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KIT Royal Tropical Institute

# Abstracts

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# Organisation

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# ORAL PRESENTATIONS

## 0.01

### ABORTIVE HIV RNA IN SERUM INVERSELY CORRELATES WITH TRANSCRIPTIONAL ACTIVITY OF THE HIV RESERVOIR IN PEOPLE WITH HIV

**Stefanie Kroeze**, Alexander Pasternak, Shirley Man, Jade Jansen, Theo Geijtenbeek, Neeltje Kootstra

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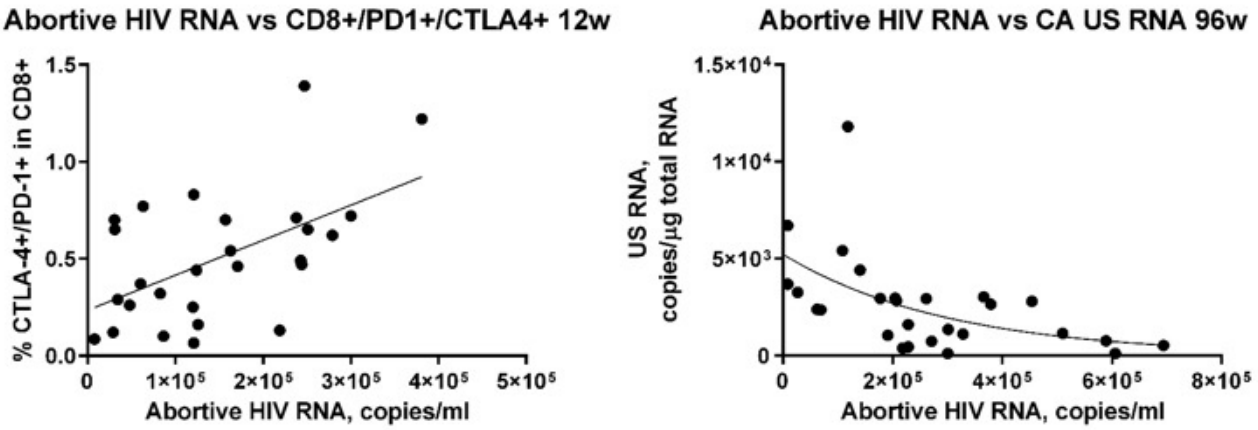
**Background**
The HIV-reservoir remains a major obstacle in HIV-cure research. Monitoring of the HIV-reservoir is a major challenge in current HIV-cure research, because established assays rely on cell-based measurements, which requires labor intensive procedures. Latent HIV-infected cells harbor abortive HIV RNA, signifying abrogated transcription elongation. We hypothesize that abortive HIV RNA in serum can be a potential biomarker of the latent HIV reservoir. It Is, however, unknown how abortive HIV RNA correlates to other virological measurements of the HIV reservoir. Here we investigate the association of abortive HIV RNA with cell associated (CA) HIV DNA (CA-DNA), CA unspliced HIV RNA (CA–US-RNA), CA multiple spliced RNA (CA-MS-RNA) , and with cellular markers of immune activation, exhaustion and senescence.

**Methods**
Abortive HIV RNA was measured in serum from people with HIV (PWH) from the Amsterdam Cohort Studies (ACS): pre-ART, 1, 2, and 5 years of ART (n=32) and 10 year of ART (n=15). The size of the RNA transcripts in serum representing abortive RNAs was assessed by fragment analysis. From 28 PWH from the ACS for whom CA-DNA, CA-US-RNA, CA-MS-RNA and immune phenotyping was available, serum abortive HIV RNA was measured. Spearman correlation was used to assess the correlation between abortive HIV RNA in serum, and cellular HIV-1 reservoir measurements and cellular biomarkers of immune activation (CD38+/HLA-DR+), exhaustion (PD1+/CTLA4+) and senescence markers (CD57+).

**Results**
Longitudinal analysis showed that abortive HIV RNA transcripts were detectable in serum of PWH for at least 10 years after ART initiation. Fragment analysis revealed that these HIV RNA transcripts in serum were short RNA transcripts (<200nt) representing indeed abortive HIV RNA transcripts. At 12 weeks of ART, abortive HIV RNA in serum correlated with CD8+ T-cell exhaustion (CD8+/PD1+/CTLA4+ r= 0.48, P=0.012; and CD8+/CTLA4+ r= 0.43, P=0.024), but not with any of the other immunological markers or viral reservoir (CA-US-RNA, CA-MS-RNA, CA-DNA). At 96 weeks of ART, abortive HIV-RNA in serum inversely correlated with CA-US-RNA (r= -0.63, P= 0.0005), but not with CA-MS-RNA, CA-HIV-DNA nor any of the immunological markers.

**Conclusion**
We show that short abortive HIV RNAs are detectable in serum from PWH during long-term ART. Short abortive HIV RNA was associated with CD8+ T-cell exhaustion during early ART and inversely correlated with CA US RNA during long term ART. These findings suggest that abortive HIV RNA in serum is reflective of the latent HIV reservoir as CA US RNA is a measure of residual transcriptional activity.

