**Supplement to: Improving adherence to daily PrEP among MSM in Amsterdam by providing feedback via a mobile application: results of a randomised clinical trial**

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### Changes to methods after trial design

The primary outcome in the protocol was defined as good adherence (i.e. [TFV-DP] ≥ 700 fmol/punch, however, we used its complement, poor adherence ([TFV-DP] < 700 fmol/punch), in these analyses to facilitate interpretation of results.

According to protocol participants were to be included at their 3 or 6 month study visits. Some participants were included during the 9 and 12 month study visits (n=27 and n=2, respectively). Since participants included during the 12-month study visit could not have been exposed to the intervention before the first sample was collected, these were excluded from per-protocol analyses. Participants included during their 9-month study visits were included in the per-protocol cohort.

### Sample size calculations

At the time of protocol writing, we assumed that 260 of the 376 participants (69%) would choose dPrEP, and that 210 (81%) of those would agree to participate in the RCT. Furthermore, we assumed that after taking into account loss-to-follow-up, switching to edPrEP and missing DBS, we would have data of 150 participants for analysis (n=75 in the intervention arm and n=75 in the control arm). Assuming that the proportion with good adherence would be 70% among those in the intervention arm, and 50% among those in the control arm, and using an alpha of 5%, we would have 70% power to demonstrate this difference as significant. If the proportion with good adherence would be 80% in the intervention arm and 60% in the control arm, we would have 76% power to demonstrate a significant effect. If the proportion with good adherence would be 90% in the intervention arm and 70% in the control arm, we would have 86% power to demonstrate a significant effect.

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| **Supplementary table S1**: Comparison of AMPrEP baseline characteristics between randomised participants included in primary per-protocol analysis of the RCT and those not included. AMPrEP study, Amsterdam, 2015-2016. | | | | | | | |
|  | **Total (n=227)** | | **Not included in primary analyses (n=61)** | | **Included in primary analyses (n=166)** | | **p value** |
|  | **n** | **%a** | **n** | **%a** | **n** | **%a** | **χ2** |
| **Demographic characteristics** |  |  |  |  |  |  |  |
| Age (years) |  |  |  |  |  |  |  |
| Median [IQR] | 37 | [30-47] | 36 | [27-43] | 39 | [32-47] | **0.0066†** |
| Age (categorised) |  |  |  |  |  |  | 0.13 |
| 20 to 34 | 80 | 35% | 27 | 44% | 53 | 32% |  |
| 35 to 44 | 74 | 33% | 20 | 33% | 54 | 33% |  |
| 45 to 73 | 73 | 32% | 14 | 23% | 59 | 36% |  |
| Gender identity |  |  |  |  |  |  | 0.73‡ |
| Male | 226 | 100% | 61 | 100% | 165 | 99% |  |
| Transgender woman | 1 | 0% | 0 | 0% | 1 | 1% |  |
| Self-declared ethnicity |  |  |  |  |  |  | 0.39 |
| White | 197 | 87% | 51 | 84% | 146 | 88% |  |
| Non-white | 30 | 13% | 10 | 16% | 20 | 12% |  |
| Place of residency in the Netherlands |  |  |  |  |  |  | 0.42 |
| Amsterdam | 139 | 61% | 40 | 66% | 99 | 60% |  |
| Other | 88 | 39% | 21 | 34% | 67 | 40% |  |
| Education level |  |  |  |  |  |  | 0.63 |
| No college/university | 58 | 26% | 17 | 28% | 41 | 25% |  |
| College/university | 169 | 74% | 44 | 72% | 125 | 75% |  |
| Employmentb |  |  |  |  |  |  | 0.81‡ |
| Employed | 180 | 81% | 47 | 78% | 133 | 82% |  |
| Unemployed | 7 | 3% | 2 | 3% | 5 | 3% |  |
| Other (retired, volunteer, disabled, student) | 36 | 16% | 11 | 18% | 25 | 15% |  |
| Net monthly income in Euro'sc |  |  |  |  |  |  | **0.016** |
| ≤1700 | 59 | 27% | 24 | 41% | 35 | 22% |  |
| 1701-2950 | 97 | 45% | 19 | 32% | 78 | 49% |  |
| >2950 | 61 | 28% | 16 | 27% | 45 | 28% |  |
| Living situation |  |  |  |  |  |  | **0.022** |
| Alone | 116 | 51% | 33 | 54% | 83 | 50% |  |
| With partner | 75 | 33% | 13 | 21% | 62 | 37% |  |
| With parents/flatmates | 36 | 16% | 15 | 25% | 21 | 13% |  |

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| Steady relationshipd |  |  |  | |  | |  | |  | | **0.009** | |
| No | 125 | 56% | 42 | | 70% | | 83 | | 50% | |  | |
| Yes | 100 | 44% | 18 | | 30% | | 82 | | 50% | |  | |
| Sexual preferencee |  |  |  | |  | |  | |  | | 0.91 | |
| Exclusively homosexual | 173 | 77% | 47 | | 77% | | 126 | | 76% | |  | |
| Not exclusively homosexual | 53 | 23% | 14 | | 23% | | 39 | | 24% | |  | |
|  |  |  |  | |  | |  | |  | |  | |
| **Sexual behaviour** |  |  |  | |  | |  | |  | |  | |
| Number of sex partnersf |  |  |  | |  | |  | |  | |  | |
| Median [IQR] | 18 | [10-33] | 16 | | [10-30] | | 20 | | [10-36] | | 0.39† | |
| Number of condomless anal sex episodes with casual partnersf | | | | | | |  | |  | |  | |
| Median [IQR] | 11 | [5-24] | | 10 | | [4-18] | | 12 | | [5-24] | | 0.36† | |
| Sexually transmitted infectionsg |  |  | |  | |  | |  | |  | | 0.93 | |
| No | 135 | 59% | | 36 | | 59% | | 99 | | 60% | |  | |
| Yes | 92 | 41% | | 25 | | 41% | | 67 | | 40% | |  | |
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| **Mental health characteristics and drug use** |  |  | |  | |  | |  | |  | |  | |
| Sexual compulsivity scale |  |  | |  | |  | |  | |  | | 0.26 | |
| Score <24 (no indication of sexual compulsivity) | 172 | 76% | | 43 | | 70% | | 129 | | 78% | |  | |
| Score ≥24 (indication of sexual compulsivity) | 55 | 24% | | 18 | | 30% | | 37 | | 22% | |  | |
| Chemsexh |  |  | |  | |  | |  | |  | | 0.081 | |
| No | 121 | 54% | | 27 | | 44% | | 94 | | 57% | |  | |
| Yes | 104 | 46% | | 34 | | 56% | | 70 | | 43% | |  | |
| Depression or anxiety symptoms |  |  | |  | |  | |  | |  | | **0.006** | |
| MHI5 score ≥60 (no symptoms)i | 189 | 83% | | 44 | | 72% | | 145 | | 87% | |  | |
| MHI5 score <60 (symptoms)j | 38 | 17% | | 17 | | 28% | | 21 | | 13% | |  | |
| Alcohol use disorder identification test (AUDIT)e |  |  | |  | |  | |  | |  | | 0.76 | |
| Score <8 (no indication)k | 159 | 70% | | 42 | | 69% | | 117 | | 71% | |  | |
| Score ≥8 (indication)l | 67 | 30% | | 19 | | 31% | | 48 | | 29% | |  | |
| Drug use disorder identification test (DUDIT) |  |  | |  | |  | |  | |  | | 0.23 | |
| Score <8 (no indication)m | 130 | 57% | | 31 | | 51% | | 99 | | 60% | |  | |
| Score ≥8 (indication)n | 97 | 43% | | 30 | | 49% | | 67 | | 40% | |  | |
| Level of concern about acquiring HIVo |  |  | |  | |  | |  | |  | | 0.59 | |
| Low | 36 | 16% | | 11 | | 18% | | 25 | | 15% | |  | |
| Neutral to high | 191 | 84% | | 50 | | 82% | | 141 | | 85% | |  | |

