The questionnaire survey showed a relatively lower specificity (0.63, 0.61, and 0.63) but higher sensitivity (0.53, 0.50, and 0.58) than the PLP platform. Its PPV was 0.42, 0.41, and 0.40; and NPV was 0.73, 0.69, and 0.78, respectively (Table 2).

Table 2
Screening performance of the mHealth platform and traditional questionnaire for PrEP adherence among ED users across follow-up visits taking the dried blood spot as the golden standard

| Assessment Measure | Adherence Status | DBS Adherent | DBS Non-adherent | Total | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|---|---|
| ***Week 6*** | | | | | | | | |
| | ***Total*** | ***52*** | ***88*** | ***140*** | | | | |
| **PLP** | Adherent | 10 (TP) | 32 (FP) | 42 | 0.19 | 0.64 | 0.24 | 0.57 |
| | Non-adherent | 42 (FN) | 56 (TN) | 98 | | | | |
| | **Total** | **49** | **97** | **146** | | | | |
| **Questionnaire** | Adherent | 26 (TP) | 36 (FP) | 62 | 0.53 | 0.63 | 0.42 | 0.73 |
| | Non-adherent | 23 (FN) | 61 (TN) | 84 | | | | |
| **Week 12** | | | | | | | | |
| | **Total** | **35** | **53** | **88** | | | | |
| **PLP** | Adherent | 14 (TP) | 18 (FP) | 32 | 0.40 | 0.66 | 0.44 | 0.63 |
| | Non-adherent | 21 (FN) | 35 (TN) | 56 | | | | |
| | **Total** | **38** | **69** | **107** | | | | |
| **Questionnaire** | Adherent | 19 (TP) | 27 (FP) | 46 | 0.50 | 0.61 | 0.41 | 0.69 |
| | Non-adherent | 19 (FN) | 42 (TN) | 61 | | | | |
| **Week 18** | | | | | | | | |
| | **Total** | **24** | **51** | **75** | | | | |
| **PLP Platform** | Adherent | 9 (TP) | 12 (FP) | 21 | 0.38 | 0.77 | 0.43 | 0.72 |
| | Non-adherent | 15 (FN) | 39 (TN) | 54 | | | | |
| | **Total** | **26** | **62** | **88** | | | | |
| **Questionnaire** | Adherent | 15 (TP) | 23 (FP) | 38 | 0.58 | 0.63 | 0.39 | 0.78 |
| | Non-adherent | 11 (FN) | 39 (TN) | 50 | | | | |

*DBS, dry blood sample; TP, true positive; FP, false positive; FN, false negative; TN, true negative; PPV, positive predictive value; NPV, negative predictive value.

Among the daily users, the PLP platform demonstrated a specificity of 0.69, 0.59, and 0.50, and a sensitivity of 0.65, 0.86, and 0.86 at week 6, 12, and 18, respectively. The PPV was 0.85, 0.78, and 0.64; and the NPV values was 0.42, 0.71, and 0.77, respectively. The questionnaire survey's specificity (0.25, 0.11, and 0.21) was much lower than the platform; however, the sensitivity (0.80, 0.78, and 0.86) remained approximately comparable to that of the PLP platform. The corresponding PPV was 0.85, 0.64, and 0.63; and the NPV was 0.18, 0.20, and 0.50, respectively (Table 3).

Table 3
Screening performance of the mHealth platform and traditional questionnaire for PrEP adherence among daily users across follow-up visits taking the dried blood spot as the golden standard.

| Assessment Measure | Adherence Status | DBS Adherent | DBS non-adherent | Total | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|---|---|
| ***Week 6*** | | | | | | | | |
| | ***Total*** | ***43*** | ***16*** | ***59*** | | | | |
| **PLP** | Adherent | 28 (TP) | 5 (FP) | 33 | 0.65 | 0.69 | 0.85 | 0.42 |
| | Non-adherent | 15 (FN) | 11 (TN) | 26 | | | | |
| | **Total** | **43** | **8** | **51** | | | | |
| **Questionnaire** | Adherent | 34 (TP) | 6 (FP) | 40 | 0.79 | 0.25 | 0.85 | 0.18 |
| | Non-adherent | 9 (FN) | 2 (TN) | 11 | | | | |
| **Week 12** | | | | | | | | |
| | **Total** | **29** | **17** | **46** | | | | |
| **PLP** | Adherent | 25 (TP) | 7 (FP) | 32 | 0.86 | 0.59 | 0.78 | 0.71 |
| | Non-adherent | 4 (FN) | 10 (TN) | 14 | | | | |
| | **Total** | **36** | **18** | **54** | | | | |
| **Questionnaire** | Adherent | 28 (TP) | 16 (FP) | 44 | 0.78 | 0.11 | 0.64 | 0.20 |
| | Non-adherent | 8 (FN) | 2 (TN) | 10 | | | | |
| **Week 18** | | | | | | | | |
| | **Total** | **21** | **20** | **41** | | | | |
| **PLP Platform** | Adherent | 18 (TP) | 10 (FP) | 28 | 0.86 | 0.50 | 0.64 | 0.77 |
| | Non-adherent | 3 (FN) | 10 (TN) | 13 | | | | |
| | **Total** | **29** | **19** | **48** | | | | |
| **Questionnaire** | Adherent | 25 (TP) | 15 (FP) | 40 | 0.86 | 0.21 | 0.63 | 0.50 |
| | Non-adherent | 4 (FN) | 4 (TN) | 8 | | | | |

*DBS, dry blood sample; TP, true positive; FP, false positive; FN, false negative; TN, true negative; PPV, positive predictive value; NPV, negative predictive value.

In the sensitivity analysis, the result of the accuracy analysis for daily users yielded improved specificity of the platform and comparable sensitivity as well, suggesting the robustness of the diagnostic performance estimates across different adherence definitions (Table S2).

# 4. Discussion

This study developed an EMA-based mHealth platform to monitor real-time medication adherence among real-world e-consumers of PrEP, and adopted two complementary approaches, the DBS–assessed drug concentrations as a gold standard and conventional questionnaires surveys as a comparison, to evaluate the accuracy of the platform based on an 18-week screening cohort involving both ED and daily PrEP users. To the best of our knowledge, this study is among the first studies to validate an EMA-based self-reported adherence monitoring tool against pharmacologic biomarkers in a real-world PrEP population. Previous studies have applied EMA approaches to monitor PrEP-related behaviors; however, few have evaluated EMA-derived adherence reports against objective measures such as DBS. By triangulating the digital, survey, and pharmacologic data, the findings offer important empirical evidence on the accuracy of applying EMA in digital behavioral monitoring in real-world settings.

