

Supplementary Materials

Hepatitis C virus infection is uncommon at baseline and during follow-up among individuals using PrEP in the Dutch national PrEP program between 2019-2022.

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Appendix A. Detailed information about collected data on HCV infections over time.

During 2019-2020, available data on HCV infection indicated a positive or negative HCV test. When positive, information regarding the presence of infectious viral particles was collected. In 2021, positive HCV tests were categorized into recent (seroconversion ≤ 12 months ago), chronic (seroconversion > 12 months ago), spontaneously cleared/treated HCV infection or HCV stage unknown. Additionally, information regarding the presence of infectious viral particles was collected. In 2022, positive HCV tests were categorized into infectious, spontaneously cleared/treated and stage unknown.

Supplementary Table 1. Summary of the available data and reconstructed data on anti-HCV and HCV-RNA

Available data		Reconstructed data	
Variable levels		Anti-HCV	HCV-RNA
2019-2020 ^a			
HCV negative	Infectious (NA)	Negative	Negative
HCV positive	Infectious (yes)	Positive	Positive
HCV positive	Infectious (no)	Positive	Negative
HCV positive	Infectious (missing/not tested)	Positive	Missing
2021 ^a			
HCV negative	Infectious (NA)	Negative	Negative
HCV recent infection	Infectious (yes)	Positive	Positive
HCV recent infection	Infectious (no)	Positive	Negative
HCV recent infection	Infectious (missing/not tested)	Positive	Missing
HCV chronic infection	Infectious (yes)	Positive	Positive
HCV chronic infection	Infectious (missing/not tested)	Positive	Missing
HCV spontaneously cleared or treated		Positive	Negative
HCV status unknown	Infectious (yes)	Positive	Positive
HCV status unknown	Infectious (no)	Positive	Negative
HCV status unknown	Infectious (missing/not tested)	Positive	Missing
2022 ^a			
HCV negative		Negative	Negative
HCV infectious		Positive	Positive
HCV spontaneously cleared or treated		Positive	Negative
HCV status unknown		Positive	Missing

Explanation of variables: During 2019-2020, HCV infection indicated an individual had tested positive or negative for HCV, and if positive, information regarding the infection being infectious was provided, albeit often not assessed or left missing. In 2021, positive HCV tests were categorized into recent (≤ 12 months), chronic (> 12 months), spontaneously cleared or treated HCV infection or HCV stage unknown along with whether the infection was infectious. In 2022, positive HCV tests were categorized into infectious, spontaneously cleared or treated and stage unknown.

^a Date collected during this calendar year.

Abbreviations: HCV, Hepatitis C virus; NA, Not applicable; RNA, Ribonucleic acid.

Supplementary Table 2. Summary of determinants being evaluated of prevalent and incident HCV infection

Determinant	Determinant categories	Evaluated for prevalent or incident analysis or both	Time-fixed or time-updated
Use of PrEP in the preceding 12 months before the first visit in the NPP	Yes vs. no	Prevalent analysis	NA
Age (in years)	NA	Both	Time-updated
Key population	MSM vs. transgender person	Both	Time-fixed
Region of origin	Dutch vs. other than Dutch	Both	Time-fixed
Educational level	<college degree vs. ≥college degree	Both	Time-fixed
PrEP regimen choice at first visit	Daily vs. event-driven	Prevalent analysis	NA
PrEP regimen ^{12M}	Daily vs. event-driven	Incident analysis	Time-updated
Number of sex partners (continuous) ^{6M}	NA	Both	Time-updated
Receptive CAS ^{6M}	Yes vs. no	Both	Time-updated
Sex work ^{6M}	Yes vs. no	Both	Time-updated
Diagnosed with an anal gonorrhoea/chlamydia or syphilis infection at each visit	Yes vs. no	Both	Time-updated
IDU ^{6M}	Yes vs. no	Both	Time-updated
Chemsex ^{a,6M}	Yes vs. no	Both	Time-updated

All determinants were self-reported, except for STI diagnosis.

