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Abstracts

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Correspondence to:
organisation@nchiv.org

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AOPL: Abstract Oral Plenary presentations

AOPL-**01**

Promoting indicator condition-guided testing for HIV in the hospital setting (PROTEST 2.0): Baseline results of a multicentre intervention study

Saskia Bogers[1], Maarten Schim van der Loeff[2], Udi Davidovich[2], Marc van der Valk[1], Kees Brinkman[3], Godelieve de Bree[1], Peter Reiss[1], Jan van Bergen[4], Suzanne Geerlings[1]

[1]*Department of Internal Medicine, Amsterdam University Medical Centers, Amsterdam, Netherlands*

[2]*Department of Infectious Diseases, Public Health Service Amsterdam, Amsterdam, Nederland*

[3]*Department of Internal Medicine, Onze Lieve Vrouwe Gasthuis, Amsterdam, Netherlands*

[4]*Department of General Practice, Amsterdam University Medical Centers, Amsterdam, Nederland*

Background

Timely diagnosis of HIV is a key focus point in efforts towards ending the HIV epidemic. Indicator Condition (IC) guided HIV testing is a cost-effective way to identify people living with HIV who currently remain undiagnosed. It is unknown to what extent hospitals are applying IC-guided testing strategies. We assessed IC-guided HIV testing in hospitals in the Amsterdam region to identify opportunities for improvement.

Methods

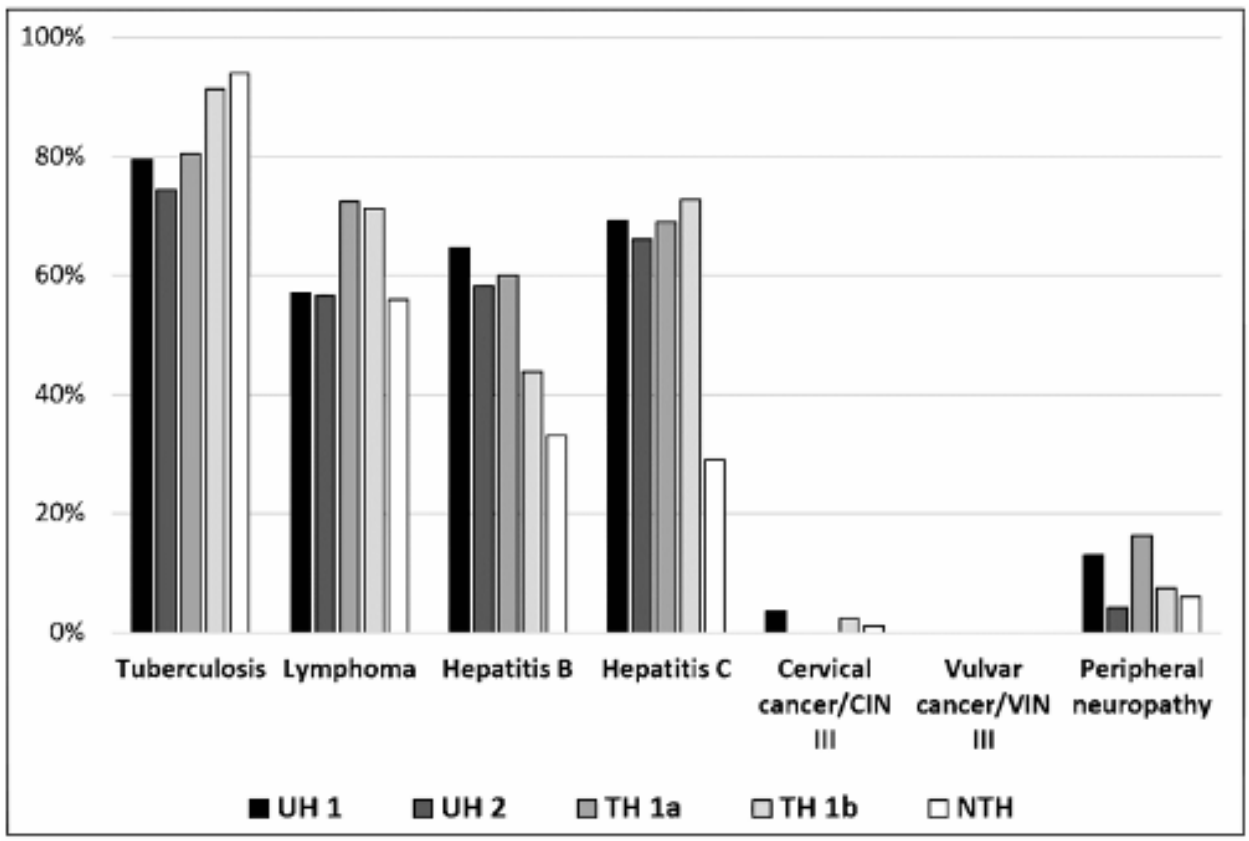
We present the baseline results of a multicentre intervention study taking place in two university hospitals (UH), two teaching hospitals (TH; one with two locations), and one non-teaching hospital (NTH). Seven ICs were selected for this study: tuberculosis (TB), lymphoma, hepatitis B (HBV), hepatitis C (HCV), cervical carcinoma including cervical intraepithelial neoplasia grade III (CC), vulvar carcinoma including vulvar intraepithelial neoplasia grade III (VC), and peripheral neuropathy (PN). Patients ≥18 years not known to have an HIV infection and diagnosed with one of the selected ICs in 2015-2020 were eligible. We included all eligible patients in UH 1, and screened a random sample of maximum 500 patients per IC in the other hospitals. Data on patient characteristics and HIV testing were extracted from electronic health records including scanned documents. Primary endpoint was the HIV test ratio: proportion of patients with an IC who were tested for HIV within 3 months around IC diagnosis. Secondary endpoint was the positivity percentage: percentage of HIV test performed that were positive.

Results

A total of 4,331 patients were included in 2 UH, 1 TH (2 locations) and 1 NTH. HIV test ratios within 3 months around diagnosis were highest amongst TB patients (range 74-94%). The test ratio varied considerably across hospitals and ICs, with ranges of 50/90(56%)-105/145(72%) in lymphoma, 5/15(33%)-113/175(65%) in HBV, 2/7(29%)-24/33(73%) in HCV, 0/68(0%)-16/452(4%) in CC and 4/97(4%)-16/98(16%) in PN patients. No VC patients were tested for HIV. Eleven patients tested HIV positive within 3 months around IC diagnosis through IC-guided testing, yielding an overall positivity percentage of 0.8%, of whom 55% (6/11) had lymphoma. Of these 11 newly diagnosed patients with HIV, 10 had a CD4 count <350 cells/mm^3.

Conclusions

Our results show IC-guided testing can identify people with previously undiagnosed HIV infection, but is insufficiently practiced across hospitals in the selected ICs. Tailored interventions are required per IC to improve IC-guided HIV testing, in order to reduce the proportion of people with undiagnosed HIV and to some extent late presentation and in the Netherlands.



CIN: cervical intraepithelial neoplasia. NTH: non-teaching hospital. TH: teaching hospital. UH: university hospital. VIN: vulvar intraepithelial neoplasia

*AOPL-**01:** HIV test ratio within 3 months around diagnosis by study site and indicator condition*

AOPL-**02**

Improving the HIV testing cascade: adequate identification of patients with HIV indicator conditions in hospitals by electronic registration systems On behalf of the #AWARE.hiv project group

Carlijn Jordans[1], Katie Hensley[1], Marius Vogel[1], Jeroen Van Kampen[1], Charles Boucher[1], Femke Mollema[2], Jet Gisolf[3], Rachida El Moussaoui[4], Gonneke Hermanides[5], Renée Finkenflügel[6], Bart Rijnders[1], Annelies Verbon[1], Casper Rokx[1]

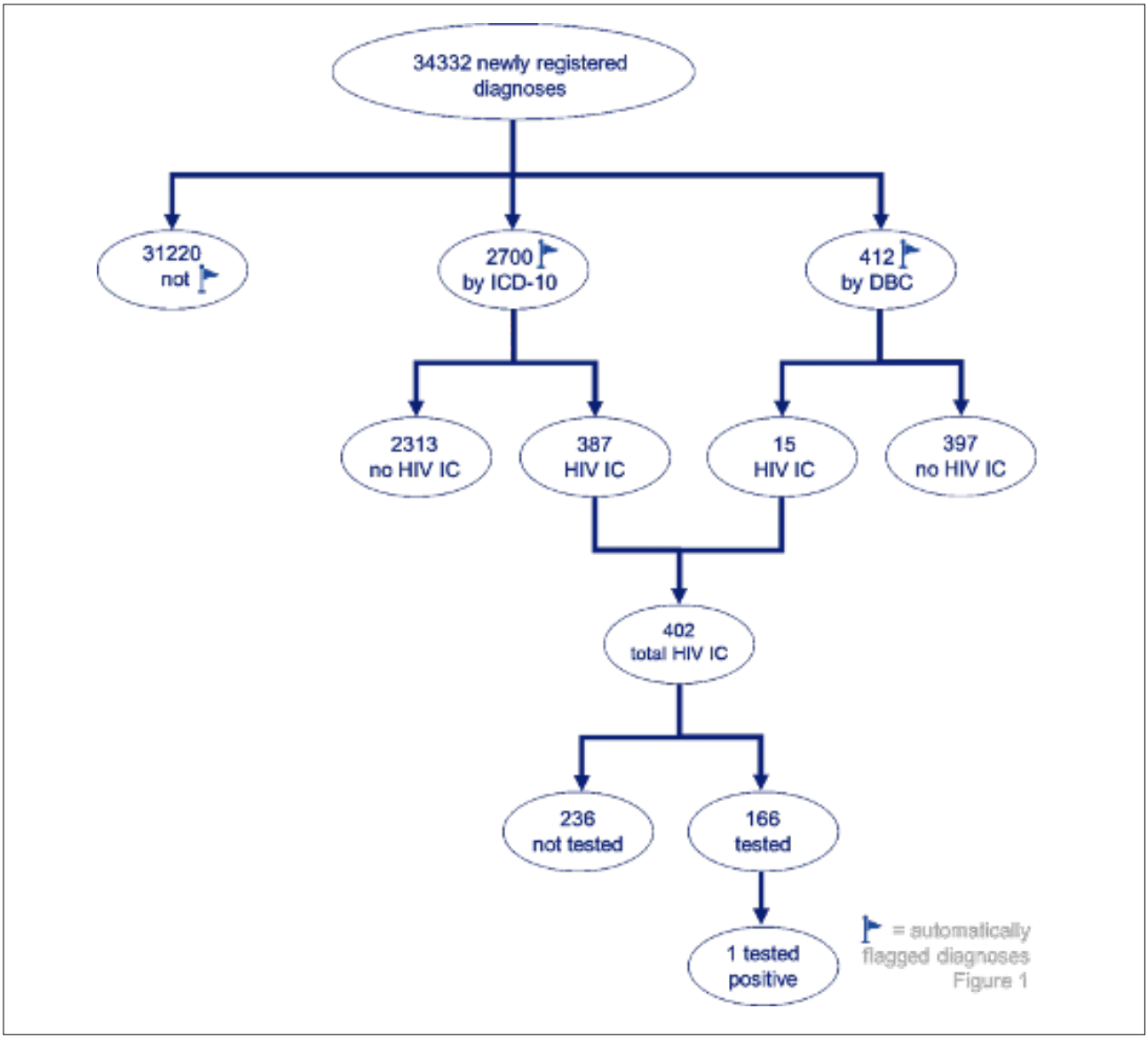
[1]Erasmus MC, Rotterdam, Netherlands
[2]Haaglanden Medisch Centrum, Den Haag, Netherlands
[3]Rijnstate Ziekenhuis, Arnhem, Netherlands
[4]Maasstad ziekenhuis, Rotterdam, Netherlands
[5]Rode Kruis Ziekenhuis, Beverwijk, Netherlands
[6]HIV vereniging, Amsterdam, Netherlands

Background
The majority of patients with an HIV infection visit physicians for HIV-related medical reasons in the years prior to their HIV diagnosis. These HIV indicator conditions provide early opportunities to test for HIV. The #AWARE.hiv project aims to improve HIV indicator condition driven testing. One of the key challenges is the adequate identification of patients with possible indicator conditions in hospitals which is the first step in triggering the HIV testing cascade.

Materials and methods
Single center prospective implementation project at Erasmus University Medical Center Rotterdam. The principle objective is to assess if patients with indicator conditions can be identified in hospitals that use electronic ICD-10 data registration systems, which are routinely used in Dutch healthcare and are mandatory to be registered by physicians. An extensive list was constructed of all ICD-10 codes related to HIV indicator conditions.
We created a two-step approach to identify possible indicator conditions by automatic ICD-10 screening and cross-compared by standardized health insurance codes used in the Netherlands (DBC).
Data were collected on all patients ≥ 18 years who entered care between January 1st 2020 and June 1st 2020. All identified ICD-10/DBC were systematically reviewed by HIV treating physicians for HIV indicator conditions. We evaluated the feasibility and sensitivity of the screening method by ICD-10 and the proportion indicator condition HIV test rate.

Results
Identifying patients with possible indicator conditions using electronic registrations within existing institutional ICT infrastructures was possible. Out of 34332 newly registered diagnoses 2700 (7.9%) were flagged by ICD-10 of which 387 (14.3%) were HIV indicator conditions. DBC screening yielded an additional 412 flagged diagnoses containing 15 indicator conditions. 166 out of these 402 (41%) have been adequately tested for HIV. 1 (0.6%) was found positive for HIV (*figure 1*).
The findings indicate a gap between HIV indicator condition identification and HIV testing rate. Recommendation of HIV testing in national guidelines seems to have a positive effect on HIV testing behavior (*table 1*). ICD-10 screening for indicator conditions had 96% sensitivity, 93% specificity, 14% positive predictive value and >99% negative predictive value.

Conclusions
In hospitals using electronic patient files with mandatory ICD-10 coding existing ICT infrastructures can help to identify patients with HIV indicator conditions. Our data confirms the gap between indicator condition identification and HIV testing. Future studies aim at improving this gap.



*AOPL-**02:** Figure 1*

Table 1

Top 10 HIV indicator condition	**N (%)**	**HIV test**
Hepatitis A + B + C*	45 (11)	36 (80)
Lymphoma*	42 (10)	31 (74)
Cervical cancer	39 (10)	0
Cervical dysplasia	33 (8)	2 (6)
Sexually transmitted infections*	26 (6)	8 (31)
Peripheral neuropathy	22 (5)	1 (5)
Unexplained chronic renal impairment	18 (4)	11 (61)
Lymphocytic meningitis	16 (4)	11 (61)
Seborrheic dermatitis/exanthema	14 (3)	1 (7)
Unexplained chronic diarrhea	14 (3)	1 (7)

* HIV testing recommended in national guideline

*AOPL-**02:** Table 1*

AOPL-**03**

Large regional variation across the Netherlands in the number of people living with undiagnosed HIV

Ard van Sighem[1], Eline Op de Coul[2], Noëmi Nijsten-Pennings[3], Denise Twisk[4], Nicole H.T.M. Dukers-Muijrers[5], Birgit van Benthem[2], Silke David[2], Peter Reiss[1]

[1]*Stichting HIV Monitoring, Amsterdam, Netherlands*

[2]*National Institute for Public Health and the Environment, Bilthoven, Netherlands*

[3]*Public Health Service (GGD) Gelderland-Zuid, Nijmegen, Netherlands*

[4]*Public Health Service (GGD) Rotterdam-Rijnmond, Rotterdam, Netherlands*

[5]*Public Health Service (GGD) South Limburg, Maastricht, Netherlands*

Background

The Netherlands aims to move to zero new HIV infections by 2030. To achieve this aim, accurate regional-level estimates of the number of people with HIV, in particular the undiagnosed population, may provide relevant information for developing tailor-made interventions.

Methods

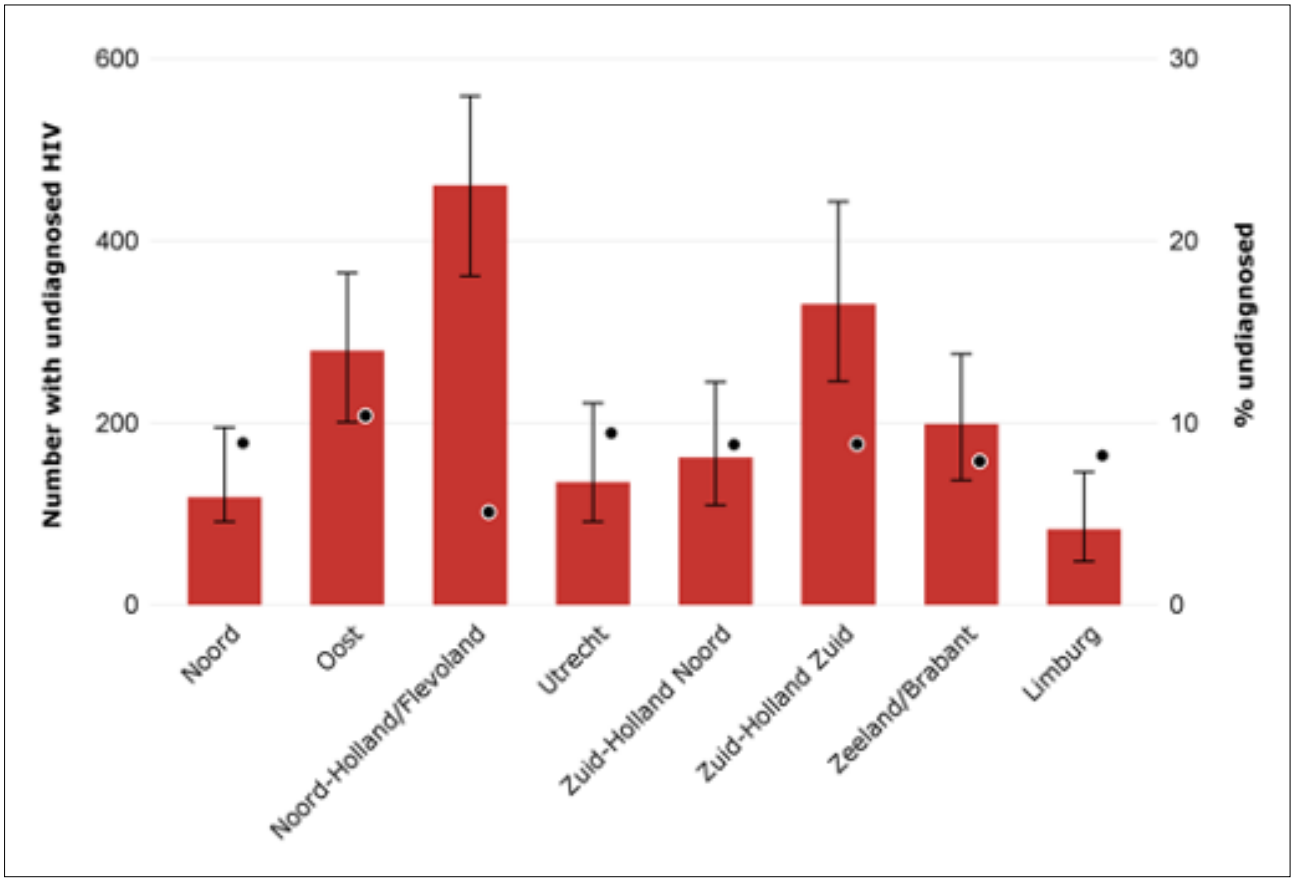
From the ATHENA national HIV cohort, we retrieved annual data during 2002-2019 on newly-diagnosed HIV-1 infections in individuals living in each of the eight sexually transmitted infection (STI) public health surveillance regions in the Netherlands. We excluded migrants originating outside of the Netherlands with documented HIV diagnosis before arrival. HIV diagnoses in 2015-2019 were adjusted for reporting delay by estimating the delay distribution using the European Centre for Disease Prevention and Control (ECDC) HIV Estimates Accuracy Tool. The ECDC HIV Modelling Tool, a CD4 count-based back-calculation method, was used to estimate annual numbers of newly-acquired HIV infections in each region during 2002-2019 and the distribution of time between infection and diagnosis by calendar year of infection. Using these estimates we then calculated the number of people remaining undiagnosed by the end of each year. Bootstrap techniques were used to calculate 95% confidence intervals (CI). The total number of people living with HIV in 2019 was estimated by adding the estimated number of undiagnosed individuals to the observed number of diagnosed HIV-positive individuals living in each region.

Results

During 2002-2019, 18,789 people were newly diagnosed in the eight regions in the Netherlands; for 253 (1%) the region was unknown. After excluding 1,093 migrants already diagnosed before arrival, estimates of undiagnosed individuals were based on the remaining 17,696 individuals. The total number of people living with undiagnosed HIV fell by 56% (95% CI, 49-60) from 4,010 (3,870-4,150) in 2010 to 1,770 (1,570-2,030) in 2019. In 2019, numbers undiagnosed varied from 80 (50-150) in Limburg to 330 (250-440) in Zuid-Holland Zuid and 460 (360-560) in Noord-Holland/Flevoland; the latter two regions accounted for 45% of people with undiagnosed HIV (*Figure*). The total number of people living with HIV in the eight regions was estimated at 23,560 (23,370-23,820), including 9,020 (8,920-9,110) in Noord-Holland/Flevoland and 3,740 (3,660-3,860) in Zuid-Holland Zuid. Proportions undiagnosed varied between 5% and 10% (*Figure*).

Conclusions

Numbers of people living with undiagnosed HIV greatly vary by STI surveillance region. Our results may be useful for developing interventions on a regional level, although a further breakdown on an even more granular level may be warranted for regions with largest numbers of undiagnosed individuals.



*AOPL-**03:** Figure 1 - Number (left axis, bars) and proportion (right axis, dots) of individuals remaining undiagnosed by the end of 2019 in each of the eight STI surveillance regions*

AOPL-**04**

Lower incidence of viral blips: another finding to favor the use of INSTI-based cART

Suzan Dijkstra, Marije Hofstra, Tania Mudrikova, Andy Hoepelman, Berend Van Welzen
University Medical Center Utrecht, Utrecht, Netherlands

Background
Blips are frequently encountered during the treatment of HIV. Although their etiology and clinical significance are subject of debate, their occurrence often leads to additional diagnostic testing and uncertainties by both patient and physician. Prior studies reported that patients using protease inhibitor (PI)-based combination antiretroviral therapy (cART) were more likely to experience blips than those receiving non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens. To our knowledge, no studies have described the occurrence of blips in patients receiving integrase strand transfer inhibitors (INSTIs) compared to NNRTIs and PIs. As INSTI-based cART is associated with more rapid virological suppression and superior long-term efficacy, we hypothesized that it would also display a lower incidence of blips.

Methods
A retrospective, longitudinal analysis on the incidence of blips, defined as isolated viral loads (VLs) 50-499 copies/mL preceded and followed by VLs <50 copies/mL, was performed. All virologically suppressed patients treated with two nucleos(-t)ide reverse transcriptase inhibitors plus one anchor in the UMC Utrecht during 2010-2020 were included. For patients treated with >1 eligible regimen, each regimen was analyzed separately. If detectable viremia was deemed to result from non-adherence (self-reported and documented in patient charts by the treating physician), the regimen was excluded from analysis. Factors associated with blips were identified using generalized estimating equation-based negative binomial models including all variables of interest and variables with a P<0.20 in unadjusted analyses.