Overall, compared with traditional questionnaire surveys, the EMA-based mHealth tool demonstrated a higher specificity in measuring medication adherence for both PrEP regimens (0.64 ~ 0.77 vs. 0.61 ~ 0.63 for ED, 0.50 ~ 0.69 vs. 0.11 ~ 0.25 for daily); and its sensitivity was lower when assessing adherence to the ED regimen (0.19 ~ 0.40 vs. 0.50 ~ 0.58), and was approximately equivalent for daily regimen (0.65 ~ 0.86 vs. 0.78 ~ 0.86). While lower sensitivity indicates that some adherent individuals may not be captured correctly by the platform, the higher specificity observed for the EMA-based monitoring tool compared with traditional questionnaires suggests potential value for identifying individuals who may benefit from additional adherence support. This finding is consistent with a study assessing drinking behavior using EMA-based smartphone app and daily surveys in 8 days. When validating against breathalyzer, the EMA-based app demonstrated greater specificity (0.87 vs 0.84) but lower sensitivity (0.83 vs 0.89) relative to the survey-based measures (Kianersi et al., 2024). Another study on monitoring sedentary behavior for 7 days showed that, when validating against accelerometer, the EMA-based app exhibiting a sensitivity of 0.83 and a specificity of 0.38, with no comparison being reported (Romanzini et al., 2019). The sensitivity and specificity observed in this study were lower than those reported in the two aforementioned studies, which may be attributable to two key factors. First, social desirability bias may have been more pronounced in the present study, as PrEP use remains a stigmatized behavior in this context (Wei & Raymond, 2018). Second, the longer validation interval used here (every 6 weeks) compared with the shorter intervals in prior studies (approximately 1 week) may have introduced greater reporting burden, leading to reporting fatigue and, consequently, increased reporting bias (Wang et al., 2024).

The higher specificity achieved by the EMA-based monitoring tool developed in this study compared to the traditional questionnaire represents a key public health strength. It is aligned with previous studies using electronic adherence monitoring devices in HIV treatment contexts (e.g. Wisepill) which demonstrated that real-time or near real-time recorded data tend to more accurately capture missed doses (Dworkin et al., 2020; Haberer et al., 2010). Accurate detection of non-adherence is particularly critical in PrEP implementation, as individuals with insufficient medication coverage remain at elevated risk of HIV acquisition and need

immediate interventions (Donnell et al., 2014). From a prevention standpoint, minimizing false reassurance is more consequential than maximizing detection of already-adherent users. A possible reason for the higher specificity observed in the EMA-based approach is that unlike conventional questionnaires, the EMA-based tool is designed to repeatedly capture people's daily life behaviors in a natural environment, which may help reduce recall bias in reporting risk behaviors, i.e., mitigating the possibility of reporting non-adherent behaviors as adherent behaviors (Wrzus & Neubauer, 2023). Another possible explanation is that participants with greater perceived need for adherence support may have different patterns of engagement with digital platforms, consistent with the Technology Acceptance Model, in which perceived usefulness—reflecting users perceived need for support—is a primary determinant of behavioral intention to use digital health technologies (Palos-Sanchez, Saura, Rios Martin, & Aguayo-Camacho, 2021).

Notably, the accuracy evaluation of this study was based on a prospective screening cohort of real-world e-consumers of PrEP among which the ED regimen users accounted for the majority. Compared with device-based adherence monitoring approaches, smartphone-based platforms may offer advantages in scalability and accessibility because they do not require additional hardware. The PLP platform can not only be used in e-commerce settings, but also be applied and promoted in PrEP users who obtained the medication via offline venues. Furthermore, the PLP platform showed a relatively high specificity in assessing the ED regimen's adherence, even higher than that for the daily regimen. Since the ED PrEP users comprise the majority of the real-world clients in China and the real-time adherence captures is particular challenging for this group when using traditional assessment approaches and electronic pill boxes (as the ED regimen involves episodic and event-driven dosing linked to sexual activity) (Laurent et al., 2023), this study developed an innovative tool which demonstrates strong potentials for future PrEP adherence management in China and other countries/regions with similar context. More broadly, this study may extend beyond PrEP by demonstrating that EMA, when externally validated against objective biomarkers, may serve as a robust methodological framework for real-time measurement of various medication behaviors. This shifts EMA from a descriptive digital tracking tool toward a biomarker-anchored behavioral monitoring method.

Furthermore, real-time or near real-time signals derived from the EMA-based monitoring tool can be used to trigger immediate precision interventions embedded in the same platform, such as personalized medication reminders following missed or delayed doses, behavioral nudges targeting momentary lapses in motivation, or coping-oriented prompts in response to contextual risk states (Heron & Smyth, 2010; Shiffman et al., 2008). Previous studies have suggested that staged adherence interventions combining monitoring, feedback, and tailored support may improve PrEP adherence (Chai et al., 2026). The real-time and behaviorally proximal nature of EMA data allows for temporal mapping of adherence patterns, offering opportunities for dynamic risk stratification and personalized intervention design. Additionally, the EMA data can support adaptive modulation of intervention intensity, whereby the frequency or content of the interventions can be dynamically adjusted according to observed adherence patterns and risk trajectories (Nahum-Shani et al., 2018). This linkage enables the delivery of timely, personalized, and precision adherence support. Therefore, the integration of EMA into PrEP and other health behavioral management systems represents a critical methodological step toward the development of just-in-time adaptive interventions.