^a Defined as the use of methamphetamine, GHB/GBL and/or mephedrone before or during sex

Abbreviations: CAS, condomless anal sex; GBL, γ -butyrolactone; GHB, γ -hydroxybutyric acid; HCV, hepatitis C virus; IDU, injecting drug use; MSM; men who have sex with men; NA, not applicable; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection; 6M, in the preceding 6 months; 12M, in the preceding 12 months

Supplementary Table 3. Description of the number of missing values for imputed variables

Imputed variable	Number of missing observations ^a	Number of individuals with ≥ 1 missing observations ^b
Region of origin	15 (0.02)	4 (0.04)
Educational level	2,669 (4.0)	484 (4.9)
Receptive CAS	1,132 (1.7)	930 (9.4)
Reporting sex work	2,634 (4.0)	1,922 (19.5)
IDU	42,475 (64.2)	8,922 (90.6)

^a The denominator represents the total count of observations included in the longitudinal analyses, which is a total of 66,170 observations.

^b The denominator represents the total number of individuals included in the longitudinal analyses, which is a total of 9,851 individuals.

Abbreviations: CAS, Condomless anal sex; IDU, Injecting drug use

Supplementary Table 4. Univariable determinants of past/current prevalent HCV infection at baseline combining chemsex and group sex among individuals enrolled in the Dutch national PrEP program between July 2019 and December 2022

	Total (n=10,563)		
	OR ^a	(95% CI)	p
Age per 10 years, continuous	1.57	1.31-1.88	<0.01
Key population			
MSM	Ref		0.24
Transgender	2.03	0.63-6.49	
Region of origin			
Dutch	Ref		0.34
Non-Dutch	1.28	0.78-2.11	
Educational level			
At least college degree	Ref		0.41
Less than college degree	0.80	0.46-1.38	
Use of PrEP before enrollment	3.03	1.79-5.13	<0.01
Choice of PrEP regimen			
Daily	Ref		0.62
Event driven	1.12	0.68-1.86	
Missing	1.18	0.42-3.36	
Number of sex partners per ln(n+1) increase^{6M}	1.10	0.92-1.33	0.29
Receptive CAS^{6M}	2.73	1.25-5.98	0.01
Reporting chemsex^b/group sex^{6M}	3.21	1.61-6.41	<0.01
Reporting sexwork^{6M}	0.67	0.16-2.76	0.58
STI diagnosis^c	2.37	1.29-4.37	<0.01
IDU^{6M}	6.61	2.35-18.61	<0.01

^a Indicates the relative increase or decrease in odds for each socio-economic characteristic or sexual behavior when present at NPP consultation visit.

^b Defined as the use of methamphetamine, GHB/GBL and/or mephedrone before or during sex.

^c Diagnosed with an anal chlamydia/gonorrhea or a syphilis infection at visit.

Abbreviations: CAS, Condomless anal sex; CI, Confidence interval; HCV, Hepatitis C virus; IDU, Injecting drug use; ln, natural log; OR, Odds ratio; MSM, Men who have sex with men; PrEP, Pre-exposure prophylaxis; Ref, Reference category; STI, Sexually transmitted infection; 6M, during the previous six months.

Supplementary Table 5. Univariable determinants of past/current prevalent HCV infection at baseline separating STI diagnosis among individuals enrolled in the Dutch national PrEP program between July 2019 and December 2022

	Total (n=10,563)		
	OR ^a	(95% CI)	p
Age per 10 years, continuous	1.57	1.31-1.88	<0.01
Key population			
MSM	Ref		0.24
Transgender	2.03	0.63-6.49	
Region of origin			
Dutch	Ref		0.34
Non-Dutch	1.28	0.78-2.11	
Educational level			
At least college degree	Ref		0.41
Less than college degree	0.80	0.46-1.38	
Use of PrEP before enrollment	3.03	1.79-5.13	<0.01
Choice of PrEP regimen			
Daily	Ref		0.62
Event driven	1.12	0.68-1.86	
Missing	1.18	0.42-3.36	
Number of sex partners per ln(n+1) increase^{6M}	1.10	0.92-1.33	0.29
Receptive CAS^{6M}	2.73	1.25-5.98	0.01
Reporting chemsex^b/group sex^{6M}	3.21	1.61-6.41	<0.01
Reporting sexwork^{6M}	0.67	0.16-2.76	0.58
Anal gonorrhea/chlamydia diagnosis	1.98	0.90-4.35	0.09
Syphilis diagnosis	2.16	0.67-6.93	0.20
IDU^{6M}	6.61	2.35-18.61	<0.01

^a Indicates the relative increase or decrease in odds for each socio-economic characteristic or sexual behavior when present at NPP consultation visit.