Results
A total of 1661 patients and 3405 regimens were analyzed (*Table 1*), accounting for 8902 person-years of follow-up and 24,081 VL measurements. In total, 247 patients (14.9%) demonstrated 308 blips (NNRTIs: 124, PIs: 147, INSTIs: 37). After controlling for other factors, blip incidence was significantly higher for PIs and lower for INSTIs when compared with NNRTIs (incidence rate ratios 1.368 and 0.641, respectively) (*Table 2*). Additional correlations were higher zenith VL, more frequent VL measurements, and shorter time since cART initiation. Patients experiencing blips were more likely to demonstrate persistent low-level viremia (consecutive VLs ≥50 copies/mL not classified as failure) (P<0.001) but not virologic failure (consecutive VLs ≥200 or one ≥500 copies/mL) (P=0.684). The 308 blips led to 226 extra telephonic/outpatient consultations, 165 extra VL measurements, 34 drug level measurements, and one resistance test.

Conclusions
In our cohort, use of INSTIs resulted in significantly fewer blips compared to other anchors. Although their prognostic significance is not completely clear, the use of INSTI-based cART could avoid extra diagnostic testing and uncertainties in the consultation room.

Table 1. Characteristics of included patients and regimens.

Characteristic	Patients	Regimens		
	All patients (n=1661)	NNRTI-based (n=1121)	PI-based (n=1275)	INSTI-based (n=1009)
Male sex	1343 (80.9)	939 (83.8)	921 (72.2)	863 (85.5)
Age (years)				
- At diagnosis[a]	37.2 ± 12.4	37.6 ± 11.6	37.3 ± 12.1	37.1 ± 12.8
- At start of follow-up patient	43.4 ± 11.9	-	-	-
- At start of follow-up regimen	-	45.7 ± 11.8	45.8 ± 12.0	45.7 ± 12.6
HIV transmission route				
- MSM	938 (56.5)	660 (58.9)	647 (50.7)	635 (62.9)
- Heterosexual	338 (20.3)	200 (17.8)	343 (26.9)	177 (17.5)
- Intravenous drugs	33 (2.0)	13 (1.2)	38 (3.0)	14 (1.4)
- Other/unknown	352 (21.2)	248 (22.1)	247 (19.4)	183 (18.1)
Fiebig stage at cART initiation				
- I-V	54 (3.3)	15 (1.3)	32 (2.5)	49 (4.9)
- VI	1570 (94.5)	1083 (96.6)	1231 (96.5)	935 (92.7)
- Missing	37 (2.2)	23 (2.1)	12 (0.9)	25 (2.5)
Treatment history				
- cART-naive	739 (44.5)	260 (23.2)	269 (21.1)	210 (20.8)
- Time since cART initiation (years)[a]	4.6 ± 5.1	6.4 ± 5.5	7.0 ± 6.0	7.0 ± 6.3
Lowest available $CD4^+$ (cells/mm^3)	261.1 ± 194.4	248.1 ± 178.3	224.0 ± 167.7	284.1 ± 202.0
Pretreatment $CD4^+$ (cells/mm^3)[a]	-	499.1 ± 298.1	505.3 ± 304.8	585.2 ± 286.1
Zenith VL (cop/mL)				
- <10.000	103 (6.2)	62 (5.5)	78 (6.1)	78 (7.7)
- 10.000-99.999	472 (28.4)	310 (27.7)	304 (23.8)	291 (28.8)
- 100.000-999.999	774 (46.6)	557 (49.7)	659 (51.7)	459 (45.5)
- ≥1.000.000	74 (4.5)	37 (3.3)	61 (4.8)	54 (5.4)
- Missing	238 (14.3)	155 (13.8)	173 (13.6)	127 (12.6)
Pretreatment VL (cop/mL)	-			
- Suppressed		640 (57.1)	797 (62.5)	732 (72.5)
- 50-9.999		62 (5.5)	129 (10.1)	75 (7.4)
- 10.000-99.999		179 (16.0)	135 (10.6)	113 (11.2)
- 100.000-999.999		152 (13.6)	163 (12.8)	62 (6.1)
- ≥1.000.000		10 (0.9)	22 (1.7)	7 (0.7)
- Missing		78 (7.0)	29 (2.3)	20 (2.0)
VL sampling frequency (tests/year)	-	3.1 ± 1.7	3.4 ± 2.8	3.4 ± 2.6
Follow-up duration (years)	5.4 ± 3.3	3.4 ± 2.9	2.5 ± 2.3	1.9 ± 1.5

All categorical data are expressed as numbers (%) and all continuous data are expressed as means ± standard deviations.

a. Missing data for continuous variables: age at diagnosis (10 NNRTI regimens (0.9%), 6 PI regimens (0.5%), 6 INSTI regimens (0.6%)), time since cART initiation (8 NNRTI regimens (0.7%), 6 PI regimens (0.5%), 6 INSTI regimens (0.6%)), pretreatment $CD4^+$ count (89 NNRTI regimens (7.9%), 59 PI regimens (4.6%), 63 INSTI regimens (6.2%)).

Abbreviations: cART, combination antiretroviral therapy; cop, copies; INSTI, integrase strand transfer inhibitor; MSM, men who have sex with men; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; VL, viral load.

*AOPL-**04:** Table 1*

Table 2. Generalized estimating equation-based negative binomial regression: associations with blips.

	Univariable analysis		Multivariable analysis	
	IRR (95% CI)	***P*-value**	**IRR (95% CI)**	***P*-value**
cART anchor				
- NNRTI	1		1	
- PI	1.442 (1.102-1.886)	0.008	1.368 (1.050-1.779)	0.020
- INSTI	0.601 (0.404-0.896)	0.012	0.641 (0.430-0.955)	0.029
Male sex (*vs.* female sex)	1.331 (0.912-1.941)	0.138	1.310 (0.893-1.923)	0.167
Age at diagnosis (per year increase)	1.019 (1.009-1.029)	<0.001	1.006 (0.996-1.017)	0.231
Age at start of follow-up regimen (per year increase)	1.003 (0.993-1.013)	0.584	-	-
HIV transmission route			-	-
- MSM	1			
- Heterosexual	0.788 (0.554-1.121)	0.186		
- Intravenous drugs	0.910 (0.353-2.343)	0.844		
- Other/unknown	0.912 (0.658-1.264)	0.579		
Fiebig stage VI at cART initiation (*vs.* stage I-V)	1.811 (0.604-5.436)	0.290	2.565 (0.770-8.534)	0.125
Time since cART initiation (per year increase)	0.921 (0.890-0.952)	<0.001	0.923 (0.890-0.958)	<0.001
Lowest available CD4$^+$ count (per square root cell/mm^3 increase)[a]	0.984 (0.966-1.004)	0.110	0.989 (0.967-1.012)	0.354
Zenith VL cop/mL[a]				
- <10.000	1		1	
- 10.000-99.999	2.106 (0.878-5.048)	0.095	1.927 (0.778-4.773)	0.156
- 100.000-999.999	2.918 (1.261-6.760)	0.013	2.479 (1.014-6.068)	0.047
- ≥1.000.000	5.507 (2.077-14.585)	0.001	4.491 (1.582-12.743)	0.005
VL sampling frequency (per sample/year increase)	1.230 (1.202-1.258)	<0.001	1.241 (1.210-1.274)	<0.001

a. Zenith VL and lowest available CD4$^+$ count, and not the pretreatment values, were selected for the model, as these factors were expected to have the highest influence on the viral reservoir as a potential source for blips.
Abbreviations: cART, combination antiretroviral therapy; CI, confidence interval; cop, copies; INSTI, integrase strand transfer inhibitor; IRR, incidence rate ratio; MSM, men who have sex with men; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; VL, viral load.

*AOPL-**04:** Table 2*

AOPL-**05**

A population pharmacokinetic analysis assessing the exposure of raltegravir once-daily 1200mg in pregnant women living with HIV

Vera Bukkems[1], Teun Post[2], Angela Colbers[1], David Burger[1], Elin Svensson[1]
[1]*Radboud university medical center, Nijmegen, Netherlands*
[2]*Leiden Experts on Advanced Pharmacokinetics and Pharmacodynamics (LAP&P), Leiden, Netherlands*

Background
Once-daily two 600mg tablets (1200mg QD) of raltegravir offers an easier treatment option compared to the twice-daily regimen of one 400mg tablet. No pharmacokinetic, efficacy or safety data of raltegravir 1200mg QD in pregnant women have been reported to date, and therefore this dosage is not recommended during pregnancy. This study aimed to develop a population pharmacokinetic (popPK) model to predict the pharmacokinetic profile of raltegravir 1200mg QD in pregnant women and to discuss the expected pharmacodynamic properties of this regimen during pregnancy based on concentration-effect relationships from the literature.

Methods
Data from 11 pharmacokinetic studies, including healthy and HIV-infected subjects with the 400mg and 600mg tablets and pregnant women with the 400mg tablet, were pooled (n=221) to develop the popPK model using NONMEM 7.4. One, two and three compartment models were evaluated, and various absorption models were tested to describe the variable absorption of raltegravir. Model selection was based on maximum likelihood statistics (dOFV < -3.84), physiological plausibility, precision in parameter estimates and visual predictive checks. Covariate testing was based on physiological plausibility and previously published results.
To compare the pharmacokinetic profile of raltegravir 1200mg QD in pregnant and non-pregnant women, Monte-Carlo simulations with 3000 individuals with multi-level of random effect were performed under fasted, low-fat and moderate-fat conditions. The primary criteria for efficacy was that the lower bound of the 90% confidence interval (CI) of the concentration before next dose administration (Ctrough) geometric mean ratio (GMR) of simulated pregnant/non-pregnant women had to be >0.75. The simulated GMRs were compared with the clinical data of two pregnant women using 1200mg QD raltegravir included in the Pharmacokinetics of newly developed ANtiretroviral agents in HIV-infected pregNAnt women (PANNA) study.

Results
A two-compartment model with first-order elimination and absorption through three sequential transit compartments best described the data. Drug intake under fed conditions increased the mean absorption time with 160% and a low-fat meal decreased F by 46%. A 49% lower F, with an relative standard error of 14%, was estimated in pregnant compared to non-pregnant women. The simulated raltegravir Ctrough GMR (90%CI) was 0.51 (0.41-0.63), hence not meeting the primary target for efficacy. Clinical data from two pregnant women using 1200mg QD raltegravir showed similar Ctrough ratios pregnant/non-pregnant of 0.52 and 0.46.

Conclusions
Based on the current knowledge of the raltegravir concentration-effect relationship, our results support the current recommendation of not using the raltegravir 1200mg QD regimen during pregnancy.

AOPL-**06**

Prevalence, correlates and health impact of healthcare provider counseling about undetectable equals untransmittable (u=u): findings from the Netherlands and other European Countries

Bart Lammertink[1], Sarah Stutterheim[2], Ama Appiah[3], Hiskya Plieger[1], Patricia De los Rios[4], Chinyere Okoli[3]
[1]*ViiV Healthcare, Amersfoort, Netherlands*
[2]*Maastricht University, Maastricht, Netherlands*
[3]*ViiV Healthcare, Brentford, United Kingdom*
[4]*ViiV Healthcare, Quebec, Canada*

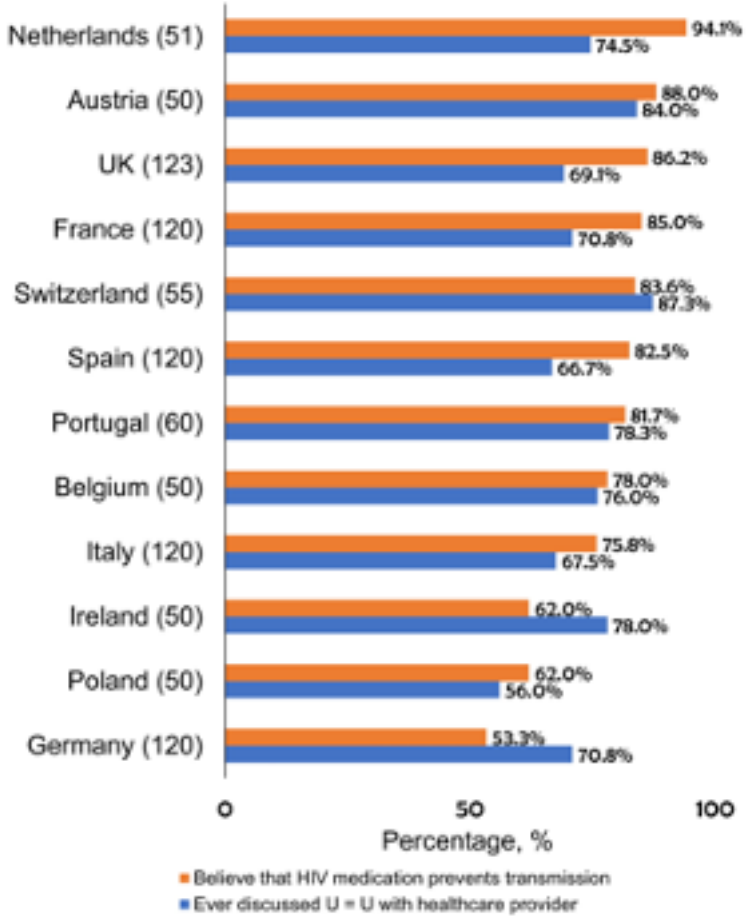
Background
U=U (undetectable=untransmittable) is an important and empowering message for PLHIV, and discussions about U=U initiated by health care providers (HCPs) are beneficial for effective HIV prevention and care. We investigated awareness of U=U and its associations with health and well-being.

Methods
Data were from the 2019 Positive Perspectives study, a web-based, 25-country survey of PLHIV on ART. Twelve European countries participated (n=969), including the Netherlands (n=51). Exposure to U=U information from an HCP was a response of “Agree”/“Strongly agree” to the statement: “My provider has told me about ‘Undetectable=Untransmittable’”. Prevalence rates for U=U were calculated, and logistic regression analyses, adjusted for age, gender, and HIV duration, were conducted.

Results
Within pooled analyses for PLHIV in Europe, 71.8%[696/969] reported that their HCP had discussed U=U with them. PLHIV exposed to U=U were more likely to believe ART prevents transmission (AOR=2.36, 95%CI=1.69-3.28), more satisfied with treatment (AOR=2.22; 95%CI=1.63-3.02), and more optimally adherent (AOR=1.70, 95%CI=1.18-2.46) than those not told about U=U. Also, PLHIV exposed to the U=U message reported better overall health (AOR=1.55, 95%CI=1.16-2.07), mental health (AOR=1.52, 95%CI=1.14-2.02), and physical health (AOR=1.48, 95%CI=1.10-1.99), and were less likely to feel stressed if someone saw their HIV medication (AOR=0.71, 95%CI=0.53-0.95). Prevalence of U=U discussions did not differ between the Netherlands (74.5%[38/51]) and other European countries, but the belief that ART prevents HIV transmission was higher among participants in the Netherlands (94.1%[48/51]) than those in Spain (82.5%[99/120], p=0.045), Portugal (81.7%[49/60], p=0.049), Belgium (78.0%[39/50], p=0.019), Italy (75.8%[91/120], p=0.005), Ireland (62.0%[31/50], p<0.001), Poland (62.0%[31/50], p<0.001), and Germany (53.3%[64/120], p<0.001), but not significantly different from Austria, UK, France, and Switzerland. U=U exposure in the Netherlands was higher among participants ≥50 years (88.0%[22/25]) than <50-year-olds (61.5%[16/26]). Higher prevalence rates were also observed among participants reporting vs not reporting that their HCP: asked if they had treatment concerns (88.5%[23/26] vs. 60.0%[15/25]), discussed new available treatments (90.6%[29/32] vs 47.4%[9/19]), and sought their view before prescribing (80.0%[36/45] vs. 33.3%[2/6]). Compared to other European countries, participants in the Netherlands reported more frequently that their HCP seeks their views before prescribing (Netherlands=88.2%[45/51]), that their HCP provides them with sufficient information to make treatment decisions (84.3%[43/51]), and that they feel they understand their treatment (90.2%[46/51]). Also, hiding HIV pills, or anticipating stress/anxiety should someone see their HIV medication, were lowest in the Netherlands (each 23.5%[12/51]).

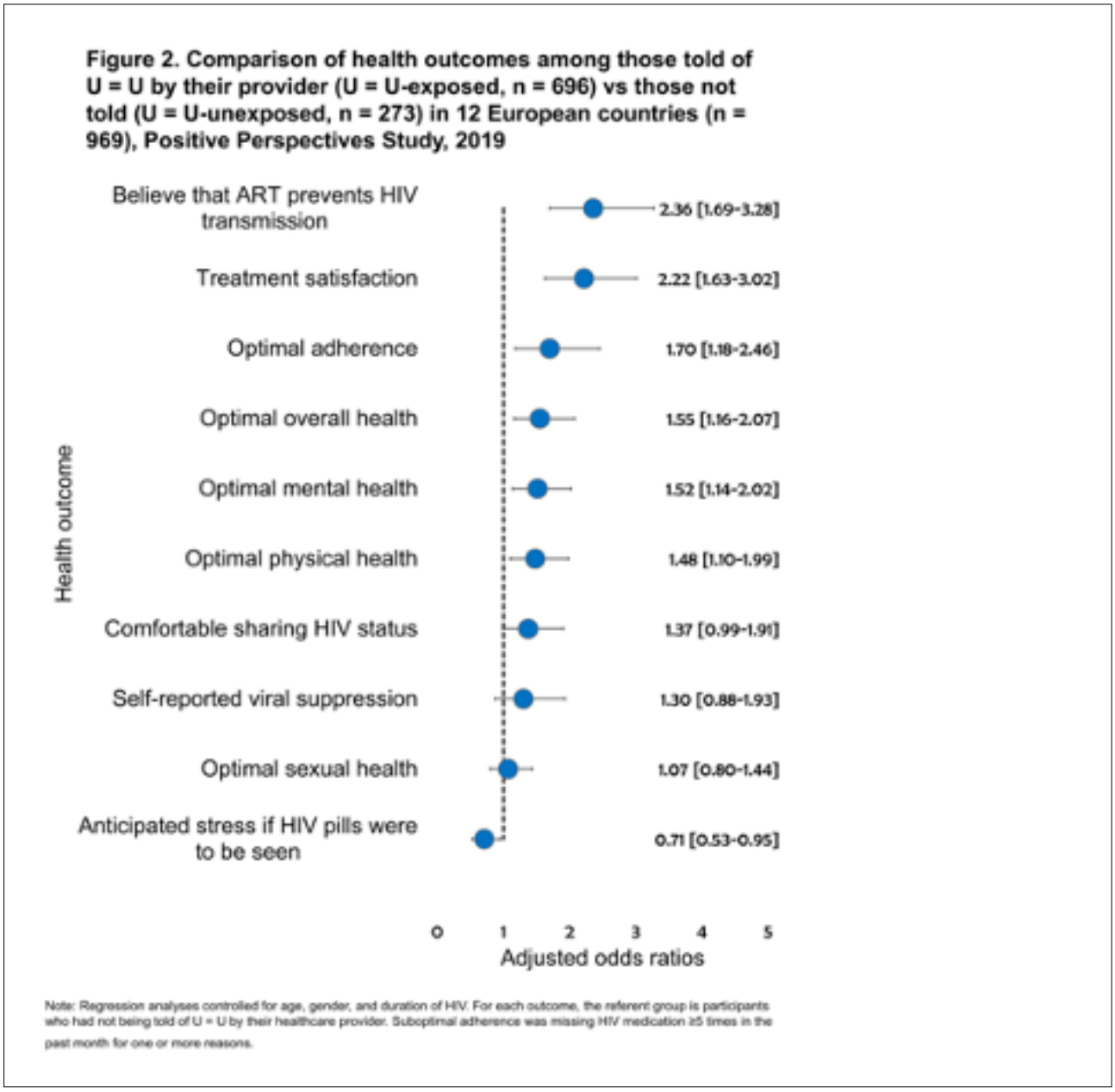
Conclusions
U=U counseling was associated with multiple facets of health and well-being, and should be prioritized in patient-provider communication.

Figure 1. Percentage of people living with HIV in the Netherlands and other European countries who reported being told of U = U by their healthcare provider [a] and the percentage who believed ART prevents HIV transmission [b], Positive Perspectives Study, 2019



[a] Exposure to U = U information from a healthcare provider was a response of "Agree"/"Strongly agree" (vs. "Disagree"/ "Strongly disagree"/ "Neither agree nor disagree") to the statement: "My provider has told me about 'Undetectable = Untransmittable'".
[b] The belief that HIV medication prevents transmission was a response of "Agree"/"Strongly agree" (vs. "Disagree"/ "Strongly disagree"/ "Neither agree nor disagree") to the statement: "My HIV medication prevents me from passing on HIV to others".

*AOPL-**06:** Figure 1*



*AOPL-**06:** Figure 2*

AOPL-**07**

HCV micro-elimination in HIV-positive individuals in the Netherlands: four years after universal access to direct-acting antivirals

Anders Boyd[1], Colette Smit[1], Bart J.A. Rijnders[2], Thijs J.W. van de Laar[3], Eliane M. Leyten[4], Wouter F. Bierman[5], Kees Brinkman[3], Mark A. Claassen[6], Jan den Hollander[7], Anne Boerekamps[2], Astrid Newsum[8], Janke Schinkel[9], Maria Prins[8], Joop Arends[10], Eline Op de Coul[11], Marc van der Valk[9], Peter Reiss[1]

[1]*Stichting HIV Monitoring, Amsterdam, Netherlands*
[2]*Erasmus MC, Rotterdam, Netherlands*
[3]*Onze Lieve Vrouwe Gasthuis, Amsterdam, Netherlands*
[4]*MC Haaglanden, Den Haag, Netherlands*
[5]*Universitair Medisch Centrum Groningen, Groningen, Netherlands*
[6]*Rijnstate Ziekenhuis, Arnhem, Netherlands*
[7]*Maasstad Ziekenhuis, Rotterdam, Netherlands*
[8]*GGD Amsterdam, Amsterdam, Netherlands*
[9]*Amsterdam University medical Centers, location Academic Medical Center, Amsterdam, Netherlands*
[10]*Universitair Medisch Centrum Utrecht, Utrecht, Netherlands*
[11]*National Institute for Public Health and the Environment, Bilthoven, Netherlands*

Background
In the Netherlands, access to direct-acting antivirals (DAA) against hepatitis C virus (HCV) infection has been unrestricted for chronic infection since 2015. We evaluated whether the nationwide incidence of HCV primary and re-infection among HIV-positive individuals has changed after 2015.

Methods
Individuals participating in the national ATHENA HIV cohort between 2000-2019 were included. Incidence rates (IR) of HCV primary infection and re-infection were calculated per calendar year using piecewise exponential survival models.