*0.01 (Figure 1)*




Correlation of abortive HIV RNA with CD8+ T-cell exhaustion and cell associated unspliced HIV RNA during ART

## 0.02

### STARTING ART EARLY AFTER HIV ACQUISITION REDUCES LONG-TERM NON-AIDS DEFINING MALIGNANCY RISK

**Iris van der Wulp**[1,2], Ferdinand Wit[2,3], Peter Reiss[1,2], Marc van der Valk[2,3]

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

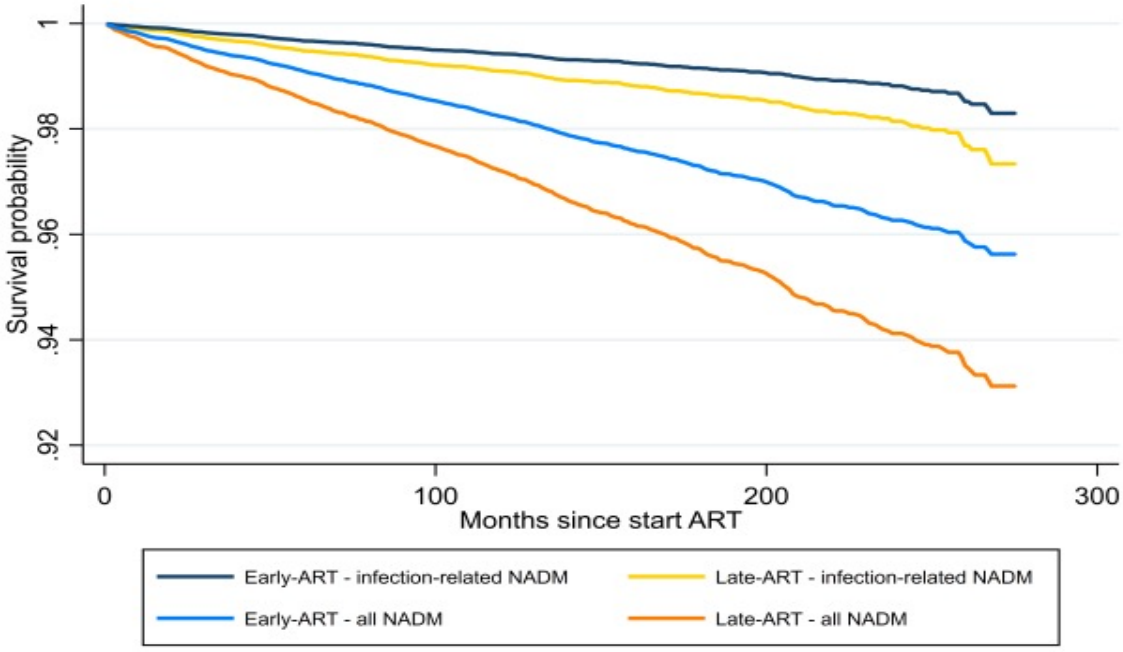
**Background**
Non-AIDS Defining Malignancies (NADM) have become a prominent cause of death in people with HIV (PWH). Evidence shows that starting antiretroviral treatment (ART) at a higher CD4 count is associated with reduced NADM risk. We aimed to investigate whether starting ART early after acquiring HIV reduces NADM risk even further.

**Methods**
We included PWH 18 years or older from the Dutch National ATHENA cohort without a known NADM diagnosis starting ART between 1/1/2000 – 31/12/2022. NADM and infection-related NADM were analyzed separately. Individuals who started ART ≤ 365 days of a last known negative HIV test or with a documented primary infection (Fiebig stages 1-5) were categorized as "Early-ART", and all others as "Late-ART" starters. Hazard Ratios (HR) for NADM were estimated by unadjusted and adjusted Cox proportional hazards models. Models were adjusted for traditional (age, sex at birth, calendar time, HIV transmission category, smoking (time-updated), and region of origin) and HIV related (time-updated CD4 count lagged by 3 months, CD4/8 ratio and time spent with HIV RNA > 1000 copies/ml) factors.

**Results**
Early-ART compared to Late-ART starters were younger (median age 34.7 vs. 39.4 years), more frequently male (94.3 vs. 80.0%), with a CD4 count > 500 cells/mm3 at ART start (42.6 vs. 18.8%), less frequently current or former smokers (39.7 vs. 44.9%), and had shorter median follow-up (68 vs. 115 months). In the Early-ART starters (n=2,036) 28 NADM occurred during 12,454 PYFU (IR 2.2/1000 PYFU) versus 1,160 NADM during 220,237 PYFU (IR 5.3/1000 PYFU) in the Late-ART starters (n=22,183). Unadjusted, Early-ART start was associated with a significantly reduced NADM hazard (HR 0.48 [95% Confidence Interval (CI) 0.33–0.69]) which was only moderately attenuated after adjustment (multivariate HR 0.63 [95% CI 0.43–0.92]). When only considering infection-related NADM, 8 events occurred in Early-ART starters (n=2,037) during 12,531 PYFU (0.6/1000 PYFU) versus 378 during 223,390 PYFU (IR 1.7/1000 PYFU) in Late-ART starters (n=22,252). Early-ART start was associated with a significantly lower infection-related NADM hazard (HR 0.38 [95% CI 0.19–0.78]) in unadjusted analysis. In our multivariable model results were similar to the all-NADM analysis, but lacked statistical significance (HR 0.64 [95% CI 0.31–1.29]).

**Conclusions**
Starting ART within 12 months of acquiring HIV or during primary infection reduces the risk of non-AIDS defining malignancy compared to starting ART later after infection. Larger studies should assess and compare the impact on individual NADM types.

*0.02 (Figure 1) Multivariable survival analyses in Early versus Late-ART.*




Infection-related NADM: hepatocellular, base of tongue, pharyngeal, tonsillar, anal, penile, vaginal, vulvar, gastric carinomas, and non-AIDS-defining lymphoma types.

## 0.03

### TARGETING HOST FACTORS DDX3 AND IAP ELIMINATES THE HIV-1 RESERVOIR IN PEOPLE LIVING WITH HIV EX VIVO

**Jade Jansen**[1,2], Stefanie Kroeze[1,2], Shirley Man[1,2], Neeltje Kootstra[1,2], Teunis Geijtenbeek[1,2]

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**Background**
The persistence of the human immunodeficiency virus-1 (HIV-1) reservoir in people living with HIV (PWH) on combination antiretroviral therapy (cART) remains the biggest obstacle to a cure. We hypothesized that interfering with HIV-1 mRNA transport while increasing sensitivity to apoptosis might specifically eliminate reactivated HIV-1 cellular reservoirs. We therefore targeted host factors Inhibitor of Apoptosis (IAP), that regulates apoptosis, and Dead-box helicase DDX3, which facilitates rev mediated HIV-1 mRNA transport and translation.

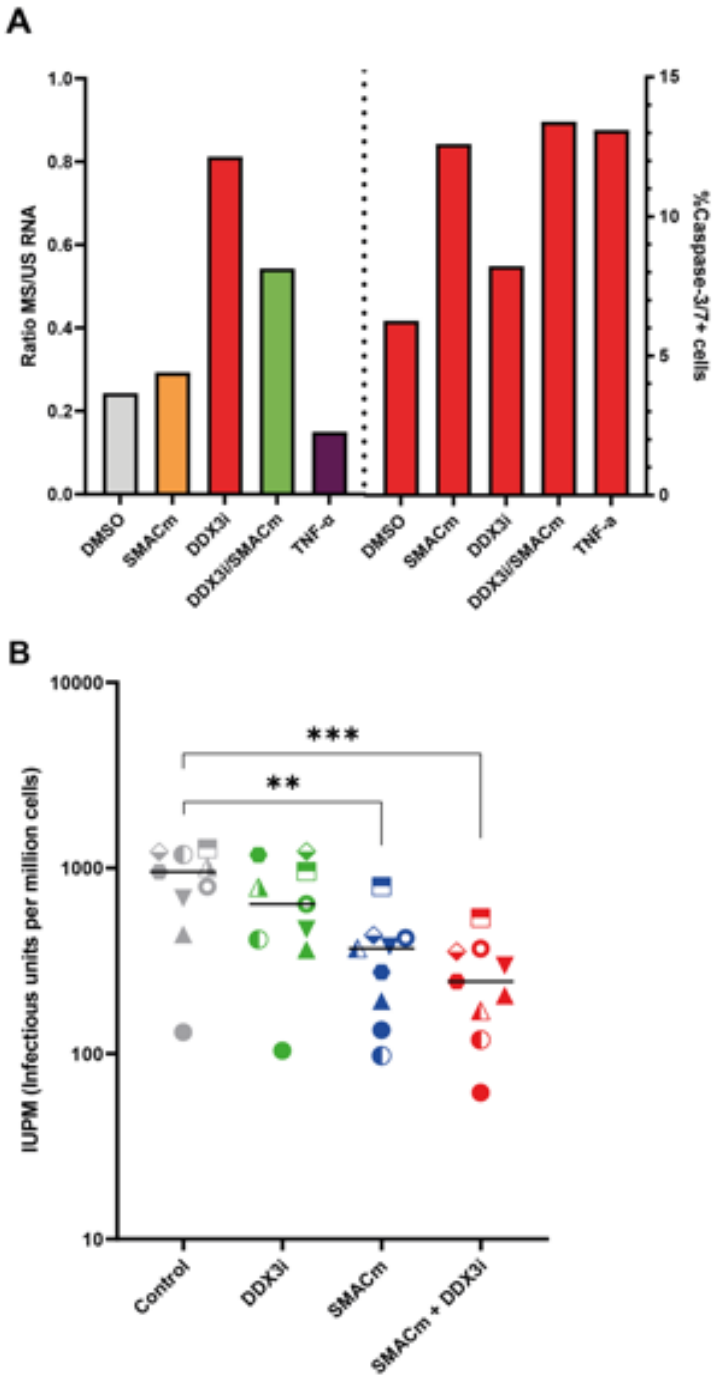
**Methods**
SUPT1-CCR5 cells were infected with NL4-3BaL, treated with DDX3 inhibitor (DDX3i), SMAC mimetic (SMACm) or the combination of both. Multiple spliced (MS) and unspliced (US) RNA was measured with RT-qPCR. Viral replication and apoptosis was determined by detecting intracellular p24 and caspase-3/7 by flowcytometry. PBMCs from PWH were treated with the compounds and the size of the inducible latent HIV-1 reservoir was measured by a newly developed ex vivo reservoir reduction assay.

**Results**
Treatment of HIV-1 infected SUPT1-CCR5 cells with a combination of DDX3i and SMACm strongly decreased the amount of HIV-1-positive cells (2.3 fold), whereas SMACm (1.2 fold) and DDX3i (1.7 fold) alone also led to a reduction of infected cells. DDX3i treatment increased MS RNA in relation to US RNA (3.3 fold increase compared to DMSO), implying an accumulation of MS RNA (Figure 1A), whereas SMACm treatment increased apoptosis (Figure 1A). The combination of both compounds (DDX3i/SMACm) led to a 2.2 fold increase of MS RNA compared to DMSO and similar induction of apoptosis compared to SMACm alone.

Strikingly, PBMCs from PWH treated with the combination of compounds (DDX3i/SMACm) reduced the inducible HIV-1 reservoir by 74% ($p=0.0006$) compared to the compounds alone with reduction of 33% and 61% ($p=0.0015$ for DDX3i and SMACm, respectively (Figure 1B).

**Conclusions**
Our research strongly suggest that a combination treatment targeting both DDX3 and IAP greatly decreased the inducible latent HIV-1 reservoir size in PWH ex vivo. We have identified the mechanism suggesting that DDX3 inhibition leads to accumulation of MS RNA while IAP inhibition with SMACm increases apoptosis of HIV-1 infected cells. The combination leads to increased apoptosis of reactivated cells most likely due to the accumulation of HIV-1 mRNA and increased sensitivity to apoptosis.

*O.03 (Figure 1) Increased MS/USRNA ratio and apoptosis by DDX3i/SMACm leads to reservoir reduction.*




Ratio of MS/US RNA by RT-qPCR after 24hr and the proportion of Caspase-3/7+ cells by flow cytomerty after 48hr treatment with the compounds (A). Reduction of the inducible latent HIV-1 reservoir size in PWH (B).

0.04

## EXPLORING AND COMPARING BIOMARKER PROFILES AND COMORBIDITY BURDEN IN PEOPLE WITH AND WITHOUT HIV: A LATENT PROFILE ANALYSIS OF THE AGEHIV COHORT STUDY

**Manon Vanbellinghen**[1,2,3], Anders Boyd[4,5], Neeltje Kootstra[6], Maarten Schim van der Loeff[1,5], Marc van der Valk[1,2,4], Peter Reiss[1,2,7]

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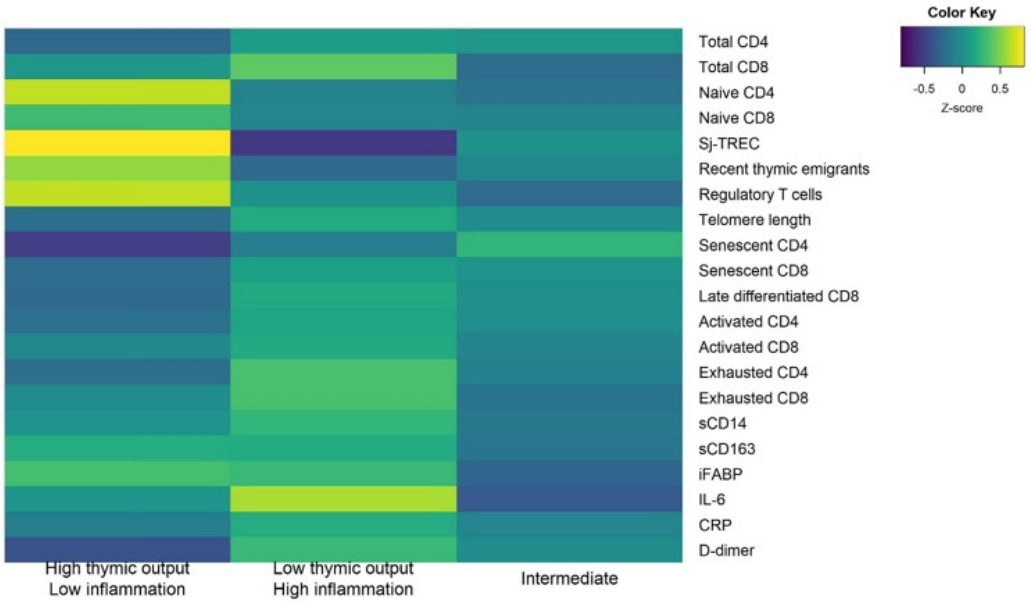
**Background**
People with HIV (PWH) experience a higher burden of ageing-associated comorbidities potentially related to ongoing inflammation and immune dysfunction. Understanding the mechanisms driving their development is crucial. We aimed to identify profiles based on immune, inflammatory and ageing biomarkers in PWH and controls. In addition, we explored the association between identified biomarker profiles and comorbidity burden over time.

**Methods**
We selected 94 PWH and 95 demographically comparable controls from the AGEhIV Cohort Study in whom baseline measurements of CD4 and CD8 T-cell subsets, soluble inflammation/immune biomarkers, telomere length and signal-joint-T-cell Receptor Excision Circle content had been determined. We constructed profiles using latent profile analysis (LPA) and examined factors associated with profile membership using multivariable logistic regression.
The association between profile membership and mean total comorbidity count over time was analyzed using a Poisson mixed-effect model, stratified by HIV-status. Comorbidities included in the total count during the 8-year follow-up comprised diabetes mellitus, non-AIDS malignancies, cardiovascular disease, osteoporosis, frailty, and chronic kidney disease.

**Results**
Three biomarker profiles were identified (Fig.1). One profile, labeled ‘High Thymic Output/Low Inflammation’ (HT/LI), present in 27 PWH and 9 Controls, showed higher proportions of naïve and regulatory T-cells, higher thymic output, and lower soluble inflammation marker levels. A second profile, labeled ‘Low Thymic Output/High Inflammation’ (LT/HI), present in 29 PWH and 26 controls, exhibited reduced thymic output, higher T-cell activation, increased soluble inflammation markers, and higher proportions of exhausted and senescent T-cells. The third and largest profile, present in 38 PWH and 60 controls, displayed a biomarker pattern ‘intermediate’ to the first and second profile.
In the multivariable analysis, only HIV-status was significantly associated with profile membership. PWH had significantly higher odds of exhibiting the HT/LI profile compared to both the HI/LT profile (OR=3.09, 95%CI=1.11-8.60, p=0.031) and the intermediate profile (OR=4.98, 95%CI=1.93-12.83, p=0.001). In PWH (Fig.2A) but not in controls (Fig.2C), those with the HT/LI profile had a significantly lower overall mean total comorbidity count (mean count=0.10, 95%CI=0.01-0.20) compared to the LT/HI (mean count=0.76, 95%CI=0.23-1.23, p< 0.001) and intermediate profile (mean count=0.55, 95%CI=0.25-0.86, p=0.002). This distinction was consistent across all follow-up visits (Fig.2B and 2D).

**Conclusion**
Exhibiting the HT/LI profile was associated with HIV-status and over time was associated with a lower comorbidity burden in PWH, but not in controls. These findings suggest that greater thymic function in PWH may be related to mitigation of chronic inflammation, thereby reducing the risk of developing ageing-associated comorbidities.

*0.04 (Figure 1) Heatmap of standarized biomarker levels for each biomarker profile in the combined cohort of PWH and controlls.*




The color displayed in each cell of the heatmap indicates the mean standardized level of the measured biomarker (i.e., z-score) within the given profile.

*0.04 (Figure 2) .*

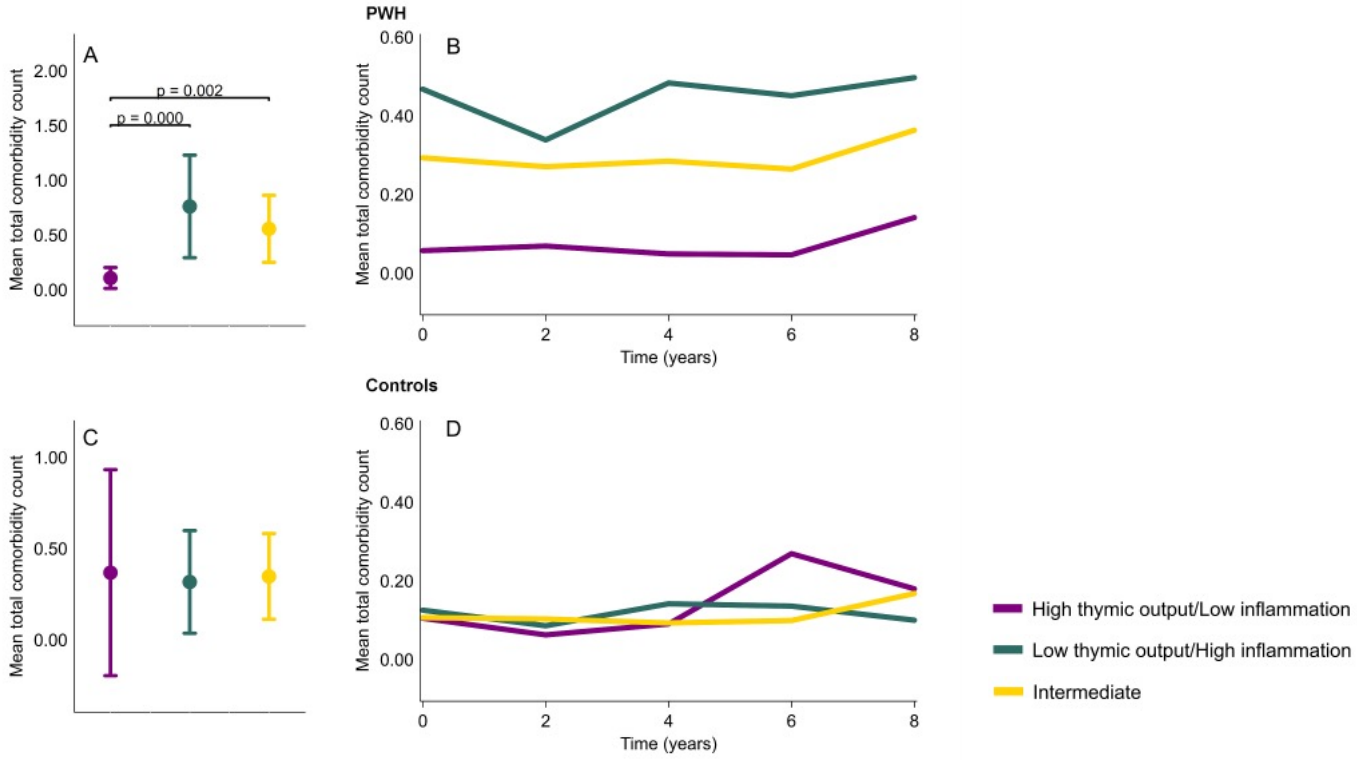



**Figure 2. Panel A and C** compare the mean total comorbidity count between profiles, as observed across all follow-up time points in PWH (**A**) and controls (**C**). **Panel B and D** illustrate the temporal course of mean total comorbidity counts at each follow-up visit, stratified by profile, in PWH (**B**) and controls (**D**). Both analyses are adjusted for age, CMV serostatus, current smoking, obesity and sex at birth.

# ORAL PRESENTATIONS

## 0.05

### BARRIERS AND MISSED OPPORTUNITIES IN PREP UPTAKE, USE AND CARE AMONG MSM WITH RECENT HIV INFECTION AND PREVIOUS PREP EXPERIENCE IN THE NETHERLANDS, 2022-2023: A QUALITATIVE STUDY

**Jeffrey Koole**[1], Maarten Bedert[2], Feline de la Court[1], Irene Bais[1], Janneke Stalenhoef[3], Tania Mudrikova[4], Ferdinand de Wit[5], Katalin Pogany[6], Birgit van Benthem[7], Maria Prins[1,2], Udi Davidovich[1,8], Marc van der Valk[2,5]

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**Background**
In the Netherlands, since 2019, HIV pre-exposure prophylaxis (PrEP) can be accessed formally [e.g., national PrEP program (NPP), general practitioner (GP)], or informally (e.g., sexual networks). Between 2018 and May 2022, 71 MSM indicated PrEP use prior to their HIV diagnosis. In this qualitative study, we aimed to identify barriers and missed opportunities in PrEP uptake, care and use among MSM recently diagnosed with HIV while formal PrEP was available in the Netherlands and have had PrEP experience.

**Methods**
HIV Monitoring Foundation (SHM) collects national data on people with HIV entering care. MSM diagnosed with HIV from 2019 onwards with PrEP experience were recruited using SHM data and HIV treatment centers. Between March 2022 and March 2023, we conducted semi-structured in-depth interviews (IDIs) on PrEP uptake, care, use and discontinuation in the context of their subsequent HIV infection.

**Results**
Of the 11 included interviewees, 2 used informal PrEP without being HIV tested before initiation, and 9 accessed formal PrEP (table 1). Of those who accessed formal PrEP, 3 tested HIV positive at PrEP intake consultation (and did not start PrEP), 4 tested positive 1-4 months after PrEP initiation, 1 discontinued PrEP and tested positive 2 months thereafter, and 1 interviewee tested positive after 2 years of daily use. All but one reported good regimen adherence. For most interviewees, initial PrEP uptake was delayed (up to 18 months) due to limited NPP capacity, and barriers for requesting PrEP from GPs (e.g., stigma on sexual behavior, lack of PrEP or sexual health expertise among GPs). PrEP care, once obtained, was generally experienced as satisfying, although missed opportunities in counseling on side-effects, adherence and practicing safer sex after discontinuation were identified. Barriers during use included side-effects and PrEP protocol/user-mismatch (e.g., burden of daily pill-taking, or complexity of event-driven regimen).

**Conclusion**
Among MSM with HIV and previous PrEP experience, PrEP uptake delay was crucial in the context of HIV seroconversion. Uptake barriers included limited national PrEP program (NPP) capacity and high threshold for requesting PrEP from GPs. New HIV diagnoses at/shortly after PrEP initiation emphasize the urgency of ensuring its timely access. Barriers for accessing PrEP through GPs and stigma on sexual behavior need to be addressed. Counseling on side-effects, adherence and safer sex post PrEP discontinuation are important for sustainable HIV prevention. Additionally, early detection of PrEP protocol/user-mismatch is required.

*0.05 (Figure 1) PrEP uptake, care and use, socio-demographic and HIV diagnosis characteristics of 11 MSM with HIV and previous PrEP experience, the Netherlands, 2022-2023.*

| # | Age, years | COB | Sex group | PrEP uptake, care, use and discontinuation | | | | | | | | | First positive HIV test result | | Estimated moment of HIV infection |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Accessed route | Country of access | Preferred route | Uptake delay[a], months | HIV test result at baseline | Regimen used | Use duration, months | Regimen adherence[f] | Reason to discontinue | Moment | Location | |
| 1 | 30-40 | NL | MSM | Sexual network (I) | NL | CSH | A few | Not performed | ED | 6 | Good | Running out of informal pills | 2 months after PrEP dinscontinuation | CSH | 1 month after PrEP discontinuation |
| 2 | 40-50 | NL | MSM | IMS (F) | N/a | N/a | N/a | Positive[c] | N/a | N/a | N/a | N/a | At baseline | IMS | Before PrEP initiation |
| 3 | 40-50 | BR | MSM | Sexual network (I) | NL | N/a | N/a | Not performed | ED | 1 | Good | Positive HIV test result | 1 month after PrEP initiation | CSH | 4 years before PrEP initiation |
| 4 | 50-60 | NL | MSM | CSH (F) | NL | CSH | 12 | Negative[d] | ED | 1 | Good | Positive HIV test result | 1 month after PrEP initiation | CSH | Before PrEP initiation |
| 5 | 60-70 | NL | MSM | CSH (F) | NL | CSH | 12 | Negative | Daily | 24 | Good | Positive HIV test result | 24 months after PrEP initiation | CSH | During PrEP use |
| 6 | 20-30 | BR | MSM | GP (F) | SA | CSH | 2[b] | Not performed[e] | Daily | 3 | Good | Positive HIV test result | 3 months after PrEP initiation | Self-test at home | Before or shortly after PrEP initiation |
| 7 | 20-30 | SU | MSM | GP (F) | NL | CSH | N/a | Negative | Daily, ED | 4 | Not good | Positive HIV test result | 4 months after PrEP initiation | CSH | During PrEP use |
| 8 | 60-70 | NL | MSM | GP (F) | NL | GP | N/a | Negative | ED | 6-7 | Good | Burden of daily pill-taking, burden of complexity of ED regimen | A few months after PrEP discontinuation | GP | After PrEP discontinuation |
| 9 | 30-40 | BR | MSM | GP (F) | NL | CSH | 12 | Negative[d] | Daily | 3 | Good | Positive HIV test result | 3 months after PrEP initiation | GP | Before PrEP start (HIV diagnostic window period) |
| 10 | 50-60 | NL | MSM | GP (F) | NL | CSH | 18 | Positive[c] | N/a | N/a | N/a | N/a | At baseline | GP | Before PrEP initiation |
| 11 | 30-40 | NL | MSM | CSH (F) | NL | CSH | 3 | Positive[c] | N/a | N/a | N/a | N/a | At baseline | CSH | <1 month before PrEP initiation |

#: interviewee number, COB: Country of birth, BR: Brazil: CSH: center for sexual health, ED: event-driven, F: formal PrEP, I: informal PrEP, GP: general practitioner, IMS: internal medicine specialist, MSM: men who have sex with men, N/a: not applicable, NL: the Netherlands, NPP: national PrEP pilot program, PrEP: HIV pre-exposure prophylaxis, SA: South-Africa, SU: Suriname, a: Time between *attempting to access PrEP* and either *PrEP intake consultation or starting PrEP*, whichever came first, b: he postponed his PrEP pursuit for 2 years because formal PrEP was not yet available, c: those having a first positive HIV test result at baseline did not start PrEP, d: presumed false-negative because of HIV diagnostic window period, e: he had a negative HIV self-test result 1 month before PrEP initiation and decided to opt out for HIV testing at baseline, f: self-reported

PrEP uptake, care and use, socio-demographic and HIV diagnosis characteristics of 11 MSM with HIV and previous PrEP experience, the Netherlands

## 0.06

### UNMASKING HIV STIGMA: PERSPECTIVES OF DUTCH HEALTHCARE PROVIDERS

**Carlijn Jordans**[1], Anne-Mae van Bruggen[1], Klaske Vliegenthart-Jongbloed[1], Sarah Stutterheim[2], Jan van Beek[1], Marion Vriesde[1], Natasja van Holten[3], Anna Roukens[3], Casper Rokx[1]

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**Background**
HIV stigma impacts the full cascade of care. Research on the perspectives of people living with HIV (PLWH) shows an increase in stigma in Dutch healthcare setting in the past decade. In this study, we investigated HIV stigma in healthcare settings from the perspective of healthcare workers (HCW) in order to provide valuable complementary insights to previous work.

**Methods**
A cross-sectional survey was conducted between April and August 2023 at two University Medical Centers (Rotterdam and Leiden). Using a standardized questionnaire for HIV stigma, we selected relevant questions for HCW in a survey. This questionnaire was distributed to all HCW by mail and through focused meetings at large departments. The primary outcome was prevalence of HIV stigma measured by one of the five indicators: 1) fear of HIV infection, 2) observed and anticipated stigma and discrimination, 3) institutional-level facilitators and barriers, 4) attitudes towards PLWHIV and, 5) barriers discussing HIV with patients. Only questionnaires with ≥1 questions on stigma indicator completed were analyzed.

**Results**
Amongst the 314 included HCW (Table 1), stigma was prevalent in all indicators (Table 2). Indicators fear of infection (74.2%) and barriers discussing HIV and risk factors (72.4%) were most prevalent. Approximately 10% of HCW believed that PLWH acquired HIV by irresponsible behavior and do not care if they infect others. Using 20 years to mark generations, HCW ≤25 years worried more about acquiring HIV at work than those ≥46 years (OR 44.3, p<0.001). They also used more precautionary measures (OR 3.0, p=0.026) and expressed more negative attitudes towards PLWH (OR 41.2, p=<0.001). Nurses worried more about getting infected than doctors (OR 2.6, p=0.003) which also correlated with more negative attitudes. With the exception of the infectious diseases department, over 50% of HCW in all departments expressed concerns about acquiring HIV at work, with HCW from surgical departments taking precautionary measures most frequently. Difficulties discussing HIV-related matters were comparable across departments (range 60% - 100%).

**Conclusion**
HIV stigma is prevalent among Dutch HCW and appears to be more prominent among younger HCW. Targeted approaches to reduce stigma in healthcare are needed, particularly for younger HCW and HCW in training. Interventions should be theory and evidence-based and, in a safe and non-judgmental context, target 1) concerns about occupational infection, 2) overcoming barriers to discussing HIV with patients, and 3) reflecting on prejudices against PLWH.

*0.06 (Table 1) Participant characteristics*

| | Participants, n (%) | Median (IQR) | Missing, n (%) |
|---|---|---|---|
| **Age (years)** | | 32 (27-39) | - |
| ≤25 | 59 (18.8) | | |
| 26 – 45 | 209 (66.6) | | |
| ≥ 46 | 46 (14.6) | | |
| **Gender** | | | - |
| Female | 231 (73.6) | | |
| Male | 81 (25.8) | | |
| Other | 2 (0.6) | | |
| **Occupation** | | | - |
| Nurse | 157 (50.0) | | |
| Resident | 70 (22.3) | | |
| Medical specialist | 57 (18.2) | | |
| Other | 30 (9.5) | | |
| **Department(s)** | | | - |
| Internal medicine | 48 (15.3) | | |
| Emergency department | 35 (11.1) | | |
| Pulmonology | 27 (8.6) | | |
| Ear, nose, throat | 22 (7.0) | | |
| Neurosurgery | 20 (6.4) | | |
| Gastroenterology/hepatology | 19 (6.1) | | |
| Cardiothoracic surgery | 19 (6.1) | | |
| Oncology | 15 (4.8) | | |
| Acute admission department | 12 (3.8) | | |
| Gastroenterology/hepatology/surgery | 11 (3.5) | | |
| Dermatology | 11 (3.5) | | |
| Surgery | 10 (3.2) | | |
| Infectious diseases | 9 (2.9) | | |
| other | 56 (17.8) | | |
| **City of work** | | | - |
| Rotterdam | 282 (89.8) | | |
| Leiden | 28 (8.9) | | |
| Other | 4 (1.3) | | |
| **Years worked in healthcare** | | 8.0 (4.9-15.0) | 2 (0.6) |
| **Number of treated patients with HIV per year** | | 4.0 (IQR 2.0-8.0) | - |
| **Received training on the following topics:** | | | - |
| HIV stigma and discrimination | 31 (10.2) | | |
| Infection control and universal precautions | 132 (42.0) | | |
| Patient's informed consent, privacy, and confidentiality | 127 (40.4) | | |
| Key population stigma and discrimination | 47 (15.0) | | |
| Received no training in one of these topics | 136 (43.3) | | |
| **Received any of above training** | 178 (56.7) | | |

*0.06 (Table 2) Prevalence of stigma indicators*

| *The five HIV stigma indicators measured by an adapted version of the standardized questionnaire 'Measuring HIV stigma and discrimination among health facility staff: indicator monitoring tool' ** | | | |
|---|---|---|---|
| ***Fear of HIV infection*** | | | |
| **Worry of HIV when conducting the following activities:** | **Not worried, n (%)** | | **Worried, n (%)** |
| Touch clothing of a patient living with HIV (n=313) | 284 (90.7) | | 29 (9.3) |
| Dress wounds of a patient living with HIV (n=298) | 94 (31.5) | | 204 (68.5) |
| Draw blood from a patient living with HIV (n=296) | 71 (24.0) | | 225 (76.0) |
| **Any worry to get HIV infected (n=314)** | | **No, n (%) 81 (25.8)** | **Yes , n (%) 233 (74.2)** |
| **Use of precautionary measures when providing care to patients living with HIV:** | **No, n (%)** | | **Yes, n (%)** |
| Avoid physical contact (n=303) | 283 (93.4) | | 20 (6.6) |
| Wear double gloves (n=302) | 252 (83.4) | | 50 (16.6) |
| **Any use of precautionary measures (n=303)** | | **No, n (%) 238 (78.5)** | **Yes, n (%) 65 (21.5)** |
| ***Observed stigma and discrimination*** | | | |
| **Observed at your health facility in the last 12 months** | **Never, n (%)** | | **At least once, n (%)** |
| Healthcare providers unwilling to care for a patient living with HIV (n=252) | 243 (96.4) | | 9 (3.6) |
| Healthcare providers providing poorer quality of care to a patient living with HIV compared to other patients (n=252) | 235 (93.3) | | 17 (6.7) |
| **Any observed stigma and discrimination (n=253)** | | **No, n (%) 231 (91.3)** | **Yes, n (%) 22 (8.7)** |
| ***Institutional facilitators and barriers*** | | | |
| **Policies on discrimination** | **No, n (%)** | **Yes, n (%)** | **Don't know, n (%)** |
| I will get in trouble at work if I discriminate against patients living with HIV (n=307) | 14 (4.6) | 176 (57.3) | 117 (38.1) |
| My health facility has written guidelines to protect patients living with HIV from discrimination (n=309) | 7 (2.3) | 57 (18.4) | 245 (79.3) |
| **Policies on reducing the risk of HIV infection** | **Agree, n (%)** | | **Disagree, n (%)** |
| There are adequate supplies in my health facility that reduce my risk of becoming infected with HIV (n=309) | 298 (96.4) | | 11 (3.6) |
| There are standardized procedures/protocol in my health facility that reduce my risk of becoming infected with HIV (n=309) | 287 (92.9) | | 22 (7.1) |
| ***Attitudes towards people living with HIV*** | | | |
| **Level of agreement with the following statements:** | **Agree, n (%)** | | **Disagree, n (%)** |
| Most people living with HIV do not care if they infect other people (n=302) | 27 (8.9) | | 275 (91.1) |
| People living with HIV should feel ashamed of themselves (n=302) | 3 (1.0) | | 299 (99.0) |
| People get infected with HIV because they engage in irresponsible behaviors (n=301) | 33 (11.0) | | 268 (89.0) |
| Women living with HIV should be allowed to have babies if they wish (n=301)** | 265 (88.0) | | 36 (12.0) |

| **Any negative attitudes (n=302)** | **Yes, n (%) 80 (26.5)** | **No, (%) 222 (73.5)** |
|---|---|---|
| ***Barriers discussing HIV and risk factors with patients*** | | |
| **Level of difficulty discussing the following topics:** | **Easy, n (%)** | **Difficult, n (%)** |
| The possibility of an HIV infection (n=240) | 135 (56.2) | 105 (43.8) |
| The need to test for HIV (n=244) | 201 (82.4) | 43 (17.6) |
| Risk factors for HIV (n=244) | 168 (68.9) | 76 (31.1) |
| HIV-related topics when a patient is accompanied by a family member (n=251) | 77 (30.7) | 174 (69.3) |
| **Any difficulties discussing HIV and risk factors (n=257)** | **No, n (%) 71 (27.6)** | **Yes, n (%) 186 (72.4)** |

* Reference:
https://www.healthpolicyproject.com/pubs/49_StandardizedBriefQuestionnaireMeasuringSD.pdf
** This statement was inverted in the 'any negative attitudes' section as women living with HIV should be allowed to have babies is a positive attitude towards people living with HIV

0.07

## STI TESTING RATES AMONG PREP USERS RANDOMIZED TO RECEIVING 3-MONTHLY OR 6-MONTHLY PREP MONITORING WITHIN THE EZI-PREP TRIAL, THE NETHERLANDS: PRELIMINARY RESULTS

**Marije Groot Bruinderink**[1], Eline Wijstma[1], Vita Jongen[1,2], Sophie Boers[3], Joey Woudstra[1], Koenraad Vermey[4], Elske Hoornenborg[1,5,6], Maria Prins[1,5,6], Frenk van Harreveld[7,8], Hannelore Götz[9,10], Udi Davidovich[1,11], Maarten Schim van der Loeff[1,5,6]

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[10] *Department of Public Health, Erasmus MC, University Medical Center, Rotterdam, Netherlands*