^b Defined as the use of methamphetamine, GHB/GBL and/or mephedrone before or during sex.

Abbreviations: CAS, Condomless anal sex; CI, Confidence interval; HCV, Hepatitis C virus; IDU, Injecting drug use; ln, natural log; OR, Odds ratio; MSM, Men who have sex with men; PrEP, Pre-exposure prophylaxis; Ref, Reference category; STI, Sexually transmitted infection; 6M, during the previous six months.

Supplementary Table 6. Univariable determinants of past/current prevalent HCV infection at baseline among complete cases enrolled in the Dutch national PrEP program between July 2019 and December 2022

	Total (n=10,563)		
	OR ^a	(95% CI)	<i>p</i>
Age per 10 years, continuous	1.57	1.31-1.88	<0.01
Key population			
MSM	Ref		0.24
Transgender	2.03	0.63-6.49	
Region of origin			
Dutch	Ref		0.34
Non-Dutch	1.28	0.78-2.10	
Educational level			
At least college degree	Ref		0.45
Less than college degree	0.81	0.47-1.40	
Use of PrEP before enrollment	3.03	1.79-5.13	<0.01
Choice of PrEP regimen			
Daily	Ref		0.62
Event driven	1.12	0.68-1.86	
Missing	1.18	0.42-3.36	
Number of sex partners per ln(n+1) increase^{6M}	1.10	0.92-1.33	0.29
Receptive CAS^{6M}	2.68	1.22-5.88	0.01
Reporting chemsex^b/groupsex^{6M}	2.44	1.49-3.99	<0.01
Reporting sexwork^{6M}	0.67	0.16-2.74	0.58
STI diagnosis^c	2.37	1.29-4.37	<0.01
IDU^{6M}	6.47	2.63-15.90	<0.01

^a Indicates the relative increase or decrease in odds for each socio-economic characteristic or sexual behavior when present at NPP consultation visit.

^b Defined as the use of methamphetamine, GHB/GBL and/or mephedrone before or during sex.

^c Diagnosed with an anal chlamydia/gonorrhea or a syphilis infection at visit.

Abbreviations: CAS, Condomless anal sex; CI, Confidence interval; HCV, Hepatitis C virus; IDU, Injecting drug use; ln, natural log; OR, Odds ratio; MSM, Men who have sex with men; PrEP, Pre-exposure prophylaxis; Ref, Reference category; STI, Sexually transmitted infection; 6M, during the previous six months.

Supplementary Table 7. Univariable determinants of incident HCV infection separating STI diagnosis among individuals enrolled in the Dutch national PrEP program between July 2019 and December 2022.

	IRR ^a	Total (n=9,851) (95% CI)	p
Age per 10 years, continuous	1.19	0.98-1.44	0.08
Key population			
MSM	Ref		0.81
Transgender	0.79	0.11-5.68	
Region of origin			
Dutch	Ref		0.45
Non-Dutch	1.22	0.73-2.05	
Educational level			
At least college degree	Ref		0.22
Less than college degree	0.68	0.37-1.26	
PrEP regimen^{12M}			
Daily	Ref		0.34
Event driven	0.79	0.48-1.31	
Missing	^b		
Number of sex partners per ln(n+1) increase^{6M}	0.93	0.74-1.17	0.56
Receptive CAS^{6M}	2.59	1.12-6.02	0.03
Reporting chemsex^c/group sex^{6M}	1.83	1.01-3.30	0.05
Reporting sex work^{6M}	^d		
Anal gonorrhoea/chlamydia diagnosis	2.32	1.18-4.55	0.02
Syphilis diagnosis	2.45	0.77-7.80	0.13
IDU^{6M}	6.15	2.20-17.18	<0.01

^a Indicates the relative increase or decrease in IR for each socio-economic characteristic or sexual behavior when present at NPP consultation visit.

^b No incident HCV infections were among those who identified as transgender and whose PrEP regimen was missing at any of the consultation visits.

^c Defined as the use of methamphetamine, GHB/GBL and/or mephedrone before or during sex.

^d Sex work was excluded because all incident infections were among those who did not report sex work.