Results
Among 24,488 individuals without prior HCV, 712 cases of HCV primary infection were documented (IR=29/1,000 person-years, 95%CI=2.7-3.1). The highest IR was observed in men who have sex with men (MSM) (4.4/1,000 person-years, 95%CI=4.1-4.8) and lower among people who inject drugs (PWID) (0.4/1,000 person-years, 95%CI=0.1-2.4) and other key populations (0.4/1,000 person-years, 95%CI=0.2-0.5). In MSM, IR increased in 2007 (IR=8.3/1,000 person-years) and fluctuated between 4.6 and 8.5/1,000 person-years from 2008-2015. In 2016, IR declined to 3.2 cases/1,000 person-years and remained steady between 2.1 and 3.1/1000 person-years from 2017-2019. Among 1866 individuals with a previous HCV infection, 274 HCV re-infections were documented (IR=26.9/1,000 person-years, 95%CI=23.9-30.3). The highest IR was observed in MSM (38.5/1,000 person-years, 95%CI=33.9-43.7) and was lower among PWID (10.9/1,000 person-years, 95%CI=3.5-33.8) and other key populations (8.9/1,000 person-years, 95%CI=6.3-12.8). In MSM, re-infection IRs fluctuated until 2015, reaching 55.6/1,000 person-years. In 2016, re-infection incidence declined to 41.4/1,000 person-years, followed by further decreases of 24.4 and 11.4/1,000 person-years in 2017 and 2019, respectively.

Conclusions
The observed sharp decline in HCV incidence among HIV-positive MSM shortly after unrestricted DAA access suggests a “treatment-as-prevention” effect. HCV incidence was already low in PWID and other groups prior to unrestricted access. Ongoing HCV transmission is occurring in MSM, as illustrated by a declining but nonetheless high rate of reinfection, stressing the need for additional preventive measures.

AOPL-**08**

HIV-specific CD8+ T-cells from elite controllers display a gene expression profile associated with increased functionality

Lisa van Pul, Ad van Nuenen, Margarita Mangas Ruiz, Agnes Harskamp, Neeltje Kootstra
Amsterdam UMC - AMC, Amsterdam, Netherlands

Background
Antiretroviral therapy (ART) is very successful, however it cannot eliminate the viral reservoir and therefore lifelong treatment of HIV infected individuals is essential. In order to gain immune control upon treatment interruption or to eradicate/reduce the viral reservoir during so-called “kick and kill” strategies, a fully effective CD8+ T-cells response is essential. Natural immune control of HIV infection is possible, and these so called elite controllers (EC) have highly efficient HIV-specific CD8+ T-cells. The aim of this study was to gain insight into the mechanisms behind CD8+ T-cell dysfunction in HIV infection.

Methods
HIV- and CMV-specific CD8+ T-cells from patients with chronic HIV infection (CHI; n=7), HLA-B*57 EC (n=6) as well as HLA-B*7 long-term non-progressors (LTNP; n=7) were isolated from cryopreserved PBMC of individuals participating in the Amsterdam Cohort Studies. In addition, CMV-specific CD8+ T cells were isolated from blood donors (BD; n=6). HIV and CMV-specific CD8+ T-cells were isolated by flow cytometry sorting using MHC class I dextramers presenting HIV or CMV peptides. Next, RNA libraries were generated and RNA sequencing was performed. Differential gene expression (DGE) analysis was performed using the EdgeR package in R and the Reactome pathway browser was used for pathway analysis.

Results
DGE analysis comparing HIV-specific CD8 T-cells of CHI and EC or LTNP identified respectively 23 or 14 differentially expressed genes (DEG) (logFC >1.5; P-value <0.1) of which most genes were upregulated in EC (15 DEGs) and LTNP (11 DEGs). Nine of these genes were differentially expressed in both EC and LTNP as compared to CHI. Pathway analysis revealed 274 different pathways and showed that most of these DEGs play a role in protein and RNA metabolism pathways, while some DEGs were also involved in infectious disease and the immune system. DGE analysis of the CMV-specific CD8 T-cells of CHI compared to those of EC or LTNP revealed a different gene expression profile compared to that of the HIV-specific CD8 T-cells.

Conclusions
HIV-specific CD8+ T-cells of EC and LTNP display a gene expression profile associated with increased protein and RNA metabolism pathways as compared to CHI. These pathways in CD8+ T-cells have previously been linked to enhanced cytotoxicity. This indicates that immune control of HIV infection in EC and LTNP is associated with increased functionality of HIV-specific CD8 T-cells. Moreover, the gene expression profile of CD8+ T-cells was virus specific, and no increased expression of inhibitory receptors was observed in CHI.

AOPL-**09**

Antibody engineering to improve Fc effector function and therapeutic application of HIV-1 bNAbs

Steven de Taeye[1], Angela Schriek1, Marloes Grobben[1], Geert-Jan Boons[2], Rogier Sanders[1], Marit Van Gils[1]
[1]*Amsterdam UMC, Amsterdam, Netherlands*
[2]*Utrecht University, Utrecht, Netherlands*

Background
Despite decades of research there is still no cure for HIV, though broadly neutralizing antibodies (bNAbs) against HIV-1 have shown great potential for the treatment of HIV-infected individuals recently. HIV-specific bNAbs are able to recognize a large percentage of circulating HIV-1 strains worldwide and have shown to delay viral rebound and reduce the latent reservoir in a subset of patients in recent studies. These results demonstrate the potential of antibodies, but also indicate that improvements are necessary before antibodies will lead to a functional cure. Recently, there is a growing interest in potentiating the effector functions of antibodies to improve the use of antibodies as therapeutics. Fc-receptors can be found on many immune cells and activating these through the Fc-tail of antibodies leads to phagocytosis, complement activation and infected cell lysis. In a recent study, the administration of a TLR ligand in combination with antibody therapy was found to delay viral rebound in a SHIV infection model, by activating immune cells and increasing killing of HIV-infected cells through the effector function of the co-administered antibody.

Methods
We designed three strategies to improve the function of broadly neutralizing antibodies (bNAbs) PGDM1400 and ACS202: (1) Fc engineering to increase Fc mediated effector function, (2) Conjugation of a TLR ligand to the Fc glycan to activate immune cells and (3) Conjugation of a toxin to the Fc glycan to facilitate direct killing of infected cells. Functional in vitro assays, such as antibody dependent cellular cytotoxicity (ADCC) and antibody dependent cellular phagocytosis (ADCP), will guide the selection of the best Fc-engineered variants.

Results
We have produced 10 different Fc-variants of bNAb PGDM1400, varying in terms of isotype, hinge length and Fc-glycosylation profile. All variants showed equal Env-binding and HIV-1 neutralization capacity compared to PGDM1400 IgG1 WT. Currently, these Fc-variants are further analysed for their Fc-dependent effector function in various in vitro assays.

Conclusions
The most promising antibody candidates in terms of Fc effector function and immune activation will be further tested on ex-vivo material from HIV-1 infected patients. Next, the contribution of these antibodies to a functional cure for HIV-1 will be tested in a therapeutic setting.

AOPL-**10**

Impact of COVID-19 measures on patterns of sexual activity and risk of HIV or STI acquisition among MSM living in the Netherlands

Philippe CG Adam[1], Eline Op de Coul[2], Paul Zantkuijl[3], Chantal den Daas[4], Wim Zuilhof[3], John de Wit[5]

[1]*Institute for Prevention and Social Research, Utrecht, Netherlands*

[2]*Rijksinstituut voor Volksgezondheid en Milieu, Bilthoven, Netherlands*

[3]*Soa Aids Netherlands, Amsterdam, Netherlands*

[4]*Aberdeen Health Psychology Group, Institute of Applied Health Sciences, University, Aberdeen, Scotland*

[5]*Utrecht University, Utrecht, Netherlands*

Background

From mid-March 2020, people in the Netherlands were encouraged to stay at home as much as possible, limit numbers of home visitors, and practice social and physical distancing with people not part of their household. In this study, we assessed the extent to which men who have sex with men (MSM) in the Netherlands adapted their sexual activity during this so-called 'intelligent lockdown', and whether they subsequently compensated for missed sexual opportunities, possibly resulting in increased HIV/STI risk.

Methods

From 20 July to 11 September 2020, adult MSM in the Netherlands were recruited through social media. Of the 4,012 eligible MSM who commenced the online survey, 55% completed the comprehensive questionnaire about their sexual behaviour, and strategies to mitigate the risk of COVID-19 and HIV infection. Overall data were collected for the second half of 2019 and the first half of 2020. Detailed data were collected for the two months before the lockdown (T1, January-February), the two months of lockdown (T2, mid-March-mid-May), and the two months following the easing of the lockdown (T3, mid-May-mid-July). We analysed responses of 1,811 MSM who were sexually active at T1 and reported data for all periods.

Results

The number of sex partners was lower in the first half of 2020 (Mdn=3.0) than in the second half of 2019 (Mdn=5.0). While all included respondents were sexually active at T1, 25.5% were sexually abstinent at T2 and 14% at T3. The proportion of sexually active respondents with more than one partner decreased between T1 and T2 (from 57.4% to 44.6%), as did participation in group sex. The proportion of respondents with more than one partner increased at T3 (53.4%), but remained below baseline, as did participation in group sex. The number of sex partners per period was lower in T2 (Mdn=1.0) than in T1 and T3 (Mdn=2.0).

Conclusions

While respondents adapted in various ways to COVID-19, including sexual abstinence, limiting numbers of partners and avoiding group sex, nearly half had more than one partner during the lockdown. Following the lockdown, most respondents re-engaged in sex, with numbers of partners similar to pre-lockdown. Comparison of numbers of sex partners with the second half of 2019 suggests that respondents did not (over)compensate for missed opportunities in the first half of 2020. While sexual activity entails a risk of COVID-19, our data so far do not suggest that the risk of HIV/STI increased in the post-lockdown period.

AOPL-**11**

The effect of COVID-19 restrictions on daily sexual behavior and pre-exposure prophylaxis use among men who have sex with men

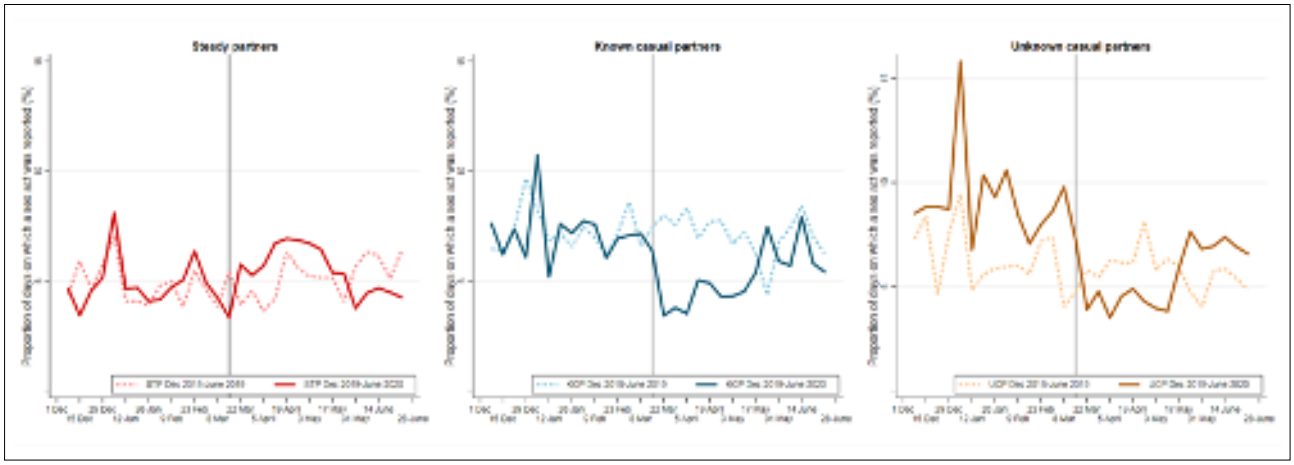
Vita Jongen, Hanne Zimmermann, Anders Boyd, Elske Hoornenborg, Mark van den Elshout, Udi Davidovich, Yvonne van Duijnhoven, Henry de Vries, Maria Prins, Maarten Schim van der Loeff, Liza Coyer
Public Health Service Amsterdam, Amsterdam, Netherlands

Background
Understanding how COVID-19 restrictions impacted sexual behavior and HIV/STI prevention choices can aid sexual health clinics prioritize care during periods of severe restrictions. We assessed how the restrictions of 15-March-2020 in the Netherlands affected sexual behaviour and PrEP- and condom-use in MSM participating in the Amsterdam PrEP (AMPrEP) demonstration project.

Methods
We used daily-collected data on (1) PrEP-use, (2) anal sex acts and (3) condom-use, according to partner type (steady [SP], known casual [KCP] and unknown casual partners [UCP]), from a mobile application used between 1-December-2019 and 30-June-2020. First, we compared the proportion of days at which each endpoint was reported before versus after 15-March-2020 using multilevel logistic regression. Second, to evaluate the effect of seasonality on anal sex, we added data of included participants from the same period the year before (i.e. 1-December-2018 through 30-June-2019, with a pseudo before-after division on 15-March-2019) to a model with an interaction between period and before-after restrictions. Third, we compared the proportion of anal sex acts covered by PrEP and/or condom before versus after 15-March-2020 using bivariate probit regression. Models were ran separately by partner type.

Results
By 1-December-2019, 302/376 (80%) AMPrEP participants were in active follow-up. We included 136/302 (45%) participants who used the app between 1-December-2019 and 30-June-2020, all MSM. By 1-December-2019, median age was 47.5 years (IQR=40-56); median follow-up since PrEP initiation was 3.9 years (IQR=3.7-4.1). The proportion of days with PrEP-use decreased from 74% to 58% before and after 15-March-2020, respectively (p<0.001). The proportion of days with anal sex was higher after 15-March-2020 for sex with SP (OR=1.25;95%CI=1.09-1.44) and lower for sex with KCP (OR=0.73;95%CI=0.64-0.82) compared to before, while these did not change the year prior (p=0.24 and p=0.59, respectively) (*Figure1*). Sex with UCP decreased after 15-March-2019 compared to before (OR=0.89;95%CI=0.80-0.99), but a more pronounced reduction was observed after 15-March-2020 (OR=0.54;95%CI=0.48-0.61). PrEP-use during sex with UCP decreased after 15-March-2020 compared to before (β=-0.36;95%CI=-0.72-0.00), and did not change with SP and KCP (p=0.16 and p=0.35, respectively). Condom-use decreased during sex with KCP (β=-0.36;95%CI=-0.67-to-0.04) and UCP (β=-0.24;95%CI=-0.46-to-0.03) after 15-March-2020 compared to before, and did not change with SP (p=0.98).

Conclusions
As per national COVID-19 recommendations, MSM limited sex acts mostly to steady partners. Decreases in sex with casual partners paralleled decreases in PrEP-use. However, continued sex with casual partners was more likely to be condomless, suggesting that continued STI testing and PrEP services are needed for PrEP-users during COVID-19 restrictions.



*AOPL-**11:** Figure 1 - Proportion of days on which sex was reported before and after the implementation of COVID-19 restrictions on 15-March-2020, and the year before*

AOPL-**12**

Never tested for HIV: directions for a targeted testing intervention among men who have sex with men

Ward P.H. van Bilsen, Hanne M.L. Zimmermann, Anders Boyd, Udi Davidovich
GGD Amsterdam, Amsterdam, Netherlands

Background
Men who have sex with men (MSM) are disproportionately affected by HIV. MSM who are unaware of their HIV-infection contribute to onward HIV transmission and are more likely to progress to severe illness. We assessed determinants of never being tested for HIV among MSM living in the Netherlands.

Methods
Between April-July 2019, we conducted a nationwide, cross-sectional survey among MSM. The survey included questions on socio-demographics, HIV-related testing behavior, sexual risk behavior and perceived severity of HIV. The survey was distributed online via gay sites/apps and social media. Multivariable logistic regression was used to investigate socio-demographic and behavioral characteristics associated with never having been tested for HIV.

Results
950 tested, HIV-negative MSM and 122 never-tested MSM completed the survey. In never-tested MSM, median age was 37 (IQR=22-51) years. The majority of this group was born in the Netherlands (n=115, 94%), resided outside a large urban area (n=105, 86%), did not have a college degree or higher (n=74, 61%), and was single (n=72, 59%). Most never-tested MSM reported a high perceived severity of HIV (n=101, 83%), while 37 (30%) reported engaging in sexual risk behavior in the preceding 6 months. In multivariable analysis, never having been tested for HIV was associated with age (adjusted odds ratio [aOR]=0.98, 95%-confidence interval [CI]=0.97-1.00, p=0.021), bisexual identity (aOR=2.93, 95%-CI=1.61-5.34, p<0.001), and not knowing others living with HIV (aOR=3.74, 95%-CI=2.28-6.13, p<0.001). Furthermore, a significant interaction was observed (p=0.001): compared to higher-educated MSM living in a large urban area, the odds for non-testing was higher among lower-educated MSM living in a rural (aOR=12.06, 95%-CI=4.00-36.38, p<0.001) or urban area (aOR=9.29, 95%-CI=3.64-23.76, p<0.001), and among higher-educated MSM living in a rural area (aOR=6.26, 95%-CI=2.42-16.23, p<0.001). There was no association between never-testing and relationship status, recent sexual risk behavior or perceived severity of HIV. When restricting analysis to MSM with recent sexual risk behavior, never-testing was only associated with not knowing others with HIV (aOR=4.91, 95%-CI=1.97-12.24, p=0.001), and bisexual identity (aOR=2.80, 95%-CI=1.09-7.18, p=0.032).

Conclusions
Based on this online sample of MSM, never testing for HIV is more common in those who were younger, had lower education level, non-urban residency, identified as bisexual, and did not know someone with HIV. Only the latter two factors were observed among those with recent sexual risk behavior. Testing interventions should be tailored to geographical location, education level, and those identifying as bisexual, while at the same time increasing the visibility of people living with HIV.

AOPL-**13**

HIV-1 Subverts the complement system to escape degradation and promote viral dissemination

Marta Bermejo Jambrina[1], Bernardien M. Nijmeijer[1], Tanja M. Kaptein[1], Carla M.S, Ribeiro[1], Doris Wilflingseder[2], Teunis B.H Geijtenbeek[1]
[1]*Amsterdam UMC-AMC, Amsterdam, Netherlands*
[2]*Institute of Hygine and Medical Microbiology, Medical University of Innsbruck, Innsbruck, Austria*

Background
Complement is an important defense mechanism against pathogens, however, its role in HIV-1 susceptibility remains unclear. Mucosal Langerhans cells (LCs) are the first immune cells to encounter HIV-1 during sexual contact and form a barrier by degrading HIV-1. Here we show that complement opsonizes HIV-1, which prevents degradation of the virus and leads to enhanced transmission by LCs.

Methods
We have used semen and serum to investigate opsonization of HIV-1 and use both primary LCs and the ex vivo human tissue transmission model to investigate HIV-1 dissemination.

Results
Non-opsonized HIV-1 did not infect LCs in the ex vivo tissue transmission model. Notably, pre-treatment of HIV-1 with semen led to HIV-1 opsonization, which enhanced LC infection and transmission to T cells. Both LC infection and transmission of complement-opsonized HIV-1 was inhibited by blocking complement receptors CR3 (CD11b/CD18) and CR4 (CD11c/CD18). Complement opsonization of HIV-1 enhanced virus uptake and fusion in LCs, leading to increased virus integration, infection and transmission. Our data suggest that complement opsonization reroutes HIV-1 away from the degradative pathway in LCs via CR3 and CR4.

Conclusions
This study strongly suggest that HIV-1 hijacks the complement system for its dissemination and imply that targeting complement factors might be effective in preventing HIV-1 transmission.

AOPL-**14**

Changes in condomless anal sex and sexually transmitted infections after PrEP initiation among men who have sex with men: a comparison of PrEP users to non-PrEP users

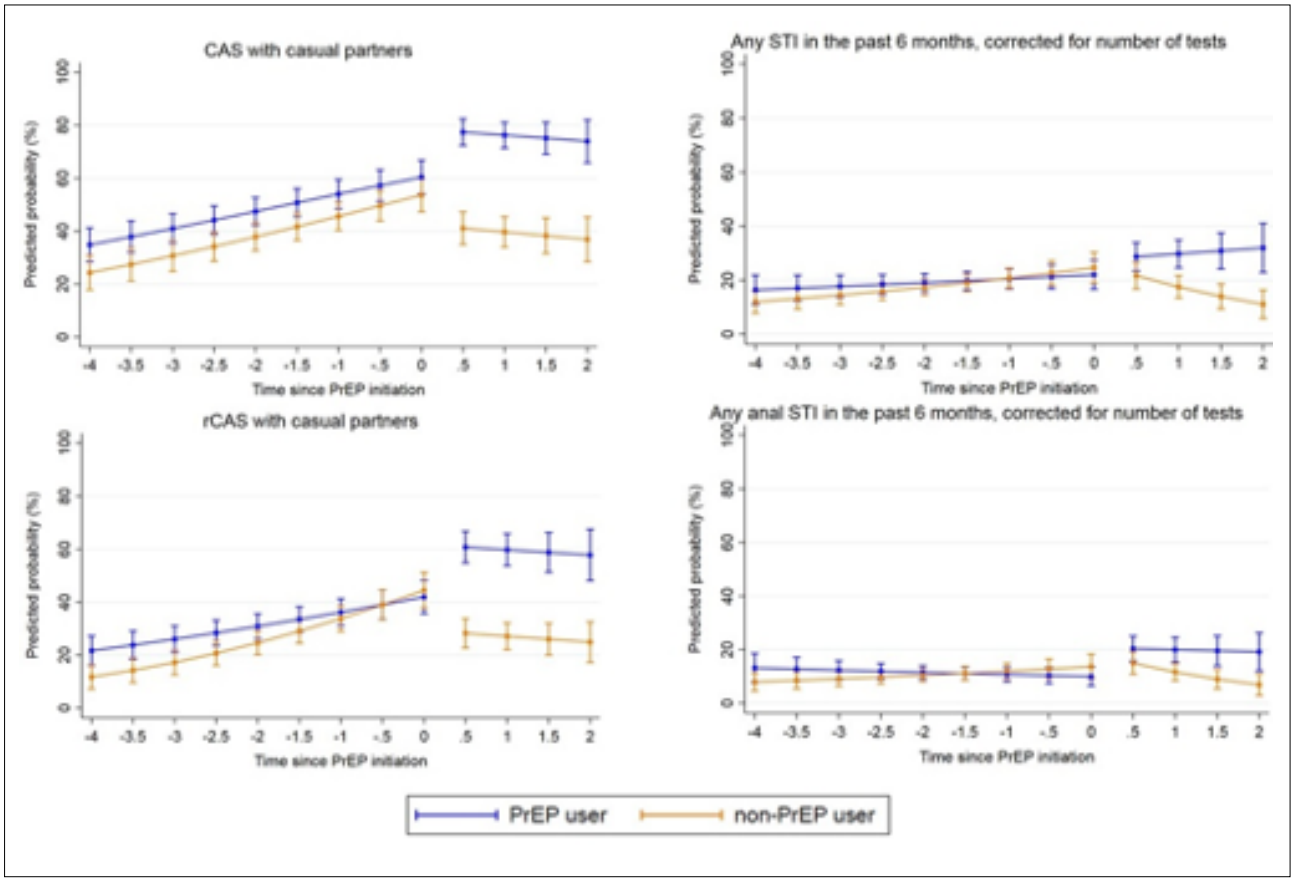
Liza Coyer[1], Anders Boyd[2], Udi Davidovich[3], Maarten Schim van der Loeff[4], Maria Prins[4], Amy Matser[1]
[1]*Public Health Service of Amsterdam, Amsterdam, Netherlands*
[2]*HIV Monitoring Foundation, Amsterdam, Netherlands*
[3]*University of Amsterdam, Department of Social Psychology, Amsterdam, Netherlands*
[4]*Amsterdam UMC, Amsterdam Infection & Immunity (AII), Amsterdam, Netherlands*

Background
People initiating HIV pre-exposure prophylaxis (PrEP) may increase condomless anal sex (CAS), and consequently, more often acquire sexually transmitted infections (STI). We assessed changes in CAS and STI after PrEP-initiation between comparable groups of men who have sex with men (MSM) from the Amsterdam Cohort Studies (ACS) who did versus who did not initiate PrEP.