Several limitations should be acknowledged in this study. First, the convenience sampling may have introduced selection bias in the reported prevalence of optimal adherence and accuracy estimation of the

PLP platform. PrEP users who were more willing to engage with mHealth platforms and more health-conscious had a higher likelihood of participating in the study and keeping a higher utilization rate of the platform than the non-participations. However, participants included in the analyses were generally comparable to excluded participants, suggesting limited evidence of selection bias. Second, as missed check-in records of the platform were treated as missing data and directly excluded from the statistical calculation, the study results might be further biased. Those who had more missing records (lower engagement with the platform) might demonstrate different adherence behaviors, but the direction of the bias was hard to gauge, because it is difficult to assume the actual medication uptake in the missed check-in days, especially among ED users whose dosing schedule is linked to sexual activities. Third, the participation rate of the platform check-in, the response rate of the questionnaire surveys, and the DBS return rates declined significantly throughout the follow-up period, reducing the effective sample size and statistical power for the accuracy evaluation. It may also introduce attrition bias. Fourth, return of the DBS was delayed. As the DBS-derived drug concentrations reflect cumulative exposure over preceding weeks, the delayed return could have shifted the effective exposure window relative to the intended assessment period, potentially attenuating agreement estimates. Last but not least, caution is warranted when generalizing these findings to other medication adherence contexts, as both the regimen characteristics and the study population (all participants were MSM in this study) differ in important ways from those of other medications, such as treatments for non-communicable diseases.

In conclusion, the study adopted PrEP medication as a real-world case to validate the accuracy of the EMA-based behavioral monitoring tool, taking the DBS-derived pharmacologic biomarkers as the gold standard and traditional questionnaires as a comparison. The findings of the higher sensitivity and lower-to-equivalent sensitivity of the EMA-based mHealth platform provide empirical evidence supporting the accuracy of EMA in capturing medication adherence in real world. The study provides accumulating evidence that EMA may serve as a valid and accessible approach for monitoring a range of health-related behaviors, with broader implications for this rapidly emerging methodological framework.

# Declarations

**Data availability:** All the relevant data were presented in the manuscript.

**Code availability:** Data analysis was completed in R. The analysis code is available at upon reasonable request.

**Acknowledgement:** We would like to express our sincere gratitude to all the participants who contributed their time and insights to this study. We extend our appreciation to HeHealth for their invaluable assistance in participant recruitment, which was crucial to the success of this project. Special thanks to RZBY health for their expertise and support in the development of the platform.

**Author Contributions:** J.Z. and Q.L. contributed equally to this work and share first authorship. J.Z., Q.L., and S.L. were responsible for conceptualization and study design. J.Z., Q.L., and HW.X. conducted the investigation and data collection. X.R., H.Z., C.L., M.Z., J.X., H.T., and H.L. contributed to methodology development and provided critical input on interpretation. J.Z. and Q.L. performed formal analysis and drafted

the original manuscript. C.R., MY.Z., Y.Z., JY.Z., YH.Z., S.H., and L.W. were involved in data curation and validation. H.X. contributed to software development and technical support. S.L. provided supervision, funding acquisition, and project administration. All authors contributed to manuscript review and editing and approved the final version.

**Ethics Declaration:** The authors declare that they have no competing interests. This study has been approved by the Institutional Review Board of Tsinghua University (THU01-20240097) on July 4th, 2024. Electronic consent will be provided from all participants. The study findings will be reported in peer-reviewed publications and presented at relevant academic conferences.

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## References

1. Bruening M, van Woerden I, Todd M, Brennhofer S, Laska MN, Dunton G (2016) A Mobile Ecological Momentary Assessment Tool (devilSPARC) for Nutrition and Physical Activity Behaviors in College Students: A Validation Study. J Med Internet Res 18(7):e209. 10.2196/jmir.5969
2. Chai PR, Lee JS, Goodman GR, Albrechta H, Hokayem J, Loo L, O'Cleirigh C (2026) PrEPSteps: A Pilot Randomized Controlled Trial to Assess the Feasibility and Acceptability of a Digital Pill-Based PrEP Adherence Intervention in Men Who Have Sex with Men with Substance Use Disorder. AIDS Behav. 10.1007/s10461-026-05049-x
3. Chu ZX, Jin X, Ye ZH, Zhu YY, Huang XJ, Wang H, Shang H (2025) Real-time digital intervention on oral pre-exposure prophylaxis adherence among MSM: randomized controlled trial. NPJ Digit Med 8(1):349. 10.1038/s41746-025-01743-7
4. Czyz EK, King CA, Al-Dajani N, Zimmermann L, Hong V, Nahum-Shani I (2023) Ecological Momentary Assessments and Passive Sensing in the Prediction of Short-Term Suicidal Ideation in Young Adults. JAMA Netw Open 6(8):e2328005. 10.1001/jamanetworkopen.2023.28005
5. Donnell D, Baeten JM, Bumpus NN, Brantley J, Bangsberg DR, Haberer JE, Celum C (2014) HIV protective efficacy and correlates of tenofovir blood concentrations in a clinical trial of PrEP for HIV prevention. J Acquir Immune Defic Syndr 66(3):340–348. 10.1097/qai.0000000000000172
6. Dworkin MS, Panchal P, Wiebel W, Garofalo R, Jimenez A, Haberer JE (2020) Experience with antiretroviral electronic adherence monitoring among young African American men who have sex with men living with HIV: findings to inform a triaged real-time alert intervention. AIDS Care 32(9):1092–1101. 10.1080/09540121.2020.1713975
7. E OM, Marshall L, Teljeur C, Harrington P, Hayes C, Moran P, Ryan M (2022) Oral pre-exposure prophylaxis (PrEP) to prevent HIV: a systematic review and meta-analysis of clinical effectiveness, safety, adherence and risk compensation in all populations. BMJ Open 12(5):e048478. 10.1136/bmjopen-2020-048478