Abbreviations: CAS, Condomless anal sex; CI, Confidence interval; HCV, Hepatitis C virus; IDU, Injecting drug use; IRR, Incidence rate ratio; ln, natural log; MSM, Men who have sex with men; Pre-exposure prophylaxis; Ref, Reference category; STI, Sexually transmitted infection; 6M, during the previous six months; 12M, during the previous twelve months.

Supplementary Table 8. Univariable determinants of incident HCV infection combining chemsex and group sex among individuals enrolled in the Dutch national PrEP program between July 2019 and December 2022.

	IRR ^a	Total (n=9,851) (95% CI)	p
Age per 10 years, continuous	1.19	0.98-1.44	0.08
Key population			
MSM	Ref		0.81
Transgender	0.79	0.11-5.68	
Region of origin			
Dutch	Ref		0.45
Non-Dutch	1.22	0.73-2.05	
Educational level			
At least college degree	Ref		0.22
Less than college degree	0.68	0.37-1.26	
PrEP regimen^{12M}			
Daily	Ref		0.34
Event driven	0.79	0.48-1.31	
Missing	^b		
Number of sex partners per ln(n+1) increase^{6M}	0.93	0.74-1.17	0.56
Receptive CAS^{6M}	2.59	1.12-6.02	0.03
Reporting chemsex^c/group sex^{6M}	1.83	1.01-3.30	0.05
Reporting sex work^{6M}	^d		
STI diagnosis^e	1.96	1.07-3.60	0.03
IDU^{6M}	6.15	2.20-17.18	<0.01

^a Indicates the relative increase or decrease in IR for each socio-economic characteristic or sexual behavior when present at NPP consultation visit.

^b No incident HCV infections were among those who identified as transgender and whose PrEP regimen was missing at any of the consultation visits.

^c Defined as the use of methamphetamine, GHB/GBL and/or mephedrone before or during sex.

^d Sex work was excluded because all incident infections were among those who did not report sex work.

^e Diagnosed with an anal chlamydia/gonorrhea or a syphilis infection at visit.

Abbreviations: CAS, Condomless anal sex; CI, Confidence interval; HCV, Hepatitis C virus; IDU, Injecting drug use; IRR, Incidence rate ratio; ln, natural log; MSM, Men who have sex with men; Pre-exposure prophylaxis; Ref, Reference category; STI, Sexually transmitted infection; 6M, during the previous six months; 12M, during the previous twelve months.

Supplementary Table 9. Univariable determinants of incident HCV infection among complete cases enrolled in the Dutch national PrEP program between July 2019 and December 2022

	IRR ^a	Total (n=9,851) (95% CI)	p
Age per 10 years, continuous	1.19	0.98-1.44	0.08
Key population			
MSM	Ref		0.81
Transgender	0.79	0.11-5.68	
Region of origin			
Dutch	Ref		0.45
Non-Dutch	1.22	0.73-2.05	
Educational level			
At least college degree	Ref		0.21
Less than college degree	0.68	0.37-1.24	
PrEP regimen^{12M}			
Daily	Ref		0.34
Event driven	0.79	0.48-1.31	
Missing	^b		
Number of sex partners per ln(n+1) increase^{6M}	0.93	0.74-1.17	0.56
Receptive CAS^{6M}	2.62	1.13-6.07	0.03
Reporting chemsex^c/group sex^{6M}	1.84	1.02-3.33	0.04
Reporting sex work^{6M}	^d		
STI diagnosis^e	1.96	1.07-3.60	0.03
IDU^{6M}	5.46	2.22-13.45	<0.01

^a Indicates the relative increase or decrease in IR for each socio-economic characteristic or sexual behavior when present at NPP consultation visit.

^b No incident HCV infections were among those who identified as transgender and whose PrEP regimen was missing at any of the consultation visits.

^c Defined as the use of methamphetamine, GHB/GBL and/or mephedrone before or during sex.

^d Sex work was excluded because all incident infections were among those who did not report sex work.

^e Diagnosed with an anal chlamydia/gonorrhea or a syphilis infection at visit.

Abbreviations: CAS, Condomless anal sex; CI, Confidence interval; HCV, Hepatitis C virus; IDU, Injecting drug use; IRR, Incidence rate ratio; ln, natural log; MSM, Men who have sex with men; Pre-exposure prophylaxis; Ref, Reference category; STI, Sexually transmitted infection; 6M, during the previous six months; 12M, during the previous twelve months.