Methods
MSM responded to questions on behaviors in the preceding 6 months and were tested for HIV and STI (chlamydia, gonorrhea, syphilis) biannually. We matched HIV-negative MSM who initiated PrEP between 1-January-2015 and 31-December-2019 (PrEP initiators) 1:1 to MSM who did not initiate PrEP (controls) using time-dependent propensity scores based on age, number of casual partners, chemsex, CAS with casual partners and any STI diagnosis in the 6 months before PrEP-initiation. We modeled (1) CAS and (2) receptive CAS (rCAS) with casual partners, (3) any STI, and (4) anal STI over time using logistic regression with generalized estimating equations. Models with STI as an endpoint were corrected for testing frequency. We distinguished two follow-up periods: the 4 years before and the 2 years after PrEP-initiation (for PrEP initiators) or hypothetical PrEP-initiation (for controls). We compared (1) changes over time in each period per group, (2) overall changes in endpoints before and after PrEP-initiation within each group, and (3) overall changes between groups within each period.

Results
232/850 (27.3%) MSM with a visit since 1-January-2015 ever used PrEP, of whom 198 (85%) were matched to a control. Median age of included PrEP initiators at PrEP-initiation was 42 years (IQR=34-49), 85.9% were born in the Netherlands and 78.8% had a college or university degree. Before PrEP-initiation, the proportion engaging in CAS and rCAS increased over time in both groups. In PrEP initiators, the proportion engaging in CAS (OR=1.62,95%CI=1.11-2.36), rCAS (OR=1.62,95%CI=1.15-2.27) and diagnosed with anal STI (aOR=2.46,95%CI=1.38-4.38) was on average higher after PrEP-initiation compared to before, but did not change over time after PrEP-initiation (*Figure 1*). Overall, there was no difference in endpoints between groups before PrEP-initiation, but PrEP initiators had higher odds of CAS (OR=4.89,95%CI=3.41-7.01), rCAS (OR=4.00,95%CI=2.79-5.73), any STI (aOR=1.92,95%CI=1.31-2.83) and anal STI (aOR=1.81,95%CI=1.17-2.79) than controls after PrEP-initiation.

Conclusions
CAS, rCAS and anal STI were increased in MSM after initiating PrEP compared to before and compared to a comparable group of MSM who did not initiate PrEP. These findings support regular and intensified STI screening and counseling in MSM using PrEP.



*AOPL-**14:** Figure 1 - Changes in CAS, rCAS, any STI and anal STI over time in the 4 years before and 2 years after PrEP initiation in PrEP initiators and matched controls*

AOPL-**15**

Enhancing and directing neutralizing antibody responses by ultrastabilization of HIV-1 envelope trimers and masking immunodominant epitopes

Iván del Moral Sánchez[1], Edith E. Schermer[1], Rebeca A. Russell[2], Celia C. LaBranche[3], Christopher A. Cottrell[4], Alba Torrents de la Peña[1], Sanjeev Kumar[5], Joel D. Allen[6], Philip Brouwer[1], Max Crispin[6], Andrew B. Ward[4], David Montefiori[3], Quentin Sattentau[2], Kwinten Sliepen[1], Rogier W. Sanders[1]

[1]*Amsterdam UMC, Amsterdam, Netherlands*
[2]*The Sir William Dunn School of Pathology, University of Oxford, Oxford, United Kingdom*
[3]*Department of Surgery, Duke University School of Medicine, Durham, North Carolina, United States of America*
[4]*The Scripps Research Institute, La Jolla, California, United States of America*
[5]*Department of Biochemistry, All India Institute of Medical Sciences, New Delhi, India*
[6]*School of Biological Sciences, University of Southampton, Southampton, United Kingdom*

Background
A major goal for HIV-1 vaccines is to induce broadly neutralizing antibodies (bNAbs) that neutralize most circulating viral strains. All bNAbs target the envelope glycoprotein (Env) trimer on the viral surface, which makes Env the prime constituent of many HIV-1 vaccines. Stable soluble native-like Envs, such as BG505 SOSIP trimers, can induce neutralizing antibody (NAb) responses. However, most of these Abs target strain-specific epitopes and thus only neutralize the sequence-matched BG505 virus.

Methods
Here, our aim was to improve NAb responses by generating enhanced versions of BG505 SOSIP trimers. Therefore, we generated four novel SOSIP designs (BG505 SOSIP. v9.1-v9.4) by including several mutations known to improve trimerization, stability and antigenicity of Env trimers. Additionally, we used chemical crosslinking (CL) to further stabilize SOSIP.v9.3. In order to dampen strain-specific responses, we also generated SOSIP.v9 trimers in which the BG505 strain-specific glycan hole was masked by glycans. We then characterized the biophysical, antigenic and immunogenic properties of the newly generated immunogens.

Results
All four SOSIP.v9.1-v9.4 versions produced as covalently linked trimers at equal or increased yields and presented a superior antigenic profile, compared to previous SOSIP versions. Furthermore, overall thermostability and bNAb epitope stability was increased by at least ~10 °C compared to our earlier most stable BG505 SOSIP version. Remarkably, the chemically crosslinked SOSIP.v9.3.CL trimer showed a midpoint unfolding temperature of ~91 °C.

When we compared the immunogenicity of these ultrastable BG505 SOSIP.v9 trimers to older BG505 SOSIP trimer versions in rabbits, we found that the consistency and potency of the autologous NAb responses positively correlated with increased immunogen thermostability. Significantly, rabbits that received SOSIP.v9.3.CL displayed the highest serum NAb titers. We also found that most NAb responses were directed to the immunodominant strain-specific hole in the glycan shield of BG505 Env. However, in rabbits immunized with the glycan masked trimers, we observed that this strategy efficiently redirected responses to other neutralizing epitopes without decreasing NAb titers.

Conclusions
In summary, SOSIP.v9 trimers represent a significant improvement over previous SOSIP designs. Their exceptional thermostability results in more potent and consistent NAb responses and could be highly valuable for vaccine distribution to parts of the world where reliable cold chain systems are not available. Furthermore, glycan masked versions of SOSIP.v9 might be useful platforms for designing immunogens that properly display epitopes that are more likely to induce bNAbs.

AOPO-**01**

Diagnosing HIV in the Netherlands: comparing HIV testing by general practitioners and sexual health centers in five regions

Saskia Bogers[1]*, Denise Twisk[4-6]*, Loes Beckers[2], Hannelore Gotz[3-5], Bram Meima[4,6], Michelle Kroone[7], Elske Hoornenborg[7], Alewijn Ott[8], Marleen Luning-Koster[9], Nicole Dukers-Muijers[10,11], Christian Hoebe[11,12], Karlijn Kampman[13], F. Bosma[14], Maarten Schim van der Loeff[1,7], Suzanne Geerlings[1], Jan van Bergen[2,3,15]

* These authors contributed equally to this work

[1]*Department of Internal Medicine, Division of Infectious Diseases, Amsterdam University Medical Centers, location Academic Medical Center, the Netherlands*

[2]*Department of General Practice, Amsterdam University Medical Centers, location Academic Medical Center, the Netherlands.*

[3]*Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands*

[4]*Department of Infectious Disease Control, Municipal Public Health Service Rotterdam-Rijnmond, Rotterdam, The Netherlands.*

[5]*Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands*

[6]*Department Research and Business Intelligence, Municipality of Rotterdam, Rotterdam, The Netherlands*

[7]*Department of Infectious Diseases, Public Health Service Amsterdam, Amsterdam, The Netherlands*

[8]*Certe, Department of Medical Microbiology, Groningen, The Netherlands*

[9]*Municipal Public Health Service Groningen, Groningen, The Netherlands*

[10]*Department of Health Promotion, Care and Public Health Research Institute (CAPHRI), Maastricht University, Maastricht, The Netherlands*

[11]*Department of Sexual Health, Infectious Diseases and Environmental Health, South Limburg Public Health Service, Heerlen, The Netherlands.*

[12]*Department of Medical Microbiology, Care and Public Health Research Institute (CAPHRI), Maastricht University Medical Centre (MUMC+), Maastricht, The Netherlands*

[13]*Public Health Service Twente, Enschede, The Netherlands*

[14]*Laboratory for Medical Microbiology and Public Health, Hengelo, the Netherlands*

[15]*STI AIDS Netherlands (SOA AIDS Nederland), Amsterdam, The Netherlands.*

Background

In the Netherlands, about 8% of people living with HIV are still undiagnosed and half of new cases are diagnosed late, with considerable regional variation. General practitioners (GPs) are the main sexual healthcare providers, with additional services for high-risk groups by sexual health centres (SHCs). These providers are therefore the main access point for individuals seeking HIV testing. Yet, patient characteristics, barriers to testing, and testing guidelines differ greatly between these providers. It is currently unknown how testing-practice by GPs compares to that by SHCs, and whether this differs by region. We compared HIV testing and positivity between GPs and SHCs in five Dutch regions to identify settings where HIV testing may be improved.

Methods

Laboratory data (2011-2018) on HIV testing and positivity in five Dutch regions (Amsterdam, Rotterdam, Maastricht, Twente, North-Netherlands) were used. We obtained complete data from three regions; data were missing for Maastricht 2016-2018 and for SHCs in North-Netherlands in 2015. Regional HIV testing rates per 10,000 residents ≥15 years were calculated. These were compared between providers using negative binomial generalised additive models, and were additionally stratified by sex and age (15-29y, 30-44y, 45-59y, ≥60y). Chi-squared tests were used to compare percentage positive between providers.

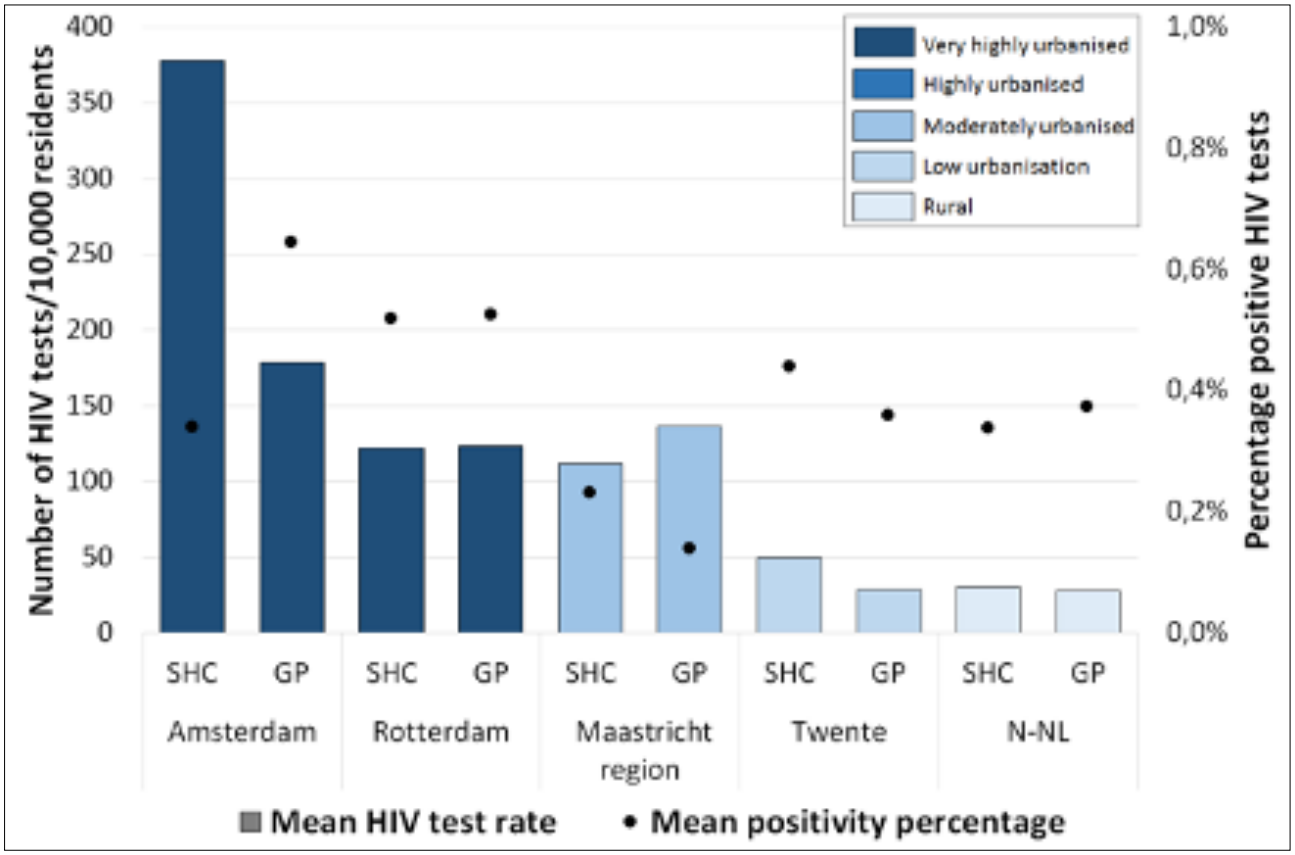
Results

Our dataset included 502,868 tests. The largest difference in testing rates between GPs and SHCs was observed in Amsterdam and Twente, where the SHC tested twice as much as GPs (Figure 1). In men, GPs' testing rates were significantly lower than the SHCs' across all regions (range rate ratio [RR]: 0.43-0.86); for women this varied per region (range RR: 0.53-1.68). Both SHCs' and GPs' testing rates decreased with increasing age of patients. Amsterdam was the only region with a significant difference in positivity between GPs and SHCs (0.6% and 0.3%, respectively, $p<0.001$). Testing rates by providers serving very highly urbanised regions were higher than those by providers serving less urbanised regions. Variation between regions of similar urbanisation was observed (e.g. Amsterdam and Rotterdam; 557 vs. 245/10,000 residents).

Conclusion

Unlike most other countries, GPs play an important role in HIV testing in the Netherlands. The contribution of GPs and SHCs to HIV testing and the percentage positive was comparable in most of the studied regions. Considering that GPs and SHCs serve different populations, more in-depth analysis involving trends over time, and applied practices per region may reveal policy improvements to achieve the Dutch ambition of HIV elimination.

AOPO: Abstract Oral Poster presentations



*AOPO-**01:** Mean number of HIV tests per 10,000 residents ≥15 years and mean HIV positivity percentage, by provider in 5 regions in the Netherlands (2011-2018)**

** Data on Maastricht includes 2011-2015. Data on 2015 in N-NL is missing.*
SHC: Sexual health centre. GP: General practitioner. N-NL: North-Netherlands.

AOPO-**02**

Testing and health-care seeking behavior preceding HIV diagnosis: directions for early-case finding among migrant and non-migrant individuals

Ward P.H. van Bilsen1[1], Janneke Bil[1], Maarten Bedert[2], Udi Davidovich[1], Ard van Sighem[3], Jan M. Prins[2], Kees Brinkman[4], Eliane Leyten[5], Fiona Burns[6], Maria Prins[1]
[1]*GGD Amsterdam, Amsterdam, Netherlands*
[2]*Amsterdam University Medical Center, Amsterdam, Netherlands*
[3]*Stichting HIV Monitoring, Amsterdam, Netherlands,*
[4]*OLVG, Amsterdam, Netherlands*
[5]*Haaglanden Medical Center, Den Haag, Netherlands*
[6]*Insitute of Global Health, London, United Kingdom*

Background
In the Netherlands, 1 out of 3 people with HIV receive their diagnosis in a late stage, which is associated with adverse clinical outcomes and ongoing HIV transmission. We assessed whether testing and health-care seeking behavior prior to HIV-diagnosis and socio-demographics differed between individuals presenting late and those who presented shortly after infection.

Methods
We used data of people living with HIV in the Netherlands who participated in the European aMASE study. Between July 2013 and June 2015, migrants and non-migrant people diagnosed with HIV within the past 5 years self-completed a survey on socio-demographics and testing and health-care seeking behavior preceding HIV-diagnosis. Testing and health-care seeking behavior were compared between early and late presenters using descriptive statistics. Using multivariable logistic regression, socio-demographic determinants of late presentation were explored. Late presentation was defined as <350/mm3 CD4+-cells or an AIDS-defining illness at time of HIV-diagnosis in the Netherlands.

Results
In total, 143 early and 101 late presenters were included, of whom respectively 59/143 (41%) and 54/101 (53%) were migrants. The majority of migrants was diagnosed in the Netherlands (109/118, 92%), and years between migration to the Netherlands and HIV-diagnosis did not differ significantly between early and late presenters (median 8 [IQR 2-24] vs. 6 [IQR 1-14] years; p=0.2). Before HIV-diagnosis, most migrant and non-migrant participants had ever been tested for HIV-infection during their lifetime (89% and 62% for early and late presenters, respectively, p<0.001), and reported healthcare use in the Netherlands in the two years preceding HIV-diagnosis (99% and 97% for early and late presenters, respectively, p=0.8). Late presenters most frequently visited a general practitioner (72%) or dentist (62%) in the two years preceding diagnosis, and 20% had been hospitalized. In these settings, only in respectively 20%, 2%, and 6% of cases an HIV-test was discussed. In multivariable analysis, late presentation was associated with older age (adjusted odds ratio [aOR]=1.04 per year, 95%-confidence interval [95%-CI]=1.01-1.07, p=0.002), and being heterosexual (compared to non-migrant men who have sex with men (MSM): migrant MSM, aOR=1.39 95%-CI=0.72-2.66; non-migrant heterosexual male aOR=5.53, 95%-CI=1.58-19.34; migrant heterosexual male aOR=11.42, 95%-CI=3.11-41.95; migrant heterosexual female aOR=3.29, 95%-CI=1.18-9.15; p<0.001).

Conclusions
Testing interventions are needed for migrant and non-migrant heterosexual individuals at risk for HIV-infection to diagnose and treat HIV-infection in an early stage. As most late presenters used health-care preceding their HIV-diagnosis in which HIV-testing was not discussed, it seems feasible to successfully roll out interventions within the existing health-care system.

AOPO-**03**

Sexual behavior and its determinants during COVID-19 restrictions among men who have sex with men in Amsterdam

Ward P.H. van Bilsen[1], Hanne M.L. Zimmermann[1], Liza Coyer[1], Lia van der Hoek[2], Neeltje A. Kootstra[2], Elske Hoornenborg[1], Maria Prins[1], Maarten Schim van der Loeff[1], Udi Davidovich[1], Amy Matser[1]
[1]*GGD Amsterdam, Amsterdam, Netherlands*
[2]*Amsterdam University Medical Center, Amsterdam, Netherlands*

Background
In response to COVID-19, far-reaching measures were introduced in the Netherlands from March, 2020 onwards. To inform future policy making on sexual health care during COVID-19 restrictions, we investigated determinants of having engaged in sex with casual partners during COVID-19 restrictions and HIV/STI positivity rates among men having sex with men (MSM) participating in the Amsterdam Cohort Study (ACS).

Methods
Normally, ACS participants are tested semi-annually for HIV/STI, and, in case of symptoms or partner notification, participants can be tested in-between study visits. Due to COVID-19, routine study visits were halted from 23-March-2020 to 1-June-2020; participants could only visit the STI-clinic when they had HIV/STI-related symptoms or really needed PrEP. On 29-May-2020, we invited all participants to complete an extra online survey on health, COVID-19 risk perceptions, beliefs and attitudes, social distancing, sexual behavior and substance use during the period of COVID-19 restrictions. We examined determinants of sex with casual partners (CSP) during COVID-19 restrictions using logistic regression. Additionally, we compared HIV/STI positivity rates before and during COVID-19 restrictions.

Results
353/683 MSM (52%; median age 47 years, IQR 38-53) completed the survey. 73% reported to have reduced the number of CSP during COVID-19 restrictions, and 11% of 125 PrEP-users discontinued PrEP. CSP during COVID-19 restrictions were reported by 133 (38%) MSM. MSM in a steady relationship and with higher educational level were less likely to report CSP (adjusted odds ratio [aOR]=0.47; 95%-confidence interval [CI]=0.24-0.92 for both). Reporting CSP was more likely among MSM with low perceived importance of preventing COVID-19 (aOR=2.59; CI=1.34-4.99), higher number of known and anonymous CSP pre-COVID-19 (i.e., in 2019) (aOR=4.63; CI=2.11-10.15 and aOR=2.58; CI=1.35-4.94 for ≥5 known CSP and ≥5 anonymous CSP, respectively, compared to no CSP), and current PrEP use (aOR=3.57; CI=1.89-6.76). Before COVID-19 restrictions, a bacterial STI was diagnosed in 19% of MSM in-between study visits and 9% when study visits and in-between study visits were pooled; there were no HIV-infections. During COVID-19 restrictions, no HIV-infections were diagnosed and the bacterial STI positivity rate was 8%.

Conclusions
During COVID-19 restrictions, the number of CSP decreased among MSM and there may have been a temporary reduction in HIV/STI transmission. Still, over one-third of MSM reported CSP and was associated, among others, with higher number of partners pre-COVID. It is important to maintain accessible HIV/STI-related testing and care as well as PrEP services for these men at times of lockdown.

AOPO-**04**

‘Not Right Now’ – Navigating sexual health services for MSM during the Covid-19 crisis in the Netherlands

Lizette Krist, Mart van Dijk, Sarah Stutterheim, Kai Jonas
Maastricht University, Maastricht, Netherlands

Background
As a result of Covid-19, access to non-essential health care has been limited. Social distancing, reduced (anonymous) clinical services, delayed requests, and reduced public transport has also made access to sexual health services difficult. This study investigated prevalence, and correlates, of HIV and renal function testing among men who have sex with men (MSM) in the Netherlands during the Covid-19 crisis.

Methods
In August 2020, 313 MSM responded to the fourth survey of a cohort of 758 MSM established in 2017 to investigate psychosocial correlates of PrEP use. We looked at the prevalence of HIV and renal function testing across the third and fourth survey, as well the role of place of residence (urban versus non-urban), educational attainment, financial hardship, age, and PrEP experience in testing.

Results
Among participants, 58.6% reported having been tested for HIV in the three months prior to the fourth survey. This was lower in non-urban versus urban (Amsterdam, Rotterdam, The Hague, Utrecht) participants (55.3% versus 63.1%).

Among participants currently taking PrEP (n=190), having been tested for HIV reduced from 93.8% at the third measurement (pre-Covid) to 75.9% during the Covid-19 crisis (urban: 77.2%, non-urban: 74.7%). Similarly, renal function test in the past three months dropped from 81.8% to 70.1%, with renal function testing also being lower among non-urban versus urban participants (66.3% versus 74.7%). Reductions in HIV and renal function testing rates in the third (pre-Covid-19) versus fourth (during Covid-19 crisis) measurement were statistically significant (ps<0.001).