8. Fonner VA, Dalglish SL, Kennedy CE, Baggaley R, O'Reilly KR, Koechlin FM, Grant RM (2016) Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. Aids 30(12):1973–1983. 10.1097/qad.0000000000001145
9. Franks J, Hirsch-Moverman Y, Loquere AS Jr., Amico KR, Grant RM, Dye BJ, Mannheimer SB (2018) Sex, PrEP, and Stigma: Experiences with HIV Pre-exposure Prophylaxis Among New York City MSM Participating in the HPTN 067/ADAPT Study. AIDS Behav 22(4):1139–1149. 10.1007/s10461-017-1964-6
10. Gillespie D, Couzens Z, de Bruin M, Hughes DA, Jones A, Ma R, Hood K (2022) PrEP Use, Sexual Behaviour, and PrEP Adherence Among Men who have Sex with Men Living in Wales Prior to and During the COVID-19 Pandemic. AIDS Behav 26(8):2746–2757. 10.1007/s10461-022-03618-4
11. Grant RM, Anderson PL, McMahan V, Liu A, Amico KR, Mehrotra M, Glidden DV (2014) Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. Lancet Infect Dis 14(9):820–829. 10.1016/s1473-3099(14)70847-3
12. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, Glidden DV (2010) Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med 363(27):2587–2599. 10.1056/NEJMoa1011205
13. Haberer JE, Bukusi EA, Mugo NR, Pyra M, Kiptinness C, Oware K, Baeten JM (2021) Effect of SMS reminders on PrEP adherence in young Kenyan women (MPYA study): a randomised controlled trial. Lancet HIV 8(3):e130–e137. 10.1016/s2352-3018(20)30307-6
14. Haberer JE, Kahane J, Kigozi I, Emenyonu N, Hunt P, Martin J, Bangsberg DR (2010) Real-time adherence monitoring for HIV antiretroviral therapy. AIDS Behav 14(6):1340–1346. 10.1007/s10461-010-9799-4
15. Hebel S, Kahn-Woods E, Malone-Thomas S, McNeese M, Thornton L, Sukhija-Cohen A, Daughtridge G (2020) Brief Report: Discrepancies Between Self-Reported Adherence and a Biomarker of Adherence in Real-World Settings. J Acquir Immune Defic Syndr 85(4):454–457. 10.1097/qai.0000000000002486
16. Hendrix CW (2013) Exploring concentration response in HIV pre-exposure prophylaxis to optimize clinical care and trial design. Cell 155(3):515–518. 10.1016/j.cell.2013.09.030
17. Heron KE, Smyth JM (2010) Ecological momentary interventions: incorporating mobile technology into psychosocial and health behaviour treatments. Br J Health Psychol 15(Pt 1):1–39. 10.1348/135910709x466063
18. Jongen VW, Hoornenborg E, van den Elshout MA, Boyd A, Zimmermann HM, Coyer L, van der Schim MF (2021) Adherence to event-driven HIV PrEP among men who have sex with men in Amsterdam, the Netherlands: analysis based on online diary data, 3-monthly questionnaires and intracellular TFV-DP. J Int AIDS Soc 24(5):e25708. 10.1002/jia2.25708
19. Kianersi S, Parker M, Ludema C, Agley J, Rosenberg M (2024) Introduction and validation of an ecological momentary assessment methodology to measure alcohol use among college students. SAGE Open 14(2):21582440241256531
20. Laurent C, Yaya I, Cuer B, Sagaon-Teyssier L, Mensah E, Dah TTE, Spire B (2023) (CohMSM-PrEP): A Multi-Country Demonstration Study From West Africa. Clin Infect Dis 77(4):606–614. 10.1093/cid/ciad221. Human Immunodeficiency Virus Seroconversion Among Men Who HaveSex With Men Who Use Event-Driven or Daily Oral Pre-Exposure Prophylaxis

21. Li Q, Zhou J, Xu Y, Zou H, Lin C, Zhang M, Luo S (2026) Medication adherence and its associated factors among oral pre-exposure prophylaxis (PrEP) users in China: The Real-world E-consumer Cohort of PrEP study. PLoS Med 23(2):e1004733. 10.1371/journal.pmed.1004733
22. Liu AY, Vittinghoff E, von Felten P, Rivet Amico K, Anderson PL, Lester R, Fuchs JD (2019) Randomized Controlled Trial of a Mobile Health Intervention to Promote Retention and Adherence to Preexposure Prophylaxis Among Young People at Risk for Human Immunodeficiency Virus: The EPIC Study. Clin Infect Dis 68(12):2010–2017. 10.1093/cid/ciy810
23. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, Gill ON (2016) Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet 387(10013):53–60. 10.1016/s0140-6736(15)00056-2
24. Molina JM, Capitant C, Spire B, Pialoux G, Cotte L, Charreau I, Delfraissy JF (2015) On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection. N Engl J Med 373(23):2237–2246. 10.1056/NEJMoa1506273
25. Nahum-Shani I, Smith SN, Spring BJ, Collins LM, Witkiewitz K, Tewari A, Murphy SA (2018) Just-in-Time Adaptive Interventions (JITAIs) in Mobile Health: Key Components and Design Principles for Ongoing Health Behavior Support. Ann Behav Med 52(6):446–462. 10.1007/s12160-016-9830-8
26. Onwubiko UN, Murray SM, Rao A, Chamberlain AT, Sanchez TH, Benkeser D, Baral SD (2024) Individual & joint associations of sexual stigma and mental distress with PrEP uptake, adherence and persistence among US gay and bisexual men. Soc Sci Med 363:117493. 10.1016/j.socscimed.2024.117493
27. Palos-Sanchez PR, Saura JR, Martin R, M., Aguayo-Camacho M (2021) Toward a Better Understanding of the Intention to Use mHealth Apps: Exploratory Study. JMIR Mhealth Uhealth 9(9):e27021. 10.2196/27021
28. Romanzini CLP, Romanzini M, Barbosa CCL, Batista MB, Shigaki GB, Ronque ERV (2019) Characterization and Agreement Between Application of Mobile Ecological Momentary Assessment (mEMA) and Accelerometry in the Identification of Prevalence of Sedentary Behavior (SB) in Young Adults. Front Psychol 10:720. 10.3389/fpsyg.2019.00720
29. Shacham E, Lew D, Xiao T, López J, Trull T, Schootman M, Presti R (2019) Testing the Feasibility of Using Ecological Momentary Assessment to Collect Real-Time Behavior and Mood to Predict Technology-Measured HIV Medication Adherence. AIDS Behav 23(8):2176–2184. 10.1007/s10461-018-2378-9
30. Shiffman S, Stone AA, Hufford MR (2008) Ecological momentary assessment. Annu Rev Clin Psychol 4:1–32. 10.1146/annurev.clinpsy.3.022806.091415
31. Songtaweesin WN, Kawichai S, Phanuphak N, Cressey TR, Wongharn P, Saisaengjan C, Puthanakit T (2020) Youth-friendly services and a mobile phone application to promote adherence to pre-exposure prophylaxis among adolescent men who have sex with men and transgender women at-risk for HIV in Thailand: a randomized control trial. J Int AIDS Soc 23(Suppl 5):e25564. 10.1002/jia2.25564. *Suppl 5*
32. Stone AA, Shiffman S (1994) Ecological momentary assessment (EMA) in behavorial medicine. *Annals of behavioral medicine*
33. Wang SD, Hatzinger L, Morales J, Hewus M, Intille S, Dunton GF (2024) Burden and Inattentive Responding in a 12-Month Intensive Longitudinal Study: Interview Study Among Young Adults. JMIR Form Res 8:e52165. 10.2196/52165

34. Wei C, Raymond HF (2018) Pre-exposure prophylaxis for men who have sex with men in China: challenges for routine implementation. J Int AIDS Soc 21(7):e25166. 10.1002/jia2.25166
35. Wray TB, Kahler CW, Monti PM (2016) Using Ecological Momentary Assessment (EMA) to Study Sex Events Among Very High-Risk Men Who Have Sex with Men (MSM). AIDS Behav 20(10):2231–2242. 10.1007/s10461-015-1272-y
36. Wrzus C, Neubauer AB (2023) Ecological Momentary Assessment: A Meta-Analysis on Designs, Samples, and Compliance Across Research Fields. Assessment 30(3):825–846. 10.1177/10731911211067538

# Figures

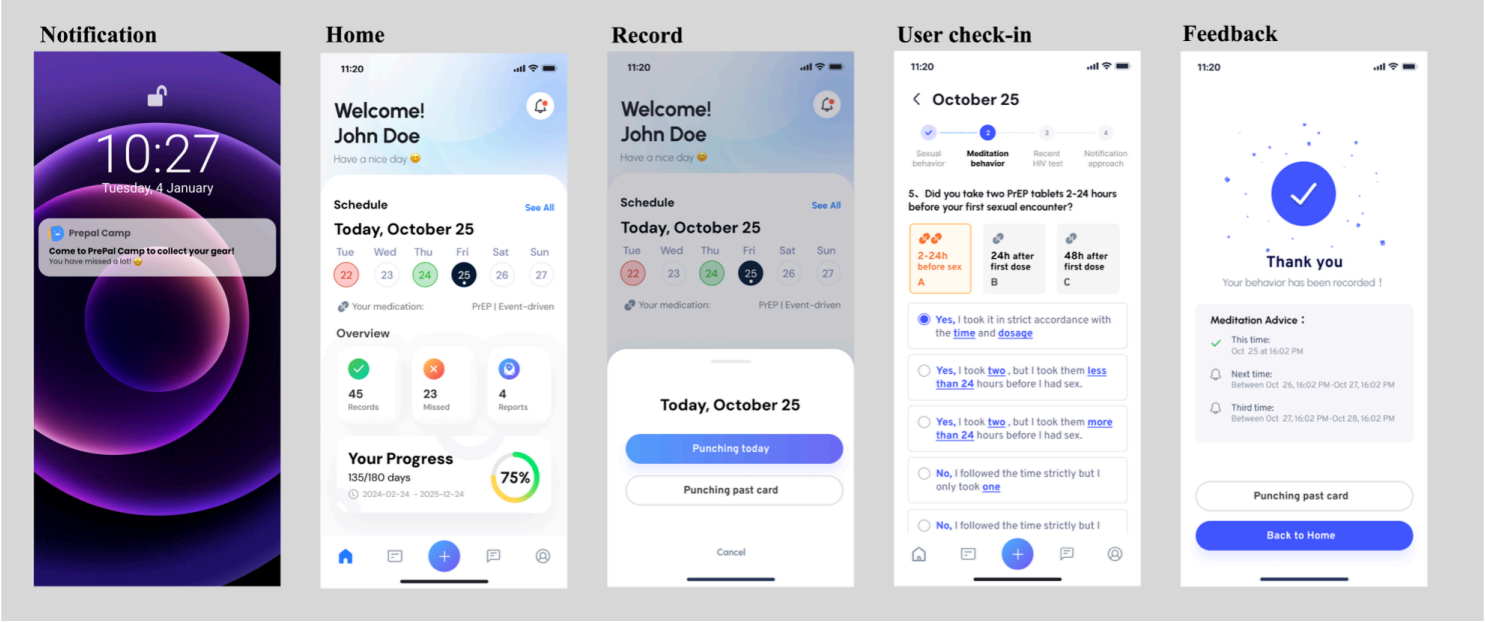



**Figure 1**

**Demonstration of the EMA-based mHealth platform (PLP) from user-end.**

Figure legend: Demonstration of the ecological momentary assessment (EMA)-based mHealth platform (PLP) from the user perspective. The figure illustrates the core functional modules of the real-time PrEP adherence monitoring and intervention system. The notification interface delivers timely reminders to prompt medication intake or reporting. The home dashboard provides a personalized overview of the dosing schedule, adherence status, and progress tracking. The record module enables users to log daily PrEP use in real time or retrospectively. The user survey module captures behavior-related information, including dosing patterns and sexual activity, to support adherence assessment. The feedback interface generates immediate, tailored medication advice based on user inputs, reinforcing adherence and informing subsequent dosing behavior.