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| Level of importance to prevent HIVo |  |  | | |  |  | | |  | | |  | | 0.63 | |
| Less than very important | 58 | 26% | | | 17 | 28% | | | 41 | | | 25% | |  | |
| Very important | 169 | 74% | | | 44 | 72% | | | 125 | | | 75% | |  | |
| Treatment for HCV infection during AMPrEP follow-upp | |  | | |  |  | | |  | | |  | | **0.0040‡** | |
| No | 215 | 95% | | | 53 | 87% | | | 162 | | | 98% | |  | |
| Yes | 12 | 5% | | | 8 | 13% | | | 4 | | | 2% | |  | |
| Yes, during RCT | 7 | 3% | | | 7 | 11% | | | 0 | | | 0% | |  | |
|  |  |  | | |  |  | | |  | | |  | |  | |
| **Allocation and regimen** |  |  | | |  |  | | |  | | |  | |  | |
| RCT allocation |  |  | | |  |  | | |  | | |  | | 0.58 | |
| Regular app | 111 | 49% | | | 28 | 46% | | | 83 | | | 50% | |  | |
| Extended app | 116 | 51% | | | 33 | 54% | | | 83 | | | 50% | |  | |
| PrEP regimen at AMPrEP baseline |  |  | | |  |  | | |  | | |  | | 0.86 | |
| Event-driven | 16 | 7% | | | 4 | 7% | | | 12 | | | 7% | |  | |
| Daily | 211 | 93% | | | 57 | 93% | | | 154 | | | 93% | |  | |
|  |  |  |  |  | | | |  | | |  | |  | |
| AMPrEP: Amsterdam PrEP demonstration project; PrEP: pre-exposure prophylaxis; IQR, interquartile range; MHI5: Mental Health Inventory-5; mo: months; RCT: randomised clinical trial; HCV: Hepatitis C Virus. | | | | | | | | | | | | |  | |
|  |  |  |  |  | | |  | | |  | | |  | |
| a Percentages may not total 100 due to rounding; b 4 missing; c 10 missing; d 2 missing; e 1 missing; f In the past 3 months prior to inclusion into AMPrEP; g Chlamydia, gonorrhoea and/or syphilis within 6 months prior to inclusion into AMPrEP; h Use of γ-hydroxybutyrate, γ-Butyrolactone, methamphetamine or mephedrone prior to or during sex in the 3 months prior to inclusion into AMPrEP, 2 missing; i No indication of an anxiety or depressive mood disorder; j Indication of an anxiety or depressive mood disorder; k No indication of an alcohol use disorder; l Indication of an alcohol use disorder; m No indication of a drug use disorder; n Indication of a drug use disorder; o Scale 1-7, dichotomised; p HCV treatment with direct-acting antivirals has shown to increase intracellular tenofovir diphosphate levels, therefore participants using these drugs during the RCT were excluded from primary analyses, †p-value calculated with Two-sample Wilcoxon rank-sum Mann-Whitney test, ‡p-value calculated with Fisher's exact test | | | | | | | | | | | | |  | |

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| **Supplementary table S2:** Baseline characteristics associated with excellent adherence ([TFV-DP] ≥ 1250 fmol/punch in DBS at 12 and 24 months); results of logistic regression analysis. AMPrEP study, Amsterdam, 2015-2018. | | | | | |
|  | **Univariable** | | | |
|  | **Excellent adherencea** | **OR** | **(95% CI)** | **p value** |
| Overall | 66/166 (40%) |  |  |  |
| **Demographic characteristics** |  |  |  |  |
| Age (per 10 years) |  | 1.1 | (0.86 to 1.5) | 0.40 |
| Age (categorised) |  |  |  |  |
| 20 to 34 | 19/56 (34%) | 1 |  | 0.49 |
| 35 to 44 | 23/51 (45%) | 1.6 | (0.73 to 3.5) |  |
| 45 to 73 | 24/59 (41%) | 1.3 | (0.63 to 2.9) |  |
| Gender identity |  |  |  |  |
| Male | 65/165 (39%) |  |  |  |
| Transgender woman | 1/1 (100%) |  |  |  |
| Self-declared ethnicity |  |  |  |  |
| White | 57/146 (39%) | 1 |  | 0.61 |
| Non-white | 9/20 (45%) | 1.3 | (0.50 to 3.3) |  |
| Place of residency in the Netherlands |  |  |  |  |
| Amsterdam | 42/99 (42%) | 1 |  | 0.39 |
| Other | 24/67 (36%) | 0.76 | (0.40 to 1.4) |  |
| Education level |  |  |  |  |
| No college/university | 17/41 (41%) | 1 |  | 0.80 |
| College/university | 49/125 (39%) | 0.91 | (0.44 to 1.9) |  |
| Employmentb |  |  |  |  |
| Employed | 53/133 (40%) | 1 |  | 1.0 |
| Unemployed | 2/5 (40%) | 1.0 | (0.16 to 6.2) |  |
| Other (retired, volunteer, disabled, student) | 10/25 (40%) | 1.0 | (0.42 to 2.4) |  |
| Net monthly income in Euro'sc |  |  |  |  |
| ≤1700 | 13/35 (37%) | 1 |  | 0.73 |
| 1701-2950 | 34/78 (44%) | 1.3 | (0.58 to 3.0) |  |
| >2950 | 17/45 (38%) | 1.0 | (0.41 to 2.6) |  |
| Living situation |  |  |  |  |
| Alone | 36/83 (43%) | 1 |  | 0.28 |
| With partner | 25/62 (40%) | 0.88 | (0.45 to 1.7) |  |
| With parents/flatmates | 5/21 (24%) | 0.41 | (0.14 to 1.2) |  |

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| Steady relationshipd |  |  |  |  |
| No | 34/83 (41%) | 1 |  | 0.80 |
| Yes | 32/82 (39%) | 0.92 | (0.49 to 1.7) |  |
| Sexual preferencee |  |  |  |  |
| Exclusively homosexual | 46/126 (37%) | 1 |  | 0.10 |
| Not exclusively homosexual | 20/39 (51%) | 1.8 | (0.89 to 3.8) |  |
|  |  |  |  |  |
| **Sexual behaviour** |  |  |  |  |
| Sexually transmitted infectionsf |  |  |  |  |
| No | 41/99 (41%) | 1 |  | 0.60 |
| Yes | 25/67 (37%) | 0.84 | (0.45 to 1.6) |  |
| Number of sex partnersg |  | 1.0 | (0.99 to 1.0) | 0.72 |
| Number of condomless anal sex episodes with casual partnersg | | 1.0 | (0.99 to 1.0) | 0.63 |
|  |  |  |  |  |
| **Mental health characteristics and drug use** |  |  |  |  |
| Sexual compulsivity scale |  |  |  |  |
| Score <24 (no indication of sexual compulsivity) | 56/129 (43%) | 1 |  | 0.076 |
| Score ≥24 (indication of sexual compulsivity) | 10/37 (27%) | 0.48 | (0.22 to 1.1) |  |
| Chemsexh |  |  |  |  |
| No | 45/94 (48%) | 1 |  | 0.022 |
| Yes | 21/70 (30%) | 0.47 | (0.24 to 0.90) |  |
| Depression or anxiety symptoms |  |  |  |  |
| MHI5 score ≥60 (no symptoms)i | 59/145 (41%) | 1 |  | 0.52 |
| MHI5 score <60 (symptoms)j | 7/21 (33%) | 0.73 | (0.28 to 1.9) |  |
| Alcohol use disorder identification test (AUDIT)e |  |  |  |  |
| Score <8 (no indication) | 45/117 (38%) | 1 |  | 0.53 |
| Score ≥8 (indication)l | 21/48 (44%) | 1.2 | (0.63 to 2.5) |  |
| Drug use disorder identification test (DUDIT) |  |  |  |  |
| Score <8 (no indication) | 42/99 (42%) | 1 |  | 0.39 |
| Score ≥8 (indication)n | 24/67 (36%) | 0.76 | (0.40 to 1.4) |  |
| Level of concern about acquiring HIVo |  |  |  |  |
| Low | 10/25 (40%) | 1 |  | 0.98 |
| Neutral to high | 56/141 (40%) | 0.99 | (0.41 to 2.4) |  |
| Level of importance to prevent HIVo |  |  |  |  |
| Less than very important | 17/41 (41%) | 1 |  | 0.80 |
| Very important | 49/125 (39%) | 0.91 | (0.44 to 1.9) |  |
|  |  |  |  |  |
| **RCT allocation** |  |  |  |  |
| Standard app | 26/83 (31%) | 1 |  | 0.027 |
| Extended app | 40/83 (48%) | 2.0 | (1.1 to 3.8) |  |
|  |  |  |  |  |
| AMPrEP: Amsterdam PrEP demonstration project; PrEP: pre-exposure prophylaxis; IQR, interquartile range; MHI5: Mental Health Inventory-5; mo: months; RCT: randomised clinical trial. | | | | | | | |
|  |  |  |  |  |  |  |  |
| a Percentages may not total 100 due to rounding; b 3 missing; c 8 missing; d 1 missing; e 1 missing; f Chlamydia, gonorrhoea and/or syphilis within 6 months prior to inclusion into AMPrEP; g In the past 3 months prior to inclusion into AMPrEP, OR per increase of 1 of the natural log of the number of sex partners/episodes; h Use of γ-hydroxybutyrate, γ-Butyrolactone, methamphetamine or mephedrone prior to or during sex in the 3 months prior to inclusion into AMPrEP, 2 missing; i No indication of an anxiety or depressive mood disorder; j Indication of an anxiety or depressive mood disorder; k No indication of an alcohol use disorder; l Indication of an alcohol use disorder; m No indication of a drug use disorder; n Indication of a drug use disorder; o Scale 1-7, dichotomised. | | | | | | | |