Additional file 2 –Differential loss-to-follow-up and motives for study discontinuation in the EZI-PrEP study (the Netherlands, 2021-2024)

Aim

We examined differential attrition in order to determine the need for applying inverse probability of censoring weights to adjust for differential attrition.

Methods

We used Cox proportional hazards regression to identify factors associated with early study discontinuation and to evaluate differences in attrition between the 6-monthly and 3-monthly monitoring group. Early study discontinuation was defined as not having completed the month 24 study visit. Discontinuation events were timed to the last recorded visit.

We included the following variables as candidate determinants for early study discontinuation: age in years (continuous), being born in the Netherlands (yes/no), completing or pursuing a university or university of applied sciences degree (yes/no), having used PrEP in the 12 months preceding enrolment (yes/no), number of sex partners in the 6 months preceding enrolment (continuous, log-transformed), reporting group sex in the 6 months preceding enrolment (yes/no), reporting chemsex in the 6 months preceding enrolment (yes/no), having any bacterial STI at the enrolment visit (yes/no), Patient Health Questionnaire (PHQ-9) score (continuous), Sexual Compulsivity Scale (SCS) score (continuous), Alcohol Use Disorders Identification Test (AUDIT) score (continuous), Drug Use Disorders Identification Test (DUDIT) score (≥8 versus <8). We included DUDIT score as a binary variable because hazards were non-proportional when including DUDIT score as a continuous variable. We included all variables as time-stable variables, based on the enrolment visit.

We estimated univariable hazard ratios (HR) along with 95% confidence intervals (CI) to identify determinants of early study discontinuation. We then added an interaction term for monitoring frequency to examine whether the association between determinants and study discontinuation differed by monitoring frequency. If a candidate determinant was associated with study discontinuation (i.e., p-value in univariable regression was <0.05) and the association differed by monitoring frequency (i.e., p-value for interaction was <0.05), we examined the association between the determinant and the primary outcome of our study (i.e., incidence of grouped bacterial chlamydia, gonorrhea, and syphilis) using Poisson regression.

We described self-reported reasons for early study discontinuation.

Results

Monitoring frequency group (i.e., 6-monthly *versus* 3-monthly) was not associated with early study discontinuation (HR=0.95 , 95%CI=0.66-1.36) (Table). Income below the minimum wage and a higher score on the PHQ-9 were associated with a shorter time until study discontinuation. Older age and having used PrEP in the 12 months preceding enrolment were associated with a longer time until study discontinuation. For none of the determinants assessed, the association with study discontinuation differed by monitoring frequency (Table).

Conclusion

We observed no evidence for differential attrition. Therefore, we did not perform inverse probability of censoring weighing to avoid differential attrition bias.

Table 1. Determinants of time until early study discontinuation from the EZI-PrEP study, the Netherlands (2021-2024): results from Cox regression analysis.

	Univariable association for determinant		Interaction term for determinant* 6-monthly monitoring frequency	
Determinant	HR [95%CI]	p-value	HR [95%CI]	p-value
Study arm				
6-monthly monitoring frequency (*vs* 3-monthly)	0.95 [0.66-1.36]	0.76	N/A	
Sociodemographic characteristics				
Age (per 10 years)	0.69 [0.57-0.82]	<0.0001	0.82 [0.57-.18]	0.28
Born in the Netherlands	1.00 [0.68-1.47]	0.99	0.84 [0.39-1.84]	0.67
Completed or pursuing a university or applied sciences degree	0.73 [0.47-1.13]	0.15	0.80 [0.33-1.91]	0.61
Income below minimum wage[1]	2.06 [1.33-3.18]	0.0011	0.87 [0.36-2.07]	0.75
PrEP use				
Used PrEP in 12 months prior to enrolment	0.45 [0.28-0.71]	0.00062	1.12 [0.45-2.82]	0.80
Intention to use PrEP daily until next monitoring visit	0.83 [0.55-1.24]	0.37	1.03 [0.66-1.61]	0.90
Sexual behaviour in the 6 months preceding enrolment				
Number of sex partners, log-transformed	1.14 [0.94-1.37]	0.18	0.74 [0.31-1.76]	0.50
Had group sex	1.04 [0.73-1.51]	0.80	1.20 [0.57-2.49]	0.63
Had chemsex 10[2]	0.80 [0.51-1.24]	0.31	1.07 [0.44-2.60]	0.89
Bacterial STI diagnoses at enrolment				
Any bacterial STI[3]	1.15 [0.73-1.82]	0.55	1.22 [0.54-3.33]	0.54
Mental wellbeing				
PHQ-9 score (per 3 points increase)	1.20 [1.07-1.33]	0.0010	1.09 [0.87-1.37]	0.45
SCS score (per 5 points increase)	0.99 [0.83-1.19]	0.95	1.09 [0.78-1.55]	0.63
AUDIT score (per 5 point increase)	1.16 [0.97-1.39]	0.10	0.83 [0.58-1.20]	0.33
DUDIT score ≥8 (vs <8)	1.28 [0.86-1.89]	0.22	0.95 [0.44-2.09]	0.91

Abbreviations: AUDIT, alcohol use disorders identification test; DUDIT, drug use disorders identification test; EZI-PrEP, e-health for zero infections-PrEP; PHQ, patient health questionnaire; PrEP, pre-exposure prophylaxis; IQR, interquartile range; SCS, sexual compulsivity scale; STI, sexually transmitted infection;

1. Minimum wage 2021: €1701 gross monthly income. https://www.rijksoverheid.nl/onderwerpen/minimumloon/bedragen-minimumloon/bedragen-minimumloon-2021.

2. Chemsex: sex under influence of one or more of the following drugs: crystal meth ('Tina'); mephedrone ('miau miau'); GHB/GBL; ketamine.

3. Any diagnosis for gonorrhea, chlamydia, or infectious syphilis (i.e., stage 1, stage 2, or early latent syphilis).