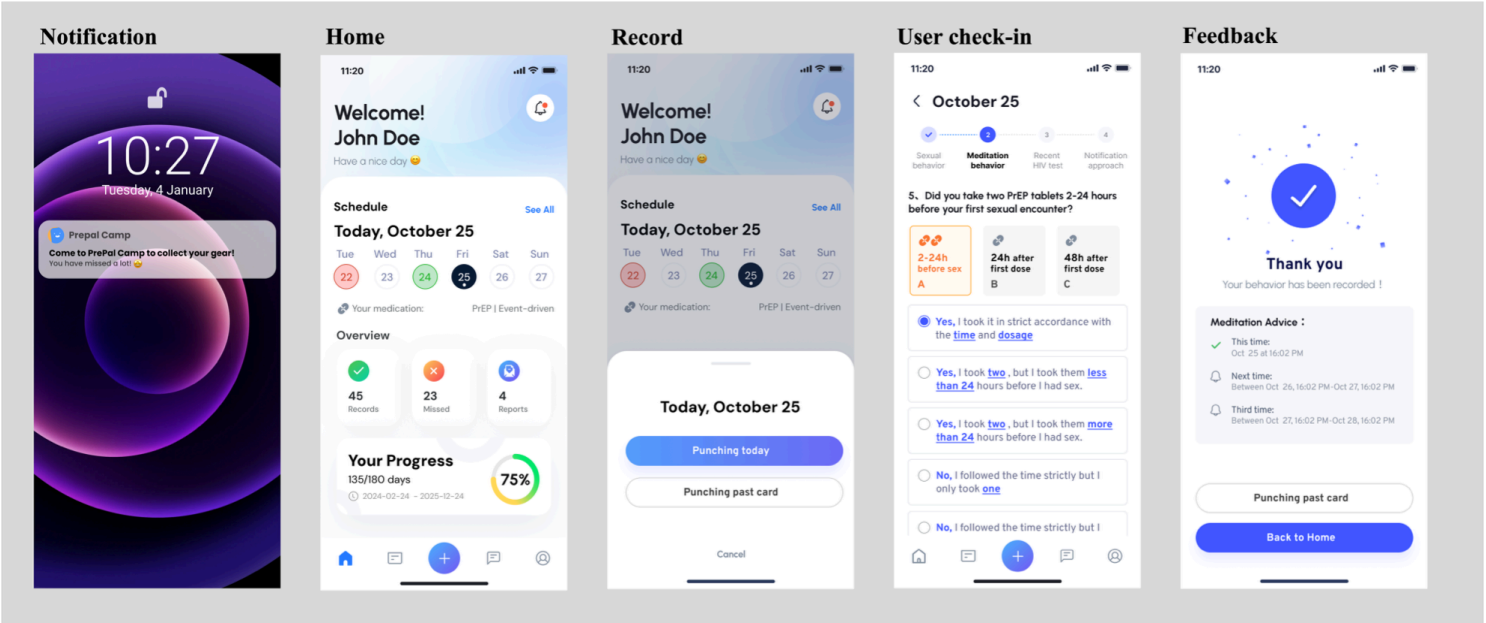
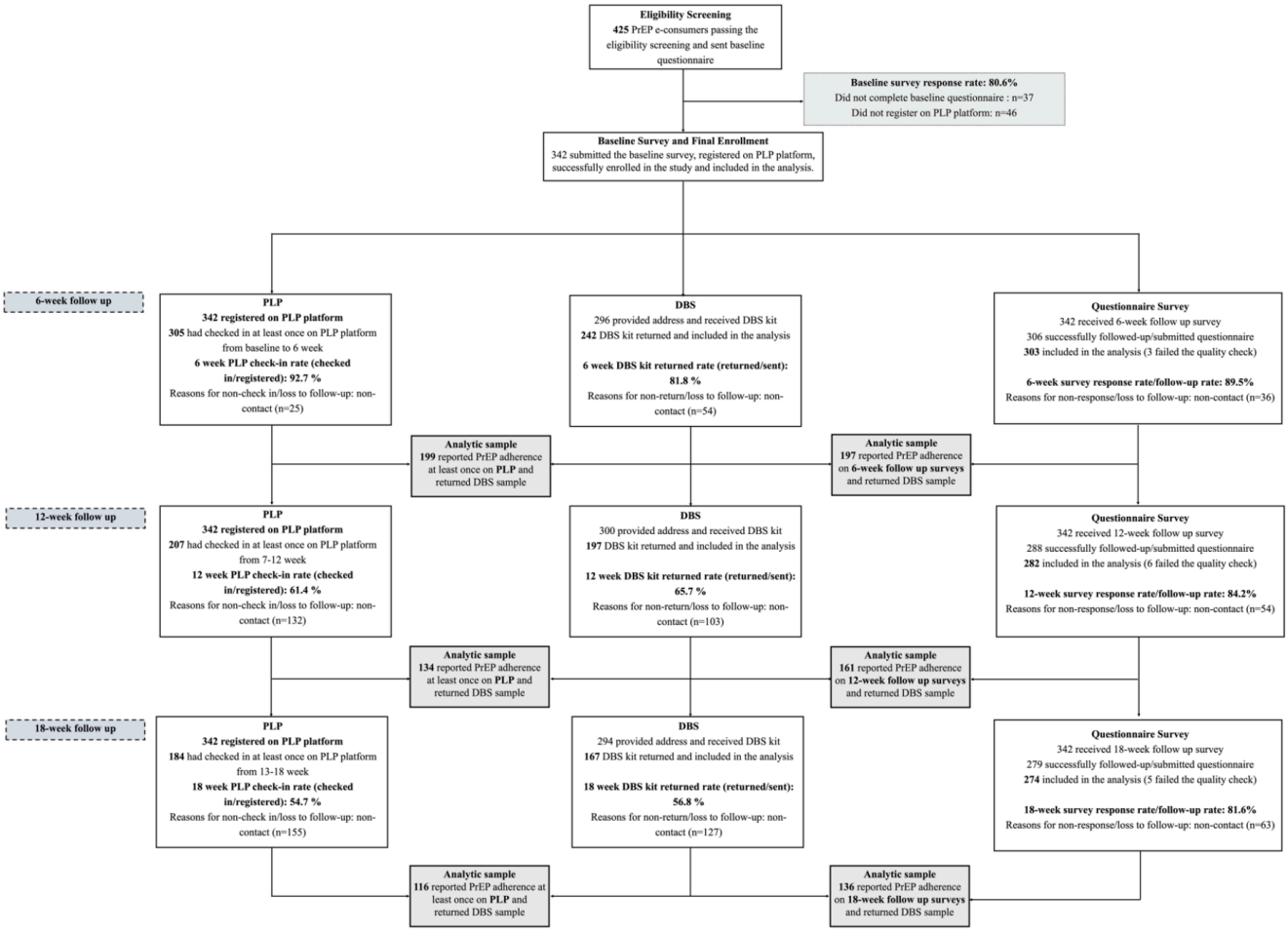



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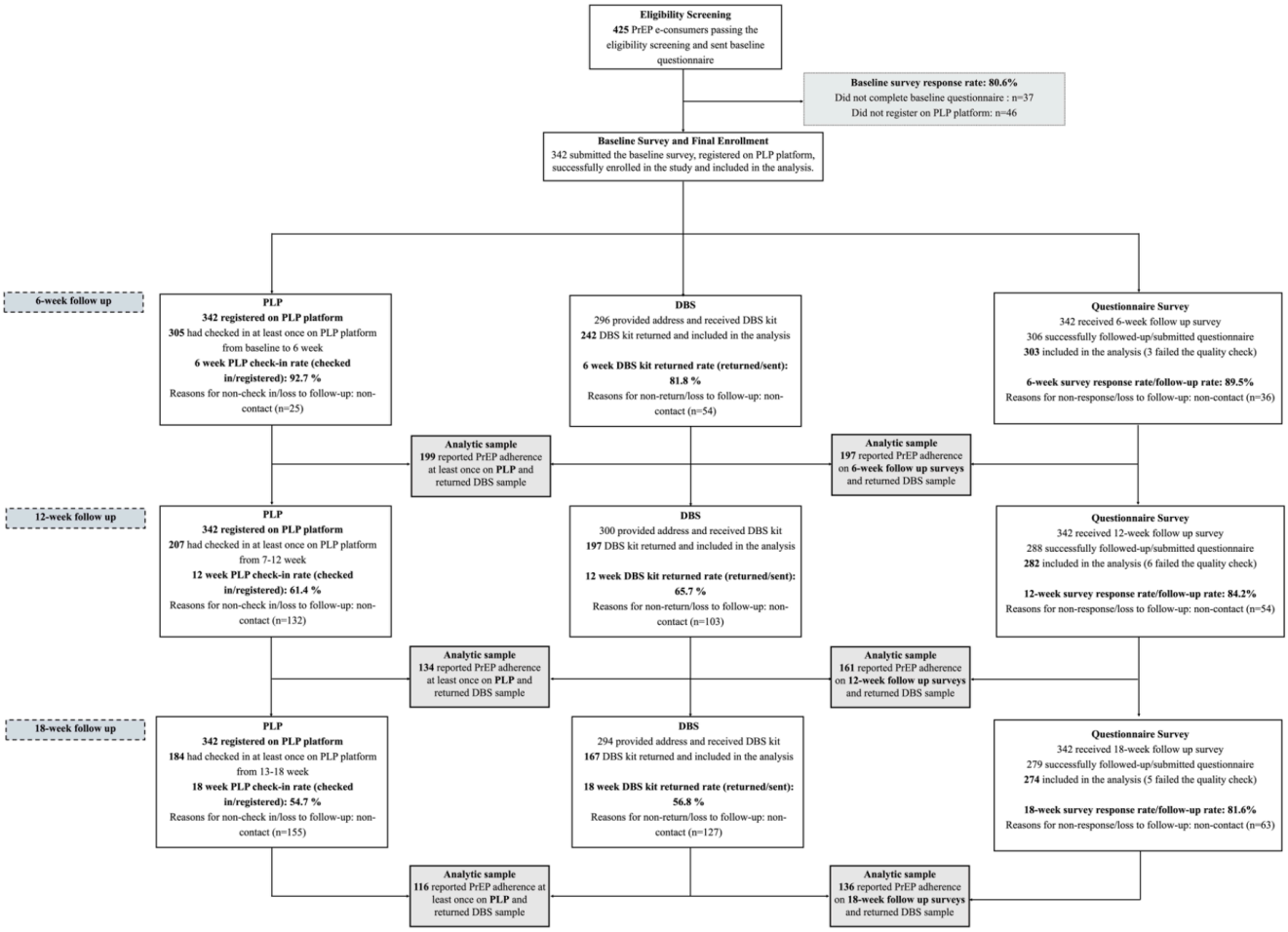
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## Figure 2

Flowchart of Study Design and Participant Follow-up.

**Figure legend:**Flow diagram of participant inclusion, follow-up, and analytic sample selection. After enrolment, participants who did not complete the baseline survey or did not register on the PLP platform were excluded. At each follow-up wave (6, 12, and 18 weeks), analytic samples were defined based on the availability of both adherence data and biological measures. For PLP-based analyses, participants were required to have at least one adherence record on the PLP platform and a returned dried blood spot (DBS) sample. For questionnaire-based analyses, participants were required to report PrEP adherence in the follow-up survey and provide a DBS sample. Separate analytic samples were therefore constructed for PLP-derived and self-reported adherence assessments. The diagram also illustrates the reduction in sample size across follow-up waves due to loss to follow-up and incomplete data.




## Figure 2

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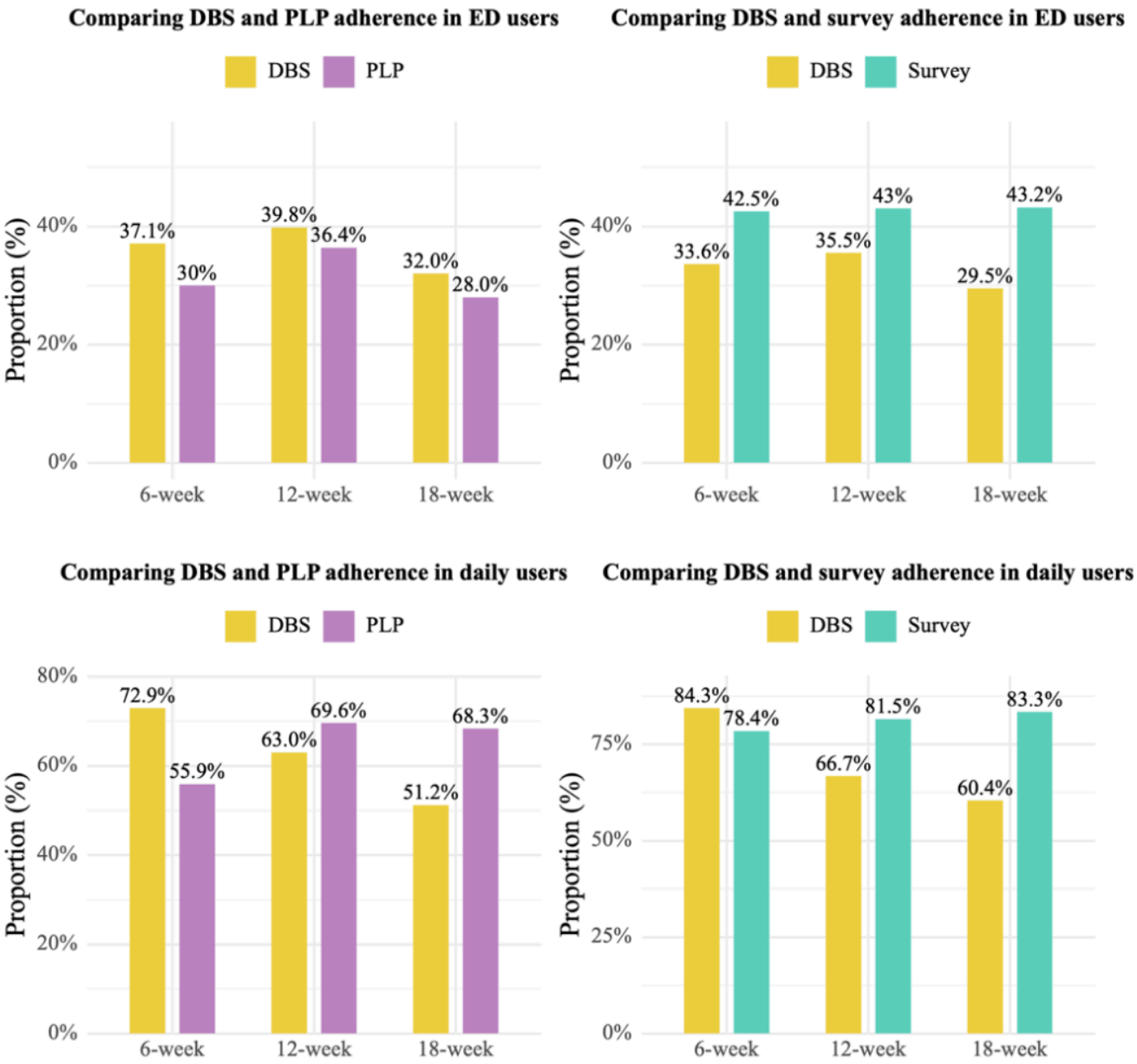



**Figure 3**

Comparison of PLP and Questionnaire Adherence with Corresponding DBS Adherence

**Figure legend:**Comparison of PrEP adherence measured by dried blood spot (DBS), the PLP platform (EMA-based monitoring), and self-reported questionnaire among event-driven (ED) and daily PrEP users at 6-, 12-, and 18-week follow-ups. Panel (a) compares DBS- and PLP-based adherence among ED users; panel (b) compares DBS- and questionnaire-based adherence among ED users; panel (c) compares DBS- and PLP-based adherence among daily users; and panel (d) compares DBS- and questionnaire-based adherence among daily users. Proportions of participants with optimal adherence are presented for each measurement approach at each follow-up time point.

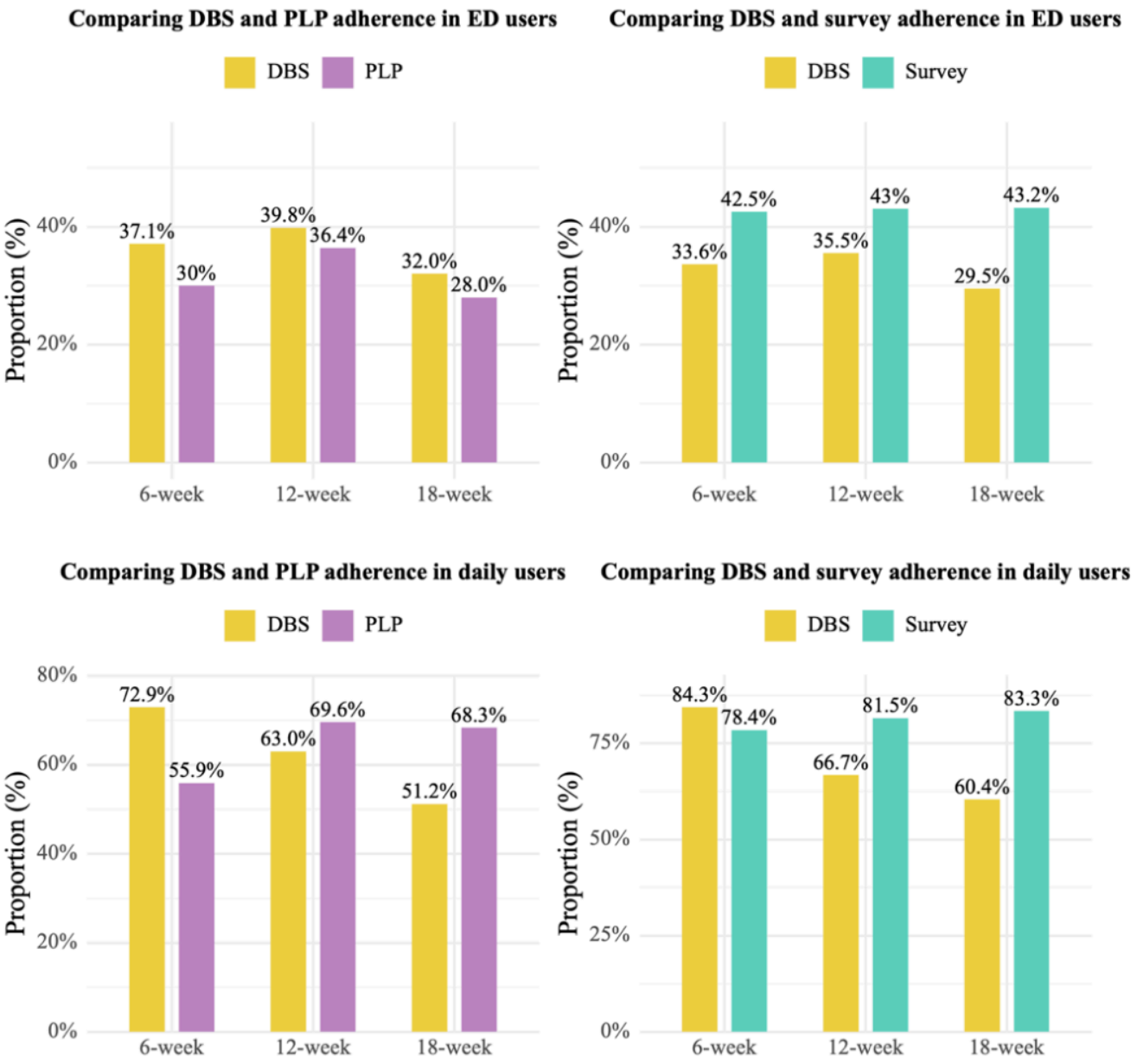



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## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTables.docx
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