Logistic regression analyses confirmed the place of residence descriptive analyses for renal testing (OR 2.66, 95% CI 1.13-6.27) but not for having had an HIV test. There was an overall association for HIV tests in the past three months with having had a renal function test in the past three months (OR 55.80, 95% CI 21.62-144.02) and having had a renal function test was associated with having tested for HIV (OR 50.86, 95% CI 20.48-126.29) respectively. No other significant correlates (educational attainment, financial hardship, age, and PrEP experience) were found.

Conclusions
As Covid-19 restrictions continue to be unpredictable, and access to sexual health care services remains precarious, health care providers should seek to proactively follow-up with MSM who normally do HIV testing, and also for renal function testing among PrEP users, even in this Covid-19 crisis. This is particularly imperative for MSM living in non-urban regions, where access to care may be more impeded than in urban areas.

AOPO-**05**

A cost-saving algorithm for initiating antiretroviral therapy in HIV naïve patients

Piter Oosterhof[1], Daoud Ait Moha[2], Gijs Geerders[2], Janneke Stalenhoef[2], Matthijs van Luin[3], David Burger[4], Kees Brinkman[2]
[1]*OLVG / Radboudumc, Amsterdam, Netherlands*
[2]*OLVG, Amsterdam, Netherlands*
[3]*Rijnstate hospital, Arnhem, Netherlands*
[4]*Radboudumc, Nijmegen, Netherlands*

Background
Many treatment naïve HIV patients are prescribed so called single tablet regimens (STRs). However, use of STRs is associated with considerable expenses. We developed an algorithm to start newly diagnosed patients with a multi-tablet regimen (MTR) and after virological suppression switch to maintenance with a STR. In this algorithm we take into account virological response, renal function, hepatitis B status and medication costs. This algorithm has been discussed as a new policy within OLVG. Here we report on our experience with this new policy.

Methods
From January to August 2020, all newly diagnosed patients with HIV who started combination antiretroviral therapy (cART) in OLVG with at least a follow-up of 3 months, were included for this analysis. Patients were prescribed first-line antiretroviral therapy (ART) with currently recommended or alternative regimens according to the DHHS Guidelines. An MTR was preferred, although deviation was possible. The MTR consisted of the backbone tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) and dolutegravir (DTG) and after one month switch to TDF/3TC/DOR, 3TC/DTG or TAF/FTC/BIC was possible. Patient data were collected from the electronic patient files. Cost savings were calculated using Dutch drug prices. The objectives were to study (1) compliance to the new policy by prescribers; (2) time to switch to maintenance; and (3) cost-savings extrapolated to yearly costs.

Results
A total of 30 patients were included in the analysis; demographic and treatment characteristics are shown in *table 1*. Twenty-five of the 30 patients (83%) started with the preferred MTR, 3 patients (=10%) started with an STR. The reasons for deviation were divers. Patient preference (i.e. compliance, swallowing complaints) were the main cause. Eighteen of the 30 patients (60%) have been switched according to the algorithm and 10 (33%) patients are still on initial treatment. The median time for switch to maintenance therapy was 2.5 months. Based on renal function and hepatitis B status, 1 patient was switched to TAF/FTC/BIC, 2 patients to 3TC/DTG and fifteen patients were switched to TDF/3TC/DOR. All patients were virological suppressed. In the total group (n=30), extrapolated to this year, drug expenses were €68.000 (29%) lower by using this algorithm compared to starting a STR directly.

Conclusions
Our algorithm for starting antiretroviral therapy in newly diagnosed patients with HIV was easy to follow and well-accepted by care-providers and patients. Our data shows a rapid virological suppression as well as significant cost savings in a small population.

Demographics n=30	
Gender, n (%)	
Male	23 (77%)
Female	7 (23%)
Mean age, years	36.6
Treatment status *(n, %)*	
Treatment details	
TDF/FTC +DTG	25 (83%)
TAF/FTC/BIC	3 (10%)
DRV/c,DTG	1 (3%)
TDF/FTC,DRV/c,DTG	1 (3%)
Number for ART pills	
1	3 (10%)
2	26 (87%)
3	1 (3%)
Reason for other regimen (n=5)	
Compliance	2 (40%)
Acute HIV	2 (40%)
Swallowing complaints	1 (20%)
Viral load (after 1 month treatment)	
> 200 copies/ml	3 (10%)
< 200 copies/ml	6 (20%)
< 50 copies/ml	21 (70%)
Treatment after algorithm (n=18)	
Initial regimen	
TDF/FTC +DTG	15 (83%)
TAF/FTC/BIC	1 (6%)
DRV/c,DTG	1 (6%)
TDF/FTC,DRV/c,DTG	1 (6%)
Time till switch from initial regimen (months)	
Median (IQR)	2.5 (2 - 6)
Regimen after switch	
TDF/3TC/DOR	15 (83%)
3TC/DTG	2 (11%)
TAF/FTC/BIC	1 (6%)

*AOPO-**05:** Table 1*

AOPO-**06**

Lower Tolerability of Initial ART in Women with HIV Infection

Sharisa Boland, Tania Mudrikova
UMC Utrecht, Utrecht, Netherlands

Background
To achieve a lifelong equally effective antiretroviral therapy (ART) for both HIV-positive men and women, sex differences affecting treatment tolerability need to be elucidated. This study explored the possible sex differences in tolerability of and response to initial ART in the first year after start of treatment.

Methods
This retrospective monocenter cohort study was conducted among the adult ART-naive HIV population getting into care at the UMC Utrecht between 2005 and 2018. Differences in the combination of initial antiretroviral agents, switching rate, virologic and immunologic responses, and adverse events leading to regimen switch were assessed. Univariate analyses for between-groups comparisons of continuous variables were conducted using the independent samples t-test, and $\chi 2$ -test and Mann-Whitney-U test for parametric and non-parametric categorical variables respectively.

Results
761 males and 117 females were eligible for analysis. Most frequently used regimen in men was NNRTI with tenofovir and lamivudine/emtricitabine (40.6%) and PI with the same backbone in women (42.7%). Significantly more women switched their initial regimen compared to men (39.3% vs. 23.9%, p<.001) with similar median time to switch (15 vs. 12 weeks, p=.842). Comparable proportions of males and females reached undetectable viral loads after six months of treatment (84.7% vs. 82.5%, p=.543) and CD4+ lymphocyte count increase after twelve months was similar (241 vs. 222, p=.281). Equal proportions of men and women reported subjective side effects (12.7% vs. 14.5%, p=.593) and showed laboratory toxicities (5.0% vs. 6.8%, p=.405) leading to regimen switch. Among men, subjective side effects mainly encompassed neurocognitive complaints (53.6%) and allergic reactions (27.8%), while among women these were gastro-intestinal (35.3%) and neurocognitive (29.4%). Adverse events were reason for regimen switch in 74.2% of men, whereas this was only in 54.4% of women. The remainder of reasons for regimen switch were divergent.

Conclusions
Although the efficacy of initial antiretroviral treatment was comparable between the sexes, females showed a lower tolerability compared to males. Most regimen switches occurred during the early treatment phase. Subjective and laboratory side effects less often appear a reason for treatment switch in women than in men. As not all switch factors are readily to predict, close follow-up after start of initial antiretroviral treatment appears to be even more important in females than in males. It should be evaluated whether the differences in switch rates between the sexes are the same when evaluating larger cohorts of patients and when using currently preferred INSTI regimens.

AOPO-**07**

The impact of sex on immune activation and inflammation dissipates in men and women with HIV after prolonged viral suppression

Albert Groenendijk, Ruben Hoogeveen, Anthonie Groothuismink, Karin Schurink, Dorine de Vries-Sluijs, Wendy van de Sande, Andre Boonstra, Annelies Verbon
Erasmus MC, Rotterdam, Netherlands

Background
Sex-based differences in immune activation have been found in viremic people with HIV after short term viral suppression. The impact of long-term viral suppression on sex-based differences in immune activation, microbial translocation and inflammation is not clear. This research sought to determine immune parameters in women and men with HIV on combination antiretroviral therapy with prolonged viral suppression, matched by CD4 nadir, age and ethnicity.

Methods
Monocyte and lymphocyte subsets were assessed with flowcytometry. Inflammatory (IL-1β , IL-6, IL-18, IL-18BP, IL-10, IL-8, IP-10, CRP, IL-37, TNF-α, sTNF-RII and IFN-γ), coagulation (D-dimer), microbial translocation ((1→3)-β-D-glucan) and monocyte activation markers (sCD14, sCD163, MCP-1, MIP-1β, MIG) were measured in plasma.

Results
In 34 women and 34 matched men with long-term viral suppression (median 73 months; interquartile range 28-160), many markers of immune and monocyte activation were still increased compared to HIV-uninfected controls. Only minor sex-based differences in immune activation were present. CD38+HLA DR+ co-expression was lower on CD4+ T and CD8+ T lymphocytes of women than of men (0.93% vs. 1.42%; p=0.021 and 1.13% vs 1.98%; p=0.055, respectively). MCP-1 levels were lower in women (p=0.006) and D-dimer was higher (p=0.018). None of the other inflammatory makers nor (1→3)-β-D-glucan levels did differ between men and women.

Conclusions
The vast majority of immune activation markers was not different in women and men with HIV, suggesting that the impact of sex on immune activation and inflammation dissipates with prolonged viral suppression.

Keywords: HIV-1, inflammation, inflammation mediators, monocytes, sex factors, female, immune activation.

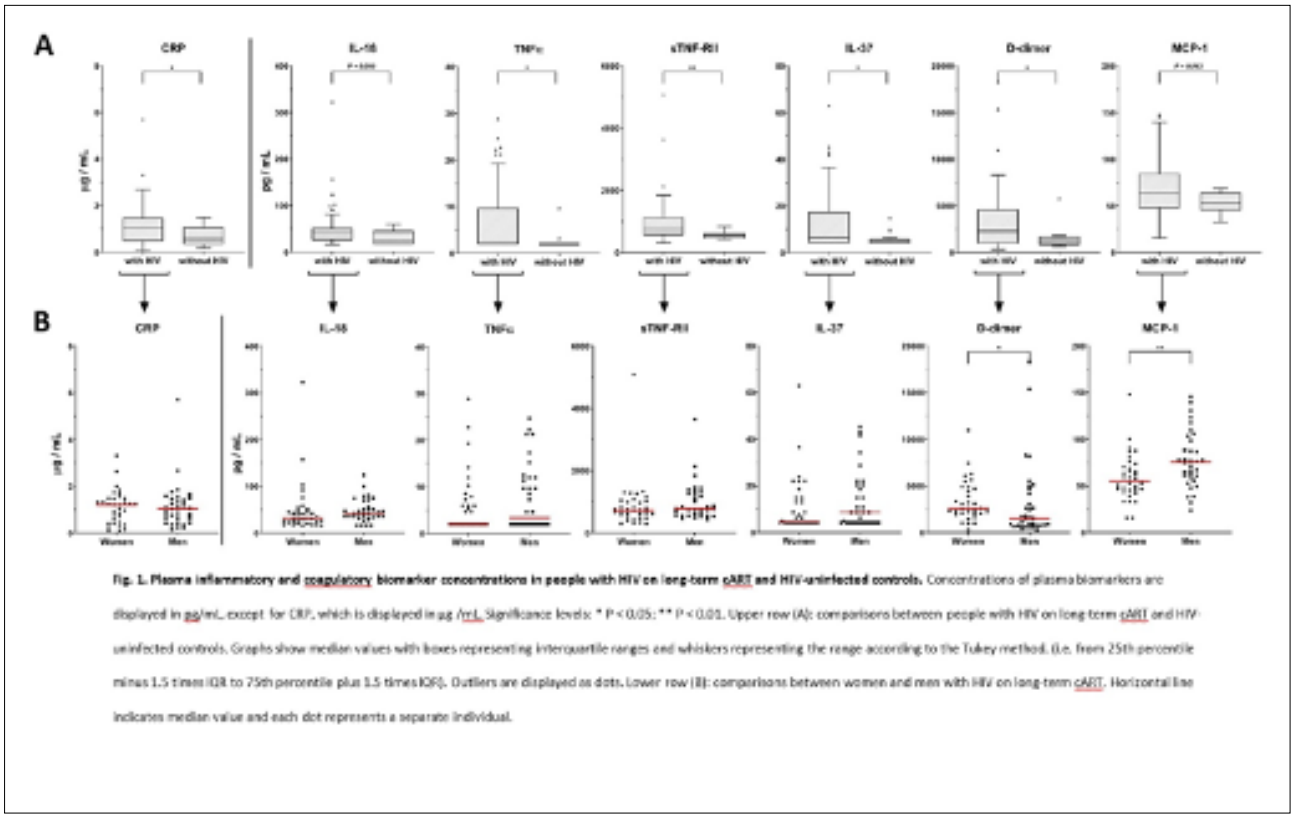
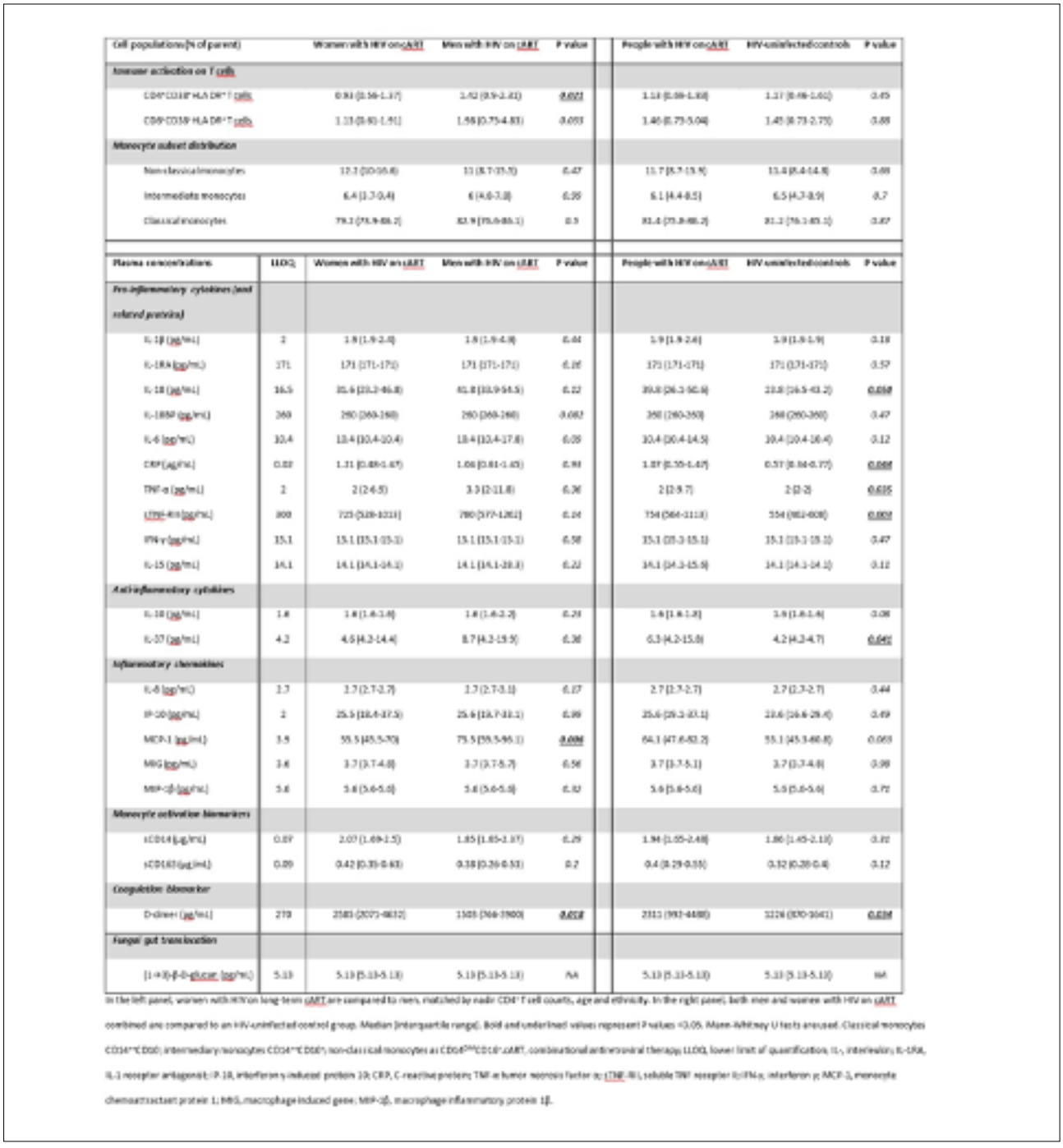


Fig. 1. Plasma inflammatory and coagulatory biomarker concentrations in people with HIV on long-term cART and HIV-uninfected controls. Concentrations of plasma biomarkers are displayed in pg/mL, except for CRP, which is displayed in µg /mL. Significance levels: * P < 0.05; ** P < 0.01. Upper row (A): comparisons between people with HIV on long-term cART and HIV-uninfected controls. Graphs show median values with boxes representing interquartile ranges and whiskers representing the range according to the Tukey method. (i.e. from 25th percentile minus 1.5 times IQR to 75th percentile plus 1.5 times IQR). Outliers are displayed as dots. Lower row (B): comparisons between women and men with HIV on long-term cART. Horizontal line indicates median value and each dot represents a separate individual.

*AOPO-**07:** Figure 1*

AOPO: Abstract Oral Poster presentations



Cell populations (% of parent)	Women with HIV on cART	Men with HIV on cART	P value	People with HIV on cART	HIV-uninfected controls	P value
Immune activation on T cells						
$CD4^+$ $CD38^+$ $HLA\text{-}DR^+$ T cells	0.91 (0.56-1.37)	1.42 (0.9-2.42)	**0.023**	1.14 (0.69-1.93)	1.17 (0.68-1.61)	0.45
$CD8^+$ $CD38^+$ $HLA\text{-}DR^+$ T cells	1.13 (0.81-1.91)	1.98 (0.75-4.83)	0.093	1.46 (0.73-5.04)	1.45 (0.73-2.75)	0.88
Monocyte subset distribution						
Non-classical monocytes	12.3 (10-16.4)	11 (8.7-15.5)	0.47	11.7 (8.7-15.9)	11.4 (8.4-14.8)	0.88
Intermediate monocytes	6.4 (3.7-9.4)	6 (4.6-7.8)	0.39	6.1 (4.4-8.5)	6.5 (4.7-8.9)	0.7
Classical monocytes	79.3 (73.9-86.2)	82.9 (76.6-86.1)	0.3	81.4 (75.8-86.2)	81.2 (76.1-85.1)	0.87

Plasma concentrations	LLOQ	Women with HIV on cART	Men with HIV on cART	P value	People with HIV on cART	HIV-uninfected controls	P value
Pro-inflammatory cytokines (and related proteins)							
IL-1β (pg/mL)	2	1.9 (1.9-2.0)	1.9 (1.9-4.9)	0.44	1.9 (1.9-2.6)	1.9 (1.9-1.9)	0.18
IL-1RA (pg/mL)	171	171 (171-171)	171 (171-171)	0.16	171 (171-171)	171 (171-171)	0.57
IL-18 (pg/mL)	16.5	35.6 (23.2-46.8)	41.8 (33.9-54.5)	0.22	39.8 (26.3-50.6)	23.8 (16.5-43.2)	**0.018**
IL-18BP (pg/mL)	260	260 (260-260)	260 (260-260)	0.082	260 (260-260)	260 (260-260)	0.47
IL-6 (pg/mL)	10.4	13.4 (10.4-10.4)	13.4 (13.4-17.8)	0.09	10.4 (10.4-14.5)	10.4 (10.4-16.4)	0.12
CRP (µg/mL)	0.03	1.31 (0.48-1.67)	1.66 (0.81-1.65)	0.93	1.37 (0.55-1.67)	0.57 (0.34-0.77)	**0.004**
TNF-α (pg/mL)	2	2 (2-6.5)	3.3 (2-11.8)	0.26	2 (2-3.7)	2 (2-2)	**0.035**
sTNF-RII (pg/mL)	300	723 (529-1211)	780 (577-1,261)	0.24	734 (566-1113)	554 (382-608)	**0.001**
IFN-γ (pg/mL)	15.1	15.1 (15.1-15.1)	15.1 (15.1-15.1)	0.58	15.1 (15.1-15.1)	15.1 (15.1-15.1)	0.47
IL-15 (pg/mL)	14.1	14.1 (14.1-14.1)	14.1 (14.1-20.3)	0.22	14.1 (14.1-15.9)	14.1 (14.1-14.1)	0.12
Anti-inflammatory cytokines							
IL-10 (pg/mL)	1.8	1.8 (1.8-1.8)	1.8 (1.8-2.2)	0.23	1.8 (1.8-1.8)	1.8 (1.8-1.8)	0.08
IL-27 (pg/mL)	4.2	4.5 (4.2-14.4)	8.7 (4.2-19.5)	0.38	6.3 (4.2-15.8)	4.2 (4.2-4.7)	**0.041**
Inflammatory chemokines							
IL-8 (pg/mL)	2.7	2.7 (2.7-2.7)	2.7 (2.7-3.1)	0.27	2.7 (2.7-2.7)	2.7 (2.7-2.7)	0.44
IP-10 (pg/mL)	2	25.5 (18.4-37.5)	25.6 (18.7-33.1)	0.89	25.6 (20.1-37.1)	23.6 (16.6-29.4)	0.49
MCP-1 (pg/mL)	3.9	55.5 (45.5-70)	75.5 (59.5-96.1)	**0.006**	66.1 (47.6-82.2)	55.1 (45.3-66.8)	0.063
MIG (pg/mL)	3.8	3.7 (3.7-4.8)	3.7 (3.7-5.7)	0.56	3.7 (3.7-5.1)	3.7 (3.7-4.8)	0.98
MIP-1β (pg/mL)	5.8	5.8 (5.6-5.8)	5.8 (5.6-5.8)	0.32	5.8 (5.6-5.8)	5.8 (5.6-5.8)	0.72
Monocyte activation biomarkers							
sCD14 (µg/mL)	0.07	2.07 (1.69-2.5)	1.85 (1.65-2.37)	0.29	1.94 (1.55-2.48)	1.86 (1.45-2.16)	0.32
sCD163 (µg/mL)	0.09	0.42 (0.33-0.63)	0.38 (0.26-0.53)	0.2	0.4 (0.29-0.55)	0.32 (0.28-0.4)	0.12
Coagulation biomarker							
D-dimer (pg/mL)	270	2583 (2072-4812)	1503 (766-3900)	**0.018**	2311 (992-4480)	1226 (870-1641)	**0.034**
Fungal gut translocation							
(1→3)-β-D-glucan (pg/mL)	5.13	5.13 (5.13-5.13)	5.13 (5.13-5.13)	NA	5.13 (5.13-5.13)	5.13 (5.13-5.13)	NA

In the left panel, women with HIV on long-term cART are compared to men, matched by nadir $CD4^+$ T cell counts, age and ethnicity. In the right panel, both men and women with HIV on cART combined are compared to an HIV-uninfected control group. Median (interquartile range). Bold and underlined values represent P values <0.05. Mann-Whitney U tests are used. Classical monocytes $CD14^{++}CD16^-$; intermediary monocytes $CD14^{++}CD16^+$; non-classical monocytes as $CD14^{dim}CD16^+$. cART, combinational antiretroviral therapy; LLOQ, lower limit of quantification; IL-, interleukin; IL-1RA, IL-1 receptor antagonist; IP-10, interferon γ-induced protein 10; CRP, C-reactive protein; TNF-α, tumor necrosis factor α; sTNF-RII, soluble TNF receptor II; IFN-γ, interferon γ; MCP-1, monocyte chemoattractant protein 1; MIG, macrophage induced gene; MIP-1β, macrophage inflammatory protein 1β.

*AOPO-**07:** Table 2 - Immune activation in women and men with HIV on long-term cART, and HIV-uninfected controls*

AOPO-**08**

Faster decline in lung function in treated HIV-positive vs. HIV-negative AGEhIV cohort participants independent of smoking behavior

Sebastiaan[1], Anders Boyd[2], Ferdinand Wit[2], Eveline Verheij[1], Maarten Schim van der Loeff[3], Neeltje Kootstra[4], Marc van der Valk[4], Reindert Van Steenwijk[4], Bradley Drummond[5], Greg Kirk[6], Peter Reiss[2]

[1]*Amsterdam Institute for Global Health and Development, Amsterdam, Netherlands*

[2]*HIV Monitoring Foundation, Amsterdam, Netherlands*

[3]*Public Health Service of Amsterdam, Amsterdam, Netherlands*

[4]*Amsterdam UMC (location AMC), Amsterdam, Netherlands*

[5]*University of North Carolina, Chapel Hill, U.S.A.*

[6]*Johns Hopkins University, Baltimore, U.S.A.*

Background

We previously reported Forced Vital Capacity (FVC) to be lower in HIV-positive versus HIV-negative participants with limited smoking-exposure at time of enrolment in the AGEhIV cohort study. We now evaluate longitudinal changes in spirometry indices, accounting for smoking and other risk factors.

Methods

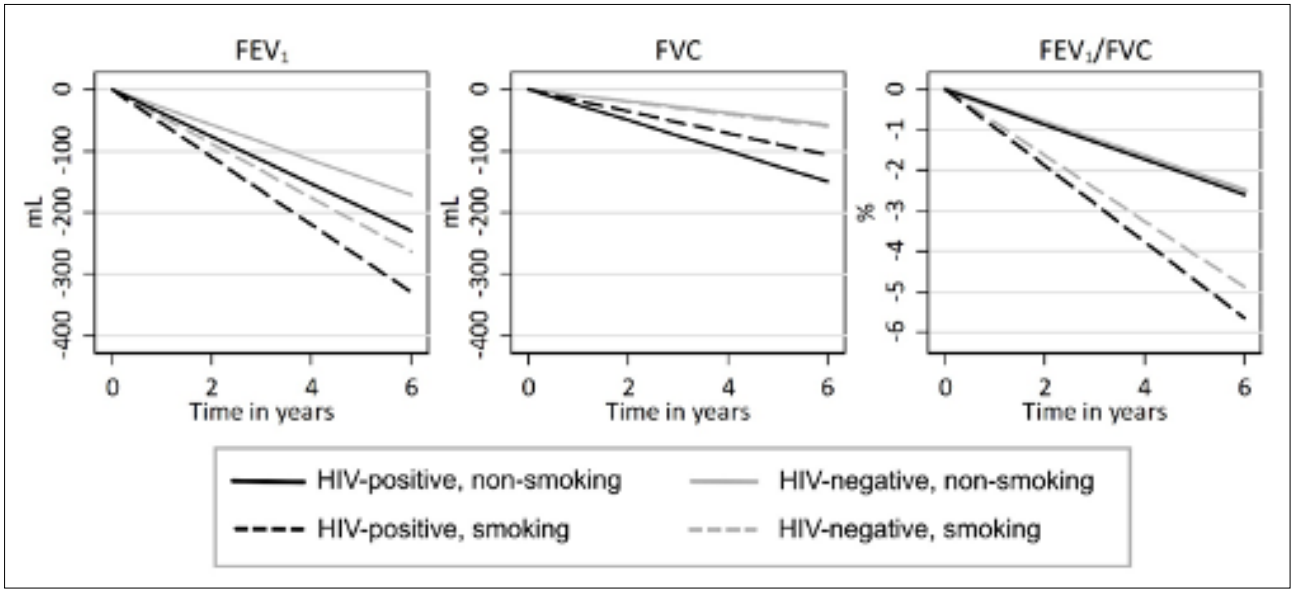
Pre-bronchodilator spirometry measurements from biennial AGEhIV cohort study visits over a median 6 years were analyzed. Adjusted declines in 1-second Forced Expiratory Volume (FEV1), FVC and FEV1/FVC were modeled using linear mixed-effects models and compared between HIV and smoking categories. Rates of FEV1 and FVC decline were evaluated in relation to CD4 and CD8 T-cell counts, C-reactive protein (CRP), Interleukin-6, soluble CD14, soluble CD163 and intestinal fatty acid-binding protein levels in separate models.

Results

500 HIV-positive and 481 HIV-negative participants were included, with median baseline age 53.2 vs. 52.5 years, (P=0.2), 89% vs. 85% male (P=0.04), 89% vs. 94% white (P<0.001), and 159 (32%) HIV-positive and 183 (38%) HIV-negative participants never smoked. HIV-positive participants were virally suppressed during 95% of study visits. Adjusted yearly declines in FEV1 as well as FVC, but not FEV1/FVC, were greater in HIV-positive than HIV-negative participants. This was the case both for participants who smoked and for those who did not smoke during follow-up (*Figure*). Compared to HIV-negative participants, HIV-positive participants had an overall adjusted additional decline in FEV1 of 10.4 mL/year, P=0.0005 and FVC of 11.5 mL/year, P=0.01 (FEV1/FVC 0.07 %/year, P=0.3), with a similar trend for never smokers (FEV1 6.0 mL/year, P=0.1; FVC 9.1 mL/year, P=0.1; FEV1/FVC 0.00 %/year, P=0.9). Higher CRP levels during follow-up were associated with accelerated declines in FEV1 and FVC among HIV-positive participants.

Conclusions

Treated HIV infection was associated with faster declines in both FEV1 and FVC, but not FEV1/FVC. These changes were not only dependent of smoking and may be partly driven by ongoing interstitial or (small-)airway damage, potentially related to increased inflammation.



*AOPO-**08:** Mean predicted declines in spirometry indices by HIV-status and smoking-status during follow-up*

AOPO-**09**

Children and adolescents perinatally infected with hiv experience few symptoms of fatigue

Anne Marleen ter Haar[1], Merel Nap-van der Vlist[2], Malon Van den Hof[1], Sanne Nijhof[2], Raphaele Litsenburg[2], Kim Oostrom[1], Lotte Haverman[1], Dasja Pajkrt[1]
[1]*Amsterdam UMC, Amsterdam, Netherlands*
[2]*UMC Utrecht, Utrecht, Netherlands*

Background
Fatigue is a commonly reported symptom among adults living with hiv and among children with chronic diseases. Fatigue can have disastrous effects on health status, including health related quality of life (HRQOL), yet fatigue is underexplored in children and adolescents perinatally infected with hiv (PHIV) in the Netherlands. This study aims to elucidate the occurrence of fatigue in PHIV receiving optimal hiv care in the Netherlands, and its impact on their HRQOL.

Methods
HRQOL and fatigue was measured using the Pediatric Quality of Life Inventory™ (PedsQL 4.0) and the PedsQL Multidimensional Fatigue Scale (MFS). The PedsQL MFS encompasses three subscales: general fatigue, sleep/rest fatigue and cognitive fatigue. Outcomes of PHIV children were compared to HIV-uninfected healthy peers (HIV-), matched for age, sex, ethnicity, socioeconomic status (SES) and adoption status. Also, outcomes were compared to a sample representing the general Dutch population and children with chronic disease (CCD). We used regression analysis to assess differences across the domains of fatigue between PHIV and the three other groups. The association between fatigue and HRQOL was identified with linear regression analysis.

Results
We enrolled 14 PHIV children and adolescents (median age 10.2 years [IQR 9.2-11.4], 93% adopted from sub-Saharan Africa at a median age of 3.3 years [IQR 2.1-4.2]) and fourteen HIV-. Results of the regression analyses are summarized in *table 1*: lower scores indicate more fatigue. Across domains of fatigue, PHIV scores were similar to those of HIV-, with the exception of a -8.9 points lower score on cognitive fatigue (p=0.212). Compared to CCD, PHIV children scored 12.8 points higher on general fatigue (p=0.037). Also, PHIV tended to report less symptoms than CCD on sleep/rest fatigue, yet PHIV scored 7.2 points lower on the cognitive fatigue scale (p=0.206). No significant differences were found between PHIV and the general Dutch population, yet PHIV reported more symptoms (-6.4 points) on the cognitive fatigue scale (p=0.196). Among PHIV, a lower score on the total fatigue scale and the cognitive fatigue scale was associated with a lower HRQoL score.

Conclusions
The results of this study suggest that PHIV children and adolescents do not necessarily experience more symptoms of fatigue than their healthy peers. Moreover, they experience significantly less general fatigue than CDD. However, PHIV children and adolescents do seem more likely to experience cognitive fatigue, which significantly predicts children's HRQOL. Further research is needed to better understand the underlying mechanisms of cognitive fatigue in PHIV.

Table 1. Mean differences in PedsQL MFS Scores in Perinatally Human Immunodeficiency Virus infected (PHIV), hiv-uninfected controls, children with chronic disease and the general Dutch population.

	Hiv-uninfected controls			*Children with chronic disease*			*General Dutch population.*		
	B*	95% CI	p	B*	95% CI	p	B*	95% CI	p
Fatigue total	-3.968	-12.9 to 5.0	0.394	4.501	-5.2 to 14.2	0.354	0.195	-6.6 to 7.0	0.955
General fatigue	-0.298	-8.3 to 7.7	0.942	12.802	0.8 to 24.8	0.037	4.685	-2.7 to 12.0	0.212
Sleep/rest fatigue	-2.679	-15.9 to 10.6	0.697	7.857	-3.1 to 18.8	0.158	2.203	-6.0 to 10.4	0.595
Cognitive fatigue	-8.929	-22.6 to 4.7	0.212	-7.161	-18.3 to 4.0	0.206	-6.366	-16.0 to 3.3	0.196

*B represents mean difference between PHIV and the comparison group. Lower scores indicate more severely fatigued.

PedsQL MFS; PedsQL multidimensional fatigue scale.

*AOPO-**09:** Table 1*

AOPO-**10**

A major reduction in estimated newly-acquired HIV infections shows the Netherlands is on track to achieve the United Nations 2020 incidence target

Ard van Sighem[1], Eline Op de Coul[2], Birgit van Benthem[2], Silke David[2], Peter Reiss[134]
[1]*Stichting HIV Monitoring, Amsterdam, Netherlands*
[2]*National Institute for Public Health and the Environment, Bilthoven, Netherlands*
[3]*Department of Global Health and Division of Infectious Diseases, Amsterdam University Medical Centers, University of Amsterdam, The Netherlands*
[4]*Amsterdam Institute for Global Health and Development, Amsterdam, The Netherlands*

Background
One of the United Nations 2020 targets is a 75% reduction in HIV incidence compared with 2010. In the Netherlands, numbers of newly-diagnosed infections have been steadily decreasing since 2010 and we investigated whether the country is on track of achieving this particular UN 2020 target.

Methods
Data on people diagnosed with HIV-1 during 2000-2019 were retrieved from the ATHENA national HIV database. We excluded people originating outside of the Netherlands with documented HIV diagnosis before arrival. Diagnoses during 2015-2019 were adjusted for reporting delay by estimating the delay distribution using the European Centre for Disease Prevention and Control (ECDC) HIV Estimates Accuracy Tool. Annual numbers of newly-acquired HIV infections were estimated with the ECDC HIV Modelling Tool, a CD4 count-based back-calculation method, for the entire population and separately for men who acquired HIV via sex with men (MSM), other men, and women.

Results
20,838 people were newly diagnosed during 2000-2019. We excluded 1,168 migrants already diagnosed before arrival, but included 5,960 migrants for whom data on pre-arrival diagnosis were not yet available. Of the 19,670 individuals included in the analysis, 11,884 (60%) were MSM, 4,137 (21%) other men, and 3,649 (19%) women. Numbers of newly-diagnosed infections decreased from 1,167 in 2010 to 580 in 2019 (*Figure*). The majority of diagnoses and estimated newly-acquired infections were in MSM. Compared with 2010, estimated HIV incidence in 2019 had declined by 72% (95% confidence interval 56–84) in the total population, 76% (61–89) in MSM, 12% (-66–72) in other men, and 83% (38–91) in women.

Conclusions
Estimated overall HIV incidence is likely to reach the UN target in 2020, and has already done so in 2019 for MSM in the Netherlands. Inherent to the nature of back-calculation methods, estimates are less precise in recent years and could not yet fully account for infections prior to immigration.

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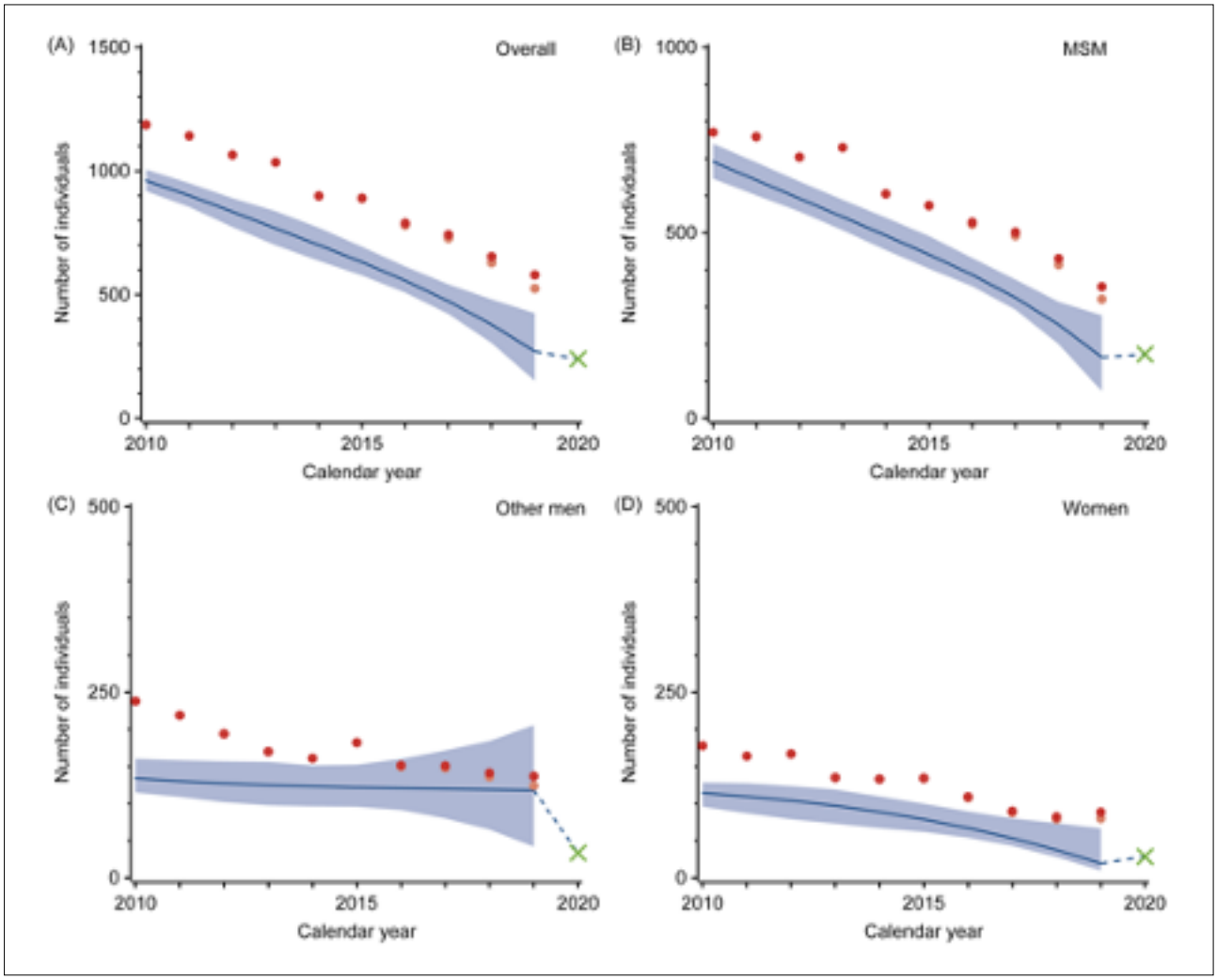

*AOPO-**10:** Figure 1*

AOPO-**11**

Daily and event-driven HIV pre-exposure prophylaxis use among men who have sex with men in Antwerp, Belgium and Amsterdam, the Netherlands: a Tale of Two Cities

Vita Jongen[1], Thijs Reyniers[2], Zorah Ypma[1], Maria Prins[1], Maarten Schim van der Loeff[1], Udi Davidovich[1], Hanne Zimmermann[1], Liza Coyer[1], Mark van den Elshout[1], Henry de Vries[1], Kristien Wouters[2], Tom Smekens[2], Bea Vuylsteke[2], Marie Laga[2], Elske Hoornenborg[1]
[1]*Public Health Service Amsterdam, Amsterdam, Netherlands*
[2]*Institute of Tropical Medicine, Antwerp, Belgium*

Background
Daily and event-driven PrEP are both efficacious in reducing the risk for HIV infection. However, event-driven PrEP is less well understood, in particular when provided as alternative to daily PrEP. We studied regimen preferences, switches and associated HIV and STI incidence.

Methods
We pooled data from a Dutch (AMPrEP) and a Belgian (Be-PrEP-ared) PrEP demonstration project. Participants were men or transgender women who have sex with men at increased risk for HIV. At baseline, participants could choose between the daily and event-driven regimen. Participants were allowed to switch between regimens at 3-monthly study visits, where they were also screened for sexually transmitted infections (STI). We assessed the proportion choosing each regimen, and the determinants of choosing the event-driven regimen, at baseline. Additionally, we assessed the incidence rate (IR) of HIV, HCV, syphilis, and chlamydia or gonorrhoea over 28 months of follow-up. We compared these IRs between regimens using an age-adjusted Poisson regression model.

Results
The pooled dataset consisted of 576 participants (n=376 AMPrEP; n=200 Be-PrEP-ared), of whom 150 (26.0%) chose event-driven PrEP at baseline. Older participants (adjusted odds ratio (aOR) 1.38 per 10 year increase, 95% confidence interval (CI) 1.15-1.64) and those unemployed (aOR 1.68, 95%CI 1.03-1.75) were more likely to initially choose event-driven PrEP. Median follow up was 26 months [interquartile range 21-27]. During follow-up, 384 participants (68.2%) did not switch between PrEP regimens, 89 (15.8%) switched once, and 90 (16.0%) switched more than once. The proportion of participants using event-driven PrEP remained stable over time (26.0% at baseline versus 26.3% at 28 months, p=0.92). Two PrEP users were newly diagnosed with HIV during follow-up (IR 0.19, 95%CI 0.05-0.75), who both chose daily PrEP. The IR of HCV and syphilis did not differ between regimens (*Table*), but the IR of chlamydia or gonorrhoea was higher among daily PrEP users (adjusted incidence rate ratio 1.58, 95%CI 1.29-1.94).

Conclusions
A quarter of participants chose event-driven PrEP at baseline. Although switching between regimens was common, the proportion of participants using event-driven PrEP remained stable over 28 months. The frequent switching suggests that participants adapt their PrEP regime to their changing needs or experiences. The lower incidence of chlamydia and gonorrhoea among event-driven PrEP users may suggest the need for less frequent STI testing in this group compared to daily PrEP users, although the IR of HCV and syphilis was similar. In spite of high incidence of bacterial STIs, HIV was uncommon.

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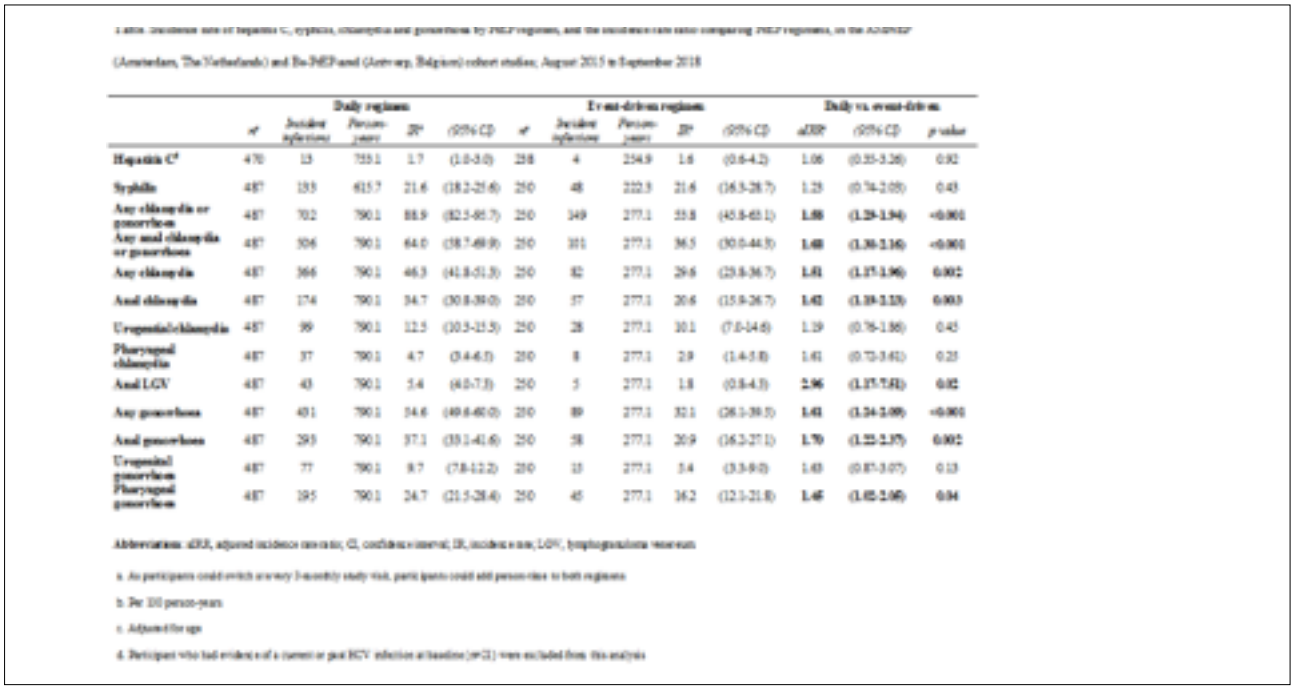

(Amsterdam, The Netherlands) and Be-PrEPared (Antwerp, Belgium) cohort studies, August 2015 to September 2018

	Daily regimen					Event-driven regimen					Daily vs. event-driven		
	n	*Incident infections*	*Person-years*	*IR*[b]	*(95% CI)*	*n*	*Incident infections*	*Person-years*	*IR*[b]	*(95% CI)*	*aIRR*[c]	*(95% CI)*	*p value*
Hepatitis C[d]	470	13	755.1	1.7	(1.0-3.0)	258	4	254.9	1.6	(0.6-4.2)	1.06	(0.35-3.26)	0.92
Syphilis	487	133	615.7	21.6	(18.2-25.6)	250	48	222.3	21.6	(16.3-28.7)	1.25	(0.74-2.05)	0.43
Any chlamydia or gonorrhoea	487	702	790.1	88.9	(82.5-95.7)	250	149	277.1	53.8	(45.8-63.1)	**1.88**	**(1.28-1.94)**	**<0.001**
Any anal chlamydia or gonorrhoea	487	504	790.1	64.0	(58.7-69.9)	250	101	277.1	36.5	(30.0-44.3)	**1.68**	**(1.30-2.16)**	**<0.001**
Any chlamydia	487	366	790.1	46.3	(41.8-51.3)	250	82	277.1	29.6	(23.8-36.7)	**1.51**	**(1.17-1.96)**	**0.002**
Anal chlamydia	487	174	790.1	34.7	(30.8-39.0)	250	57	277.1	20.6	(15.9-26.7)	**1.62**	**(1.19-2.23)**	**0.003**
Urogenital chlamydia	487	99	790.1	12.5	(10.3-15.5)	250	28	277.1	10.1	(7.0-14.6)	1.19	(0.76-1.86)	0.45
Pharyngeal chlamydia	487	37	790.1	4.7	(3.4-6.5)	250	8	277.1	2.9	(1.4-5.8)	1.61	(0.72-3.61)	0.25
Anal LGV	487	43	790.1	5.4	(4.0-7.3)	250	5	277.1	1.8	(0.8-4.3)	**2.96**	**(1.17-7.51)**	**0.02**
Any gonorrhoea	487	401	790.1	54.6	(49.6-60.0)	250	89	277.1	32.1	(26.1-39.5)	**1.61**	**(1.24-2.09)**	**<0.001**
Anal gonorrhoea	487	293	790.1	37.1	(33.1-41.6)	250	58	277.1	20.9	(16.2-27.1)	**1.70**	**(1.22-2.37)**	**0.002**
Urogenital gonorrhoea	487	77	790.1	9.7	(7.8-12.2)	250	15	277.1	5.4	(3.3-9.0)	1.63	(0.87-3.07)	0.13
Pharyngeal gonorrhoea	487	195	790.1	24.7	(21.5-28.4)	250	45	277.1	16.2	(12.1-21.8)	**1.45**	**(1.02-2.06)**	**0.04**

Abbreviations: aIRR, adjusted incidence rate ratio; CI, confidence interval; IR, incidence rate; LGV, lymphogranuloma venereum

a. As participants could switch at every 3-monthly study visit, participants could add person-time to both regimens

b. Per 100 person-years

c. Adjusted for age

d. Participant who had evidence of a current or past HCV infection at baseline (*n*=21) were excluded from this analysis

*AOPL-**11:** Table. Incidence rate of hepatitis C, syphilis, chlamydia and gonorrhoea by PrEP regimen, and the incidence rate ratio comparing PrEP regimens, in the AMPrEP*

AOPO-**12**

Time for change: transitions between HIV risk levels and determinants associated with behavior change in men who have sex with men

Daphne van Wees[1], Maartje Basten[2], Amy Matser[3], Anders Boyd[4], Ganna Rozhnova[2], Chantal den Daas[5], Mirjam Kretzschmar[2], Janneke Heijne[6]
[1]*UMC Utrecht/GGD Amsterdam, Utrecht, Netherlands*
[2]*UMC Utrecht, Utrecht, Netherlands*
[3]*GGD Amsterdam, Amsterdam, Netherlands*
[4]*GGD Amsterdam/Stichting HIV Monitoring, Amsterdam, Netherlands*
[5]*Institute of Applied Health Sciences, Aberdeen, Scotland*
[6]*National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands*

Background
As individual sexual behavior is variable over time, the timing of interventions might be vital to reducing HIV transmission. We aimed to investigate how sexual behavior has fluctuated over one decade among men who have sex with men (MSM) and identify determinants associated with change in behavior.

Methods
Data were from a longitudinal cohort study among HIV-negative MSM (Amsterdam Cohort Studies). Participants completed questionnaires about their sexual behavior during biannual visits (2008-2017). For each visit, we assigned participants to HIV risk levels based on latent classes of behavior. We modelled transitions between risk levels and identified determinants at the previous visit associated with these transitions using multi-state Markov models.

Results
We classified three risk levels (N=767, n visits=7,865): low (73% of visits), medium (22%), and high risk (5%). Modelled probabilities between visits showed that MSM were more likely to remain at the same risk level for the next visit if they were low risk (0.89) compared to medium (0.59) or high (0.57). For MSM at low risk, the probability of moving to medium and high risk was 0.10 and 0.01, respectively. For MSM at medium risk, the probability of increasing to high risk was 0.08, while the probability of decreasing to low risk was 0.33. For MSM at high risk, the probability of moving to medium and low risk was 0.34 and 0.09, respectively. Reporting “chemsex”, erection stimulants, high HIV risk perception, anal STI or syphilis in the past six months, and non-anal STI in the past six months were associated with increasing from low to medium risk (*Table 1*). Reporting “chemsex”, high HIV risk perception, and anal STI or syphilis in the past six months were associated with increasing from medium to high risk. High HIV risk perception and young age at the current visit were associated with decreasing from medium to low risk. Transitions between risk levels overall were less likely when MSM were in a steady partnership.

Conclusions
Although the majority of MSM showed no behavior change, a considerable proportion increased their HIV risk. Determinants associated with behavior change may help to identify MSM who are likely to increase risk in the near future and target interventions at these individuals, thereby reducing HIV transmission.

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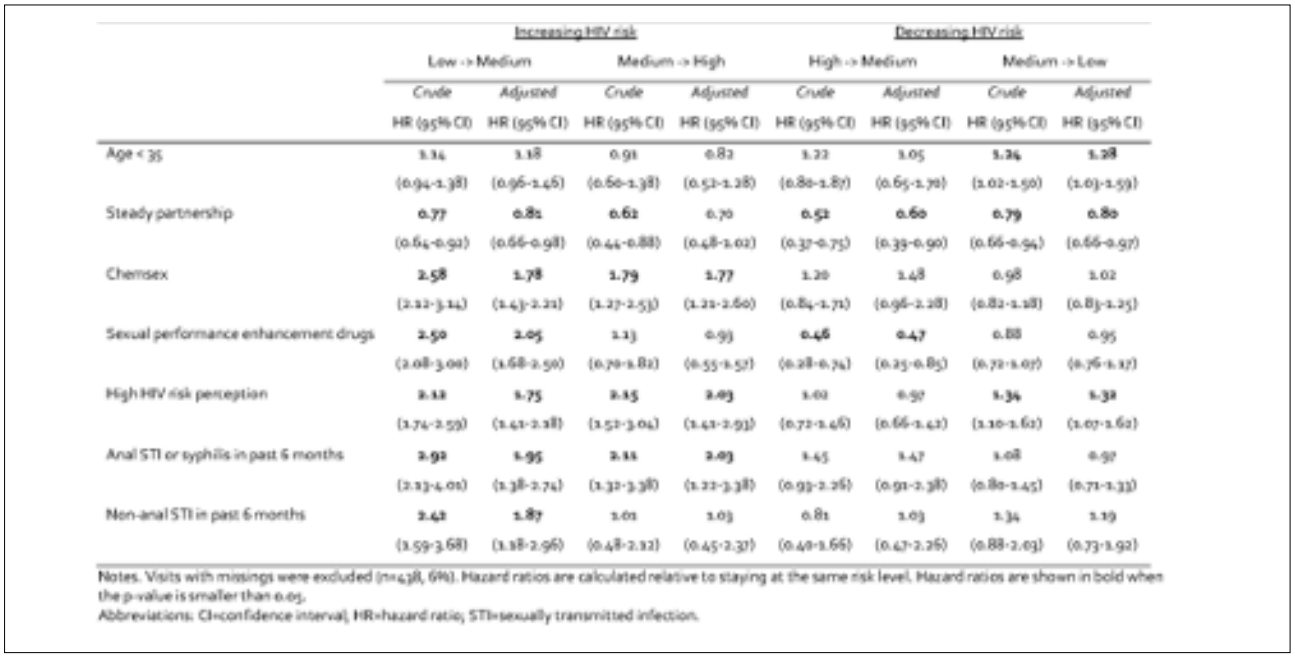


	Increasing HIV risk				Decreasing HIV risk			
	Low -> Medium		Medium -> High		High -> Medium		Medium -> Low	
	Crude	*Adjusted*	*Crude*	*Adjusted*	*Crude*	*Adjusted*	*Crude*	*Adjusted*
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Age < 35	1.14	1.18	0.91	0.82	1.22	1.05	**1.24**	**1.28**
	(0.94-1.38)	(0.96-1.46)	(0.60-1.38)	(0.52-1.28)	(0.80-1.87)	(0.65-1.70)	(1.02-1.50)	(1.03-1.59)
Steady partnership	**0.77**	**0.81**	**0.62**	0.70	**0.52**	**0.60**	**0.79**	**0.80**
	(0.64-0.92)	(0.66-0.98)	(0.44-0.88)	(0.48-1.02)	(0.37-0.75)	(0.39-0.90)	(0.66-0.94)	(0.66-0.97)
Chemsex	**2.58**	**1.78**	**1.79**	**1.77**	1.20	1.48	0.98	1.02
	(2.22-3.14)	(1.43-2.21)	(1.27-2.53)	(1.21-2.60)	(0.84-1.71)	(0.96-2.28)	(0.82-1.18)	(0.83-1.25)
Sexual performance enhancement drugs	**2.50**	**2.05**	1.13	0.93	**0.46**	**0.47**	0.88	0.95
	(2.08-3.00)	(1.68-2.50)	(0.70-1.82)	(0.55-1.57)	(0.28-0.74)	(0.25-0.85)	(0.72-1.07)	(0.76-1.17)
High HIV risk perception	**2.12**	**1.75**	**2.15**	**2.03**	1.02	0.97	**1.34**	**1.32**
	(1.74-2.59)	(1.41-2.18)	(1.52-3.04)	(1.42-2.93)	(0.72-1.46)	(0.66-1.42)	(1.10-1.62)	(1.07-1.62)
Anal STI or syphilis in past 6 months	**2.92**	**1.95**	**2.11**	**2.03**	1.45	1.47	1.08	0.97
	(2.13-4.01)	(1.38-2.74)	(1.32-3.38)	(1.22-3.38)	(0.93-2.26)	(0.91-2.38)	(0.80-1.45)	(0.71-1.33)
Non-anal STI in past 6 months	**2.42**	**1.87**	1.01	1.03	0.81	1.03	1.34	1.19
	(1.59-3.68)	(1.18-2.96)	(0.48-2.12)	(0.45-2.37)	(0.40-1.66)	(0.47-2.26)	(0.88-2.03)	(0.73-1.92)

Notes. Visits with missings were excluded (n=438, 6%). Hazard ratios are calculated relative to staying at the same risk level. Hazard ratios are shown in bold when the p-value is smaller than 0.05.
Abbreviations: CI=confidence interval, HR=hazard ratio, STI=sexually transmitted infection.

*AOPO-**12:** Table 1. Univariable and multivariable determinants of increasing (low to medium, or medium to high risk level) or decreasing HIV risk (high to medium, or medium to low risk level)*

AOPO-**13**

Long-term outcomes of first-line NNRTI-based antiretroviral treatment: results of a large multi-country cohort study in sub-Saharan Africa

Seth Inzaule[1], Stefanie Kroeze[1], Cissy Kityo[2], Margaret Siwale[3], Sulaimon Akanmu[4], Maureen Wellington[5], Marleen de Jager[6], Prudence Ive[7], Kishor Mandaliya[8], Wendy Stevens[9], Kim Steegen[7], Immaculate Nankya[2], Sonia Boender[1], Pascale Ondoa[1], Kim Sigaloff[1], Peter Mugyenyi[2], Tobias Rinke de Wit[1], Raph Hamers[1]

[1]*Amsterdam Institute for Global Health and Development, and Department of Global Health, Amsterdam, Netherlands*

[2]*Joint Clinical Research Centre, Kampala, Uganda*

[3]*Lusaka Trust Hospital, Lusaka, Zambia*

[4]*Department of Haematology and Blood Transfusion, Lagos University Teaching Ho, Lagos, Nigeria*

[5]*Newlands Clinics, Harare, Zimbabwe*

[6]*Muelmed Hospital, Pretoria, Republic of South Africa*

[7]*Clinical HIV Research Unit, University of the Witwatersrand, Johannesburg, Republic of South Africa*

[8]*Coast Province General Hospital, Mombasa, Kenya*

[9]*Department of Molecular Medicine and Haematology, University of the Witwaters, Johannesburg, Republic of South Africa*

Background

To assess long-term clinical outcomes of a large African multi-country cohort of HIV-infected adults initiating programmatic first-line ART.

Design

Multi-country cohort study at 13 sites in 6 countries, followed up to 24 months (8 sites) or 60-72 months (5 sites).

Methods

We used Kaplan Meir to estimate the cumulative incidence of retention, lost-to-follow-up and deaths, and further estimated the proportion of participants who had viral load (VL) suppression (<1000 cps/ml) and optimal CD4 cell recovery (>500mL).

Results

2,735 participants had a total follow-up time of 7,208 person-years, with a median of 24.3 months (IQR 18.7-58.3). Overall, 69.9% were retained in care, 20.1% were lost to follow-up and 10.0% had died within 72 months after ART initiation. The majority of deaths (201/240; 84%) and) of loss-to-follow-up (226/397; 57%) occurred within the first 12 months after ART initiation. The proportion of participants with viral suppression was between 91.3-93.3% at every year of follow-up among those still alive and on ART. Among those with 72 months of follow up, CD4 cell count of (median pre-ART 135 cells/mL; IQR 63-205) recovered to >500 cells/mL after 72 months of ART for 39.4% (143/363).

Conclusions

Loss-to-follow-up and deaths were high during the first year of ART, and substantially lower during long-term ART. The cohort achieved >90% viral load suppression among those on ART in successive years, but with sub-optimal immune recovery. Enhanced efforts to improve earlier ART initiation and monitor and retain patients in care during the first year, are critical for long-term ART success.

AOPO-**14**

Quality of care in a differentiated service delivery intervention in Tanzania: A mixed-methods study

Nwanneka Okere[1], Judith Meta[1], Werner Maokola[2], Giulia Martelli[3], Eric van Praag[1], Anton Pozniak[4], Tobias Rinke de Wit[1], Josien de Klerk[1], Sabine Hermans[1]

[1]*Amsterdam Institute for Global Health and Development, Amsterdam, Netherlands*

[2]*National AIDS Control Programme, Dar es Salaam, Tanzania*

[3]*Doctors with Africa (CUAMM), Shinyanga, Tanzania*

[4]*Chelsea and Westminster Hospital NHS Foundation Trust, London, United Kingdom*

Background

Differentiated service delivery (DSD) offers benefits to people living with HIV (PLHIV) - improved access, adherence, peer support, decongestion of the clinic, task shifting, and efficient service delivery. ART clubs in the community are one of the most common DSD options. However, evidence about the quality of care (QoC) delivered in DSD compared to the standard-of-care is still limited.

Methods

We conducted a mixed-methods study as part of the Test & Treat project in northwest Tanzania. We assessed QoC and explored perspectives among stable ART clients and healthcare workers (HCW) comparing between clinics and clubs (15-30 clients who usually meet within the community). The Donabedian framework which proposes three levels of assessment (structures [staff, equipment, supplies, venue], processes [time-spent, screenings, information, manner], and outcomes [viral load, CD4 count, self-worth, confidence]) structured the analysis.

Results

Among clients, 629 were surveyed (40% - club) and eight focus group discussions conducted, while among HCW, 24 were surveyed (25% - club) and 22 individual interviews conducted. Quantitative results revealed that in terms of structures, clubs fared better compared to clinics except for perceived adequacy of service delivery venue (94.4 vs 50.0% p=0.013). For processes, time-spent receiving care was significantly less in clubs than clinics (119.9 vs 49.9 mins p=0.000). Regarding outcomes, the proportion of clients with recent viral load <50 copies/ml (100 vs 94.4% p=0.000) was higher in clinics than clubs. Qualitative results indicated that quality care was perceived similarly in clinics and clubs but for different reasons. Clinics were generally perceived as places with expertise and clubs as efficient places, with peer-support and empathy. In describing QoC, HCW emphasized structure-related attributes while clients focused on processes. Outcomes-related themes such as improved client health status and self-worth were similarly perceived across clients and HCW. Confidentiality was considered very important by all clients..

Conclusions

Our results show better QoC in terms of structures and processes of care in clubs and comparable outcomes in clinics and clubs. While QoC was perceived similarly in clinics and clubs but its meaning was understood differently among clients and between clients and HCW. DSD QoC catered to the individual needs of clients, either technical care in the clinic or proximate and social care in the club. HCW understand QoC to be about good structures, clients value processes of care. Our findings are valuable to guide the DSD club model scale-up paying attention to the differential needs of clients.

AOPO-**15**

Cost Effectiveness of expanding treatment with Direct Acting Antiviral treatment to reduce Hepatitis C incidence among HIV positive MSM in Thailand

Shreoshee Mukherjee[1], Donn Colby[2], Reshmie Ramataursing[3], Stephanie Popping[1], Somchai Sriplienchan[3], Tanat Chinbunchorn[3], Nittaya Phanuphak[3], David van de Vijver[1]

[1]*Erasmus Medical Center, Rotterdam, Netherlands*

[2]*The Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda Maryland, United States of America*

[3]*Thai Red Cross HIV Research Centre, Bangkok, Thailand*

Background

Thailand experiences an expanding Hepatitis C virus (HCV) epidemic among HIV-infected men-who-have-sex-with-men (MSM) that went from zero new HCV infections before 2014 to an incidence of 45/1000 person-years in 2018. Direct acting antivirals (DAAs), although expensive, could reduce the epidemic as DAAs cure HCV infections thereby preventing its continued transmission. Therefore, costs incurred on health gains achieved is examined to progress towards WHO goals of eliminating Hepatitis C virus by 2030.

Methods

We calibrated a transmission model to the Thai HCV epidemic. We explored epidemiological impact through 2030 and economic impact over 40 years, from a provider's perspective, using 3% annual discounting rate. Base case scenario was the current treatment practise where DAAs are prescribed six months after diagnosis, and after progression to METAVIR F2. Stage F2 was compared with expanding treatment to early stage F0 and to chronic stage F1. Sofosbuvir/Ledipasvir were the DAA drugs used for this study. One-way sensitivity analysis was conducted by varying price of drugs and diagnostic tests on the cost-effectiveness.

Results

Our model predicted that continuing DAA treatment at stage F2 increases incidence by 41% (45/1000 PY 2018 to 63/1000 PY 2030), whereas incidence increases by 24% when treatment is expanded to stage F1 over F2 (56/1000 PY 2030). Starting treatment at F0 stage can reduce incidence rates by 42% for stage F0 over F2 (26/1000 PY 2030). Prevalence is reduced from 8.7% in 2018 to 1.5% in 2030, or 8.4% in 2030, if DAAs are started in stage F0 or F1, respectively. DAA treatment at F0 could avert 5938 new infections, whereas starting DAAs at F1 would avert 474 new infections by 2030. In the first seven years, earlier initiation of DAA will be more expensive compared to the current practice of postponing treatment to stage F2. After seven years, earlier treatment is cost-saving resulting in a cumulative discounted cost-saving of $5 million (F1), or $17 million (F0) as compared to $46 million for the base scenario. One-way sensitivity analysis showed that DAA price, fibrosis scan and ultrasound costs were most sensitive to cost-effectiveness, while HCV genotype costs had no impact on it.

Conclusions

DAA treatment strategy immediately after diagnosis saves costs in the future with substantial health benefits. These findings inform the Thai government on making necessary investments of expanding coverage by initiating treatment during early stage of infection to prevent HCV transmission, thereby contributing towards eliminating the epidemic by 2030.

PO-**01**

Informal PrEP: Attitudes and behaviors of PrEP users outside standard healthcare in the Netherlands

Mart Van Dijk[1], John de Wit[2], Kai Jonas[1]
[1]*Maastricht University, Maastricht, Netherlands*
[2]*Utrecht University, Utrecht, Netherlands*

Background
This presentation gives an overview of the 4-year project "PrEP among MSM in the Netherlands: attitudes, intentions, modes of acquisition and sexual risk taking", funded by AidsFonds. Prior to the implementation of subsidized PrEP in 2019 in public health centers in the Netherlands, MSM obtained PrEP via informal channels or on prescription of the general practitioner (GP), unless they were part of the AmPrEP study. This sizeable group of "informal" PrEP users is unique in its experience and challenges. The aim of this project was to investigate their experiences regarding PrEP use and accessing PrEP-related healthcare. Furthermore, we investigated attitudes and sexual behaviors of informal PrEP users and where they overlap with formal PrEP users.

Methods
A cross-sectional study (N=426) was conducted to analyze PrEP interest prior to PrEP approval in the Netherlands. A qualitative study (N=30) was conducted to explore access to PrEP and PrEP-related healthcare. A longitudinal study (N=349) was conducted to analyze predictors of PrEP uptake. In addition, the impact of PrEP on quality of sex life and HIV-related stigma was investigated with the same dataset.

Results
MSM with high-risk behavior had a higher interest in PrEP, but high-risk behaviors were not related to PrEP uptake. PrEP uptake was predicted by the price of PrEP and the financial situation. Informal PrEP users experienced difficulties accessing PrEP care at GPs, but the majority managed to get regular testing. Quality of sex life improved because of reduced fear of HIV since using PrEP, and this was not mediated by decreased condom use. PrEP may help to overcome the serodivide, as PrEP users feel more comfortable and have less anxiety when having sex with men living with HIV.

Discussion
Our data complements Dutch PrEP knowledge that is mostly related to AmPrEP data. In sum, informal use of PrEP is working quite well, but it mainly reaches MSM who are well informed about PrEP and who could afford it. For them, the transition to formal PrEP proceeded fairly fluently as soon as formal PrEP services were implemented. Attention is needed for groups that have difficulty accessing PrEP, such as less affluent MSM and migrants. Similar to formal PrEP users, the benefits of PrEP go beyond just HIV prevention: PrEP has a positive impact on the quality of sex life by reducing fear for HIV.

PO-**02**

Improving delivery, impact, and efficiency of HIV/AIDS and other health services through integration: a systematic review and meta-analysis

Caroline Bulstra[1], Jan Hontelez[1], Mortiz Otto[2], Anna Stepanova[2], Erik Lamontagne[3], Anna Yakisuk[3], Wafaa El-Sadr[4], Tsitsi Apollo[5], Miriam Rabkin[4], Rifat Atun[6], Till Barnighausen[2]

[1]*Erasmus MC, Amsterdam, Netherlands*
[2]*Heidelberg Institute of Global Health, Heidelberg University, Heidelberg, Germany*
[3]*UNAIDS, Geneva, Switzerland*
[4]*ICAP, Columbia University, New York, United States of America*
[5]*Ministry of Health and Child Care, Harare, Zimbabwe*
[6]*Harvard T.H. Chan School of Public Health, Harvard University, Boston, United States of America*

Background
The future of a sustainable HIV response depends on strategic integration of HIV services into broader health systems, yet, evidence and guidance on appropriate integration methods, standards, and targets are scarce. A comprehensive systematic synthesis of existing evidence is required to better understand the effects of service integration on the HIV service delivery cascade, HIV prevention, mortality, non-HIV health outcomes and costs.

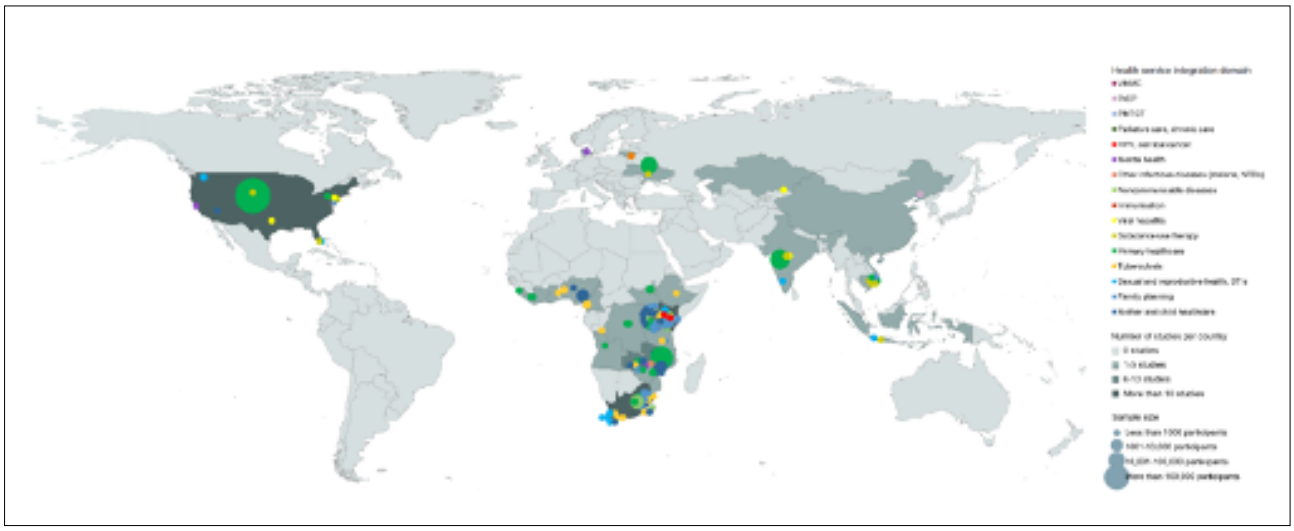
Methods
We performed a systematic review and meta-analysis to synthesise existing quantitative empirical evidence on the impact of HIV service integration with other health service areas on (i) reaching HIV epidemic control targets, (ii) service delivery efficiencies, and (iii) spill-over effects to other diseases or conditions.

Results
We identified 3,067 unique English-language studies, of which 102 were included. Most were conducted in sub-Saharan Africa. Common integration areas were maternal-and-child-healthcare, tuberculosis, primary healthcare, family planning, and sexual and reproductive health services. We found that, in almost all studies, integration led to increased uptake of HIV services and other health services; higher retention of HIV patients in care; similar or improved adherence to antiretroviral therapy and viral suppression; similar or improved HIV-free survival and/or spill-over health outcomes; and reduction in AIDS-related and non-AIDS-related mortality. Where reported, integration was relatively cost-effective, but efficiency gains from integration at the service-level are not always present.

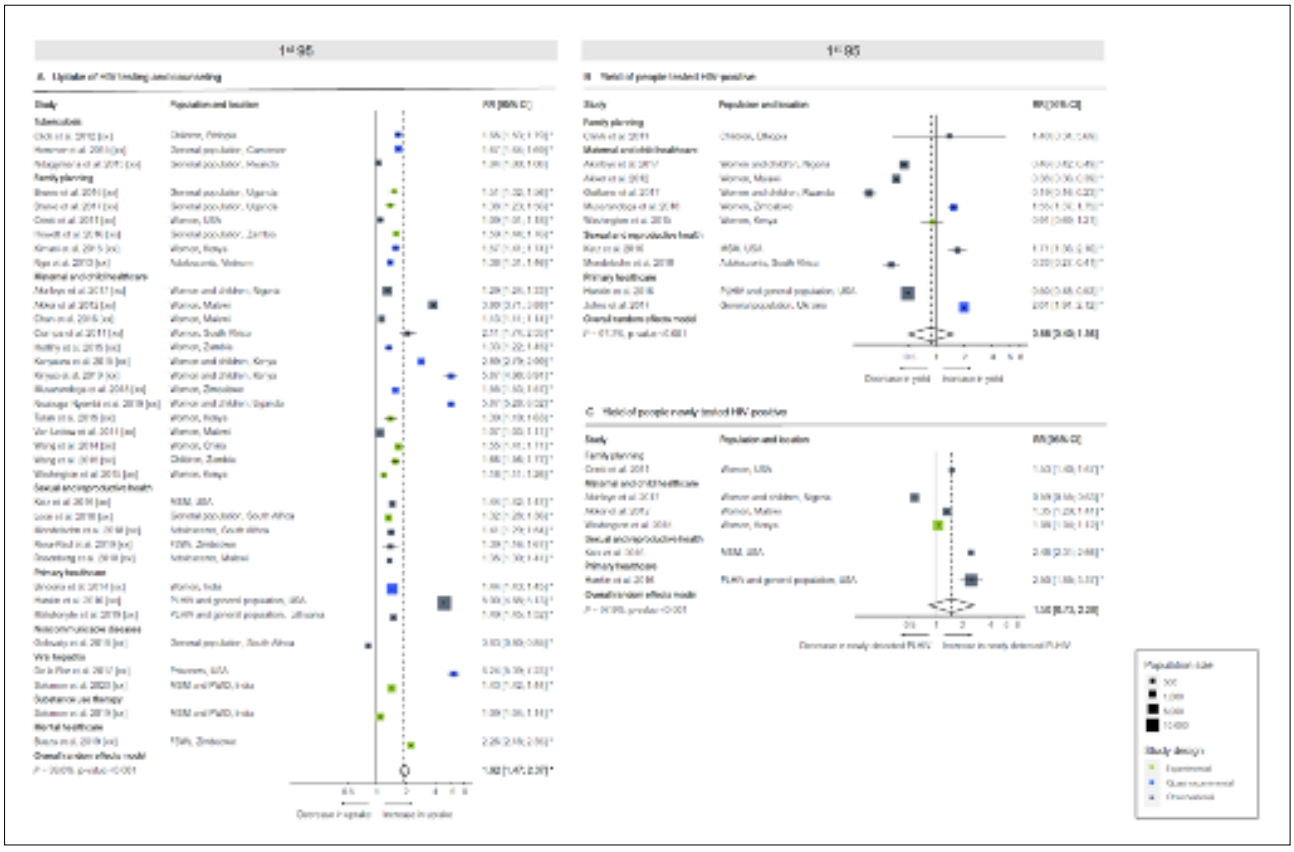
Conclusions
The existing empirical evidence indicates that integration of HIV and other health services often has a non-inferior or positive impact on service utilisation, yield and health outcomes. Integration seems to be cost-effective in diverse settings, but economies of scale or scope are not always clearly identifiable. Although current evidence supports integration in general, there is no 'one-size-fits-all' integration model, and optimal integration strategies depend on the local epidemiological and health system contexts. Nonetheless, the evidence strongly suggests that integration can be an invaluable tool toward ending AIDS by 2030, while simultaneously developing sustainable universal health coverage (UHC), a target of the Sustainable Development Goals (SDGs).

Key words: HIV, AIDS, health systems, health services, integration, integrated care, health care delivery, cost-effectiveness

PO: Posters



*PO-**02:** Figure 1 - Geographical map of the included empirical studies by type of integration*



*PO-**02:** Figure 2 - Impact of HIV services integration on outcomes related to the 95-95-95 targets as compared to non-integrated services*

PO-**03**

Systematic development of a self-stigma reduction intervention for PLHIV

Yvonne Van der Kooij[1], Sarah Stutterheim[2], Leo Schenk[3], Hannah Jansen[3], Loek Elsenburg[3], Marie Jose Kleene[4], Guido van den Berk[4], Chantal den Daas[5], Kees Brinkman[4], Arjan Bos[1]
[1]Open University, Heerlen, Netherlands
[2]Maastricht University, Maastricht, Netherlands
[3]Hello Gorgeous Foundation, Amsterdam, Netherlands
[4]OLVG Hospital, Amsterdam, Netherlands
[5]University of Aberdeen, Aberdeen, Scotland

Background
HIV-related self-stigma is a significant barrier to an effective HIV response. High levels of self-stigma have been associated with reduced health outcomes, quality of life and access to HIV care and treatment for PLHIV worldwide. Programs that effectively target self-stigma among PLHIV remain scarce. The objective of this study is to provide an overview of the development of a theory- and evidence-based intervention aimed to reduce HIV-related self-stigma and its negative effects for different key populations living with HIV in the Netherlands.

Methods
Using the Intervention Mapping (IM) approach, six steps were followed: (1) conduct a needs assessment in which data were gathered to gain a thorough understanding of self-stigma in PLHIV, (2) determine program outcomes and objectives for PLHIV and their social environment, (3) select theory-based methods and corresponding practical applications, (4) produce the program, (5) plan for adoption, implementation, and maintenance; (6) plan the program evaluation. The intervention is being developed in a collaborative manner between PLHIV, stigma researchers, and health care professionals, and will focus on two specific key populations of PLHIV in the Netherlands, namely men who have sex with men (MSM) and migrant populations.

Results
Based on our needs assessment that consisted of a systematic review, a large survey study, and interviews and focus group discussions with PLHIV, we ascertained multilevel program objectives. For the individual level (PLHIV), objectives are increasing positive beliefs about HIV and expecting positive reactions towards one's HIV status. For the environmental level, objectives are providing a supportive environment for PLHIV (social support, linkage to accurate HIV information channels and culturally sensitive support networks) and decreasing intersectional stigmas in the community. Specific behavioral determinants at the individual and environmental level such as knowledge, attitude, social norms, skills, and self-efficacy are to be targeted. Methods and applications derive from both social cognitive theories as well as empowerment theories.

Conclusions
Developing a theory- and evidence-based intervention to reduce HIV-related self-stigma and its harmful effects using the systematic IM approach holds promise and contributes to the critical gaps in knowledge about HIV-related self-stigma as well as effective intervention studies.

PO-**04**

Community-based HIV testing: experiences of lay-testers and end-users at the Aids Healthcare Foundation Checkpoint in Amsterdam

Nori Krabbenborg[1], Ralph Spijker[1], Anna Żakowicz[2], Milo De Moraes[2], Titia Heijman[3], Eline Op de Coul[1]
[1]*RIVM, Bilthoven, Netherlands*
[2]*Aids Healthcare Foundation Checkpoint, Amsterdam, Netherlands*
[3]*Public Health Service of Amsterdam, Amsterdam, Netherlands*

Background
Reaching people living with undiagnosed HIV remains a challenge. Community-based HIV test approaches are promising to overcome test barriers and to connect with 'difficult-to-reach' high-risk populations.
The community approach of AHF-Checkpoint provides free 'walk-in', rapid HIV testing at on-site and off-site (pop-up) locations. We explored the perspectives, experiences, and needs of lay providers and end-users of HIV testing at AHF-Checkpoint. Also, we evaluated to what extent adherence to the World Health Organizations' 5Cs (consent, confidentiality, counselling, correct results, connection) for HIV test services was achieved by AHF-Checkpoint.

Methods
A qualitative study with semi-structured interviews was conducted during April-June 2020 by telephone or video calling with ten lay-testers and five end-users from AHF-Checkpoint. The recorded interviews were transcribed verbatim and thematically analysed to explore perspectives, experiences and needs with those offering (lay testers) or receiving (end-users) HIV testing. Triangulation to ensure validity of data was applied by cross-verification of outcomes between the two interviewed groups.

Results
Data analysis of 15 transcripts identified four domains: 1) accessibility of HIV testing, 2) quality of community-based procedures, 3) bridging (transitional care), and 4) future strategies for service delivery. According to lay testers and end-users, AHF-Checkpoint fills a gap for people who experience barriers to HIV testing at sexual health centres or GPs by providing free, anonymous, and rapid HIV testing, especially for individuals at high-risk including LGBTQ communities and refugees. The level of trust between lay testers and end-users was highly valued by the end-users. End-users also appreciated the low threshold to test, no barriers like waiting lists, no test costs or triaging that could include referral to another test location. Needs expressed by lay providers included: being prepared for emotionally charged situations and receiving extra training to improve knowledge on STIs.
The evaluation of WHO 5Cs, showed that the Consent, Counselling, and Correct test results were realised. Confidentiality and Connection-to-care were found to be sufficient by lay providers, but improvements could be made. Confidentiality was sometimes difficult to accomplish at pop-up locations and referral barriers for HIV confirmation testing were sometimes experienced by lay providers during weekends.

Conclusions
The community-based HIV test service AHF-Checkpoint was described as a convenient and easily accessible service by end-users and lay providers. According to the WHO 5Cs approach, AHF-Checkpoint met most criteria. Optimisation of referral-to-care for STI testing or HIV confirmation can be reached by a liaison approach with external experts from the regular healthcare sector.

PO-**05**

HIV, ART and chemoprophylaxis among MSM: Results from the Dutch sample of the EMIS 2017/2018 survey

Kai Jonas[1], Haoyi Wang[1], Chantal den Daas[2], Eline Op den Coul[3], Bouko Bakker[4], Aryanti Radyowijati[5], Marije Veenstra[5], Koenraad Vermey[6], Arjan van Bijnen[6], Wim Zuilhof[6]

[1]*Maastricht University, Maastricht, Netherlands*
[2]*University of Aberdeen, Aberdeen, United Kingdom*
[3]*RIVM, Utrecht, Netherlands*
[4]*Rutgers, Utrecht, Netherlands*
[5]*Results in Health, Leiden, Netherlands*
[6]*SOAaids, Amsterdam, Netherlands*

Background
The EMIS survey is a large scale EU wide survey among MSM and provides insights into the livelihoods of MSM covering a large range of topics form sexual health, HIV prevention and treatment, substance use and mental health. We focused on HIV related topics in the Dutch subsample.

Methods
A cross-sectional study (N=3,851) was conducted in late 2017/early 2018 to investigate:
HIV testing (HIV prevalence, Knowledge gaps related to HIV, knowledge about HIV tests, treatment and prevention).
HIV treatment (HIV diagnosis, HIV treatment support)HIV chemoprophylaxis (Prevalence of PEP/PrEP use, Awareness and knowledge of PEP/PrEP, Access to PEP/PrEP, Gaps between knowledge and access of PEP/PrEP, PEP/PrEP promotion). Descriptive analysis are reported here to give a first overview over the data.

Results
In the sample, 15.7% (n=603) of the MSM had received an HIV- diagnosis. Overall, basic knowledge about HIV transmission was generally high in the whole sample. U=U (undetectable = untransmittable) is known to 2 out of 3 participants.

A sizeable minority (15.6%) had never tested for HIV; the main reasons where not knowing/being sure where to get an HIV test (29%). Among those who had ever tested for HIV, 18.6% had received a positive HIV diagnosis. The most common place for a HIV diagnosis was at a hospital/clinic outpatient setting. Ninety-five percent of those diagnosed got some form of support after their diagnosis. 77% were satisfied with the support received.
PEP is known as a form of prevention. Only 12% were unaware of PEP, and 20% were not confident that they could access PEP if they required it. Overall, only 9.4% had tried to get PEP. Among those who tried, 36.4% could not get it, and 9.9% had taken more than one course of PEP.

Knowledge about PrEP is widespread, 12% were unaware of PrEP, but only 13% indicated that a healthcare provider informed them about PrEP. Less than half (40%) were willing to use PrEP if it is available and affordable. 11% had tried to get PrEP, and overall 25.3% were taking it on a daily basis.

Discussion
Our data complements other national data and provides a valuable basis to further tailor HIV prevention measures and to improve HIV treatment. The results show three main areas to focus interventions on: HIV testing, increasing knowledge about U=U, and increasing access and use of PrEP.

PO-**06**

Social engagement and the quest for an HIV cure: A systematic review of research on the views of stakeholders of HIV cure research

Maaike A.J. Noorman[1], Chantal den Daas[2], Sarah E. Stutterheim[3], Tamika A. Marcos[3], Kai Jonas[3], John B. F. de Wit[1]
[1]*Utrecht University, Utrecht, Netherlands*
[2]*University of Aberdeen, Aberdeen, Scotland*
[3]*Maastricht University, Maastricht, Netherlands*

Background
As development of an HIV cure advances, assessing the views of the main stakeholders becomes crucial to ensure alignment between clinical progress and the needs of intended beneficiaries. By collecting and summarising existing research, this systematic review aims to provide an overview of the perspectives of HIV cure research stakeholders and identify areas for future research.

Methods
Databases PubMed, Embase, Web of Science and Scopus were searched for papers published in or before July 2020 that reported perspectives of stakeholders, directly or indirectly affected by HIV cure. Key data from included articles were extracted and tabulated. The protocol is registered in the International Prospective Register of Systematic Reviews (registration number CRD42020190942).

Results
Seventy-nine papers were included of which 38 were conceptual (i.e., theoretical, opinion – not including data) and 41 empirical (6779 stakeholders in the United States, China, South Africa, Australia, France, Thailand, and two multi-country online surveys). Across all papers, three main stakeholder groups were identified: 1) People living with HIV (PLHIV; n=5687, 83.89%), 2) the scientific community, comprised of researchers, bioethicists and project leaders (n= 230, 3.39%) and 3) other key populations (KP; n=861, 12.70%) including health workers, men who have sex with men, people who inject drugs, next of kin, community members, activists, people not living with HIV, and journalists. Research with PLHIV typically focused on cure acceptability with a utilitarian emphasis on willingness to participate in HIV cure research. Studies mostly aimed at identifying motivations for participation, characteristics that enhance participation, and perceived risks and benefits. Different perspectives of HIV cure research were highlighted by the scientific community in both conceptual papers and empirical data. Major themes included what a potential HIV cure would look like and ethical considerations in HIV cure research. Thirdly, in the heterogenous group of KP, reoccurring themes of HIV cure knowledge, HIV cure-related stigma, and communication were distinguished.

Conclusions
This review provides an overview of the three main stakeholder groups in recent HIV cure research as well as the themes and perspectives addressed in each stakeholder group. Whilst various themes were presented, not all themes were addressed by the different stakeholder perspectives. Hence, to ensure alignment between the clinical progress of the scientific community and the needs of PLHIV and KP, more socio-behavioural research into the perspectives of PLHIV and KP is needed.

PO-**07**

HIV rapid testing at AHF Checkpoint Amsterdam - COVID-19 effect on the services

Milo de Moraes[1], Anna Żakowicz[2]
[1]*AIDS Healthcare Foundation (AHF), Amsterdam, Netherlands*
[2]*AIDS Healthcare Foundation (AHF), Europe, Netherlands*

Background
By the end of 2018, an estimated 1,900 people are thought to be unaware of their HIV status in the Netherlands. A significant percentage of people who initiated ART are known to be born outside the Netherlands (40%). This group faces more barriers reaching HIV services and is more likely to present late for HIV-care. AHF Checkpoint Amsterdam provides community-based, free, 'walk-in', rapid HIV testing on-site and off-site (pop-up locations) to overcome barriers to test and reach high-risk groups including MSM and migrant populations. Due to COVID-19 AHF Checkpoint Amsterdam operations were suspended on 26thMarch 2020 and reopened with stronger safety measures on 11th May 2020.

Methods
We studied a dynamic cohort of people who used our facility from January 1st till September 21st of 2020 with a specific focus on data between May 11th till September 21st when contact-based services across the Netherlands were allowed again. AHF Checkpoint Amsterdam introduced additional safety measures and implemented an appointment-based system. After May 11thWhatsApp for scheduling appointments and performing pre-test counseling and screening was introduced.

Results
Between January and September 21st, 1190 people were tested for HIV with a total of 7 reactive cases (0.6% positivity rate). 843 (71%) people who tested were of non-Dutch origin. After May 2020, AHF Checkpoint Amsterdam performed approximately 45% of tests carried on-site in comparison to the same time in 2019. Between May 11th and September 21st, a total of 482 people tested for HIV. Among this group 3 reactive cases were detected (positivity rate 0.6%). Of the total number of people tested, 249 (52%) were MSM and 328 (68%) indicated being of non-Dutch origin. Out of the non-Dutch group 158 (48%) were MSM and 4 (1%) transgender. The 3 reactive cases belonged to the non-Dutch group, 2 were MSM and 1 transgender. Positivity rate among the non-Dutch group was 0.9%. Two clients were successfully linked to care, the third opted for self-linkage.

Conclusions
AHF Checkpoint Amsterdam was able to reintroduce its services in a safe manner to the population. The introduction of low-threshold appointment scheduling and pre-test consultation through WhatsApp successfully supported the continuation of the services fulfilling the goal to reach key affected communities. There is a need to promote community-level services to continue HIV testing in order to reach the goal of zero new HIV infections in the Netherlands.

PO-**08**

Induction of cross-reactive antibodies to human coronavirus spike proteins after SARS-CoV-2 infection and vaccination

Marloes Grobben[1], Karlijn van der Straten[1], Philip J.M. Brouwer[1], Mitch Brinkkemper[1], Tom Bijl[1], Amy W. Chung[2], Rogier W. Sanders[1], Marit J. van Gils[1]
[1]*Amsterdam UMC, Amsterdam, Netherlands*
[2]*Peter Doherty Institute for Infection and Immunity, Melbourne, Australia*

Background
There are still many unknowns about the role of SARS-CoV-2 antibodies in the immune response after infection, but evidence is appearing that previous human coronavirus (HCoV) infections may play an important role. SARS-CoV-2 is the seventh coronavirus known to infect humans and is very similar in sequence to SARS (77% spike protein sequence identity), less similar to MERS (31%) and most distinct in sequence from the common cold human coronaviruses HKU1, OC43, 229E and NL63 (25-30%).

Methods
Recombinant trimeric spike proteins of all 7 HCoVs were expressed, purified and coupled to beads. Using a custom Luminex assay, we investigated spike protein-specific IgG antibody levels in COVID-19 patients in comparison to serum and plasma of healthy donors and in cynomolgus macaques immunized with a SARS-CoV-2 spike nanoparticle vaccine.

Results
Higher IgG antibody levels against all HCoV spike proteins were observed in convalescent serum of COVID-19 patients compared to healthy donors. The results were highly significant (P<0.001) for all spikes except for coronavirus NL63, which is most distant from SARS-CoV-2 in sequence. To investigate the possibility that this is partly caused by cross-binding antibodies elicited directly by the SARS-CoV-2 infection, rather than only boosting memory of pre-existing common cold coronaviruses, we also investigated IgG antibody binding to SARS, MERS and common cold coronaviruses in cynomolgus macaques during a SARS-CoV-2 Spike Nanoparticle vaccine immunization schedule. We found that these macaques developed detectable IgG antibodies for all human coronavirus spikes in response to the vaccine, even though they were naive for all other HCoVs.

Conclusions
This study demonstrates that SARS-CoV-2 infection elicits cross-reactive HCoV antibody responses and that the induction of such responses by a vaccine seems a feasible goal. These cross-reactive antibodies and their role in future HCoV-infections need to be further investigated because the induction of cross-binding antibodies might be of great value especially for vulnerable populations such as HIV-infected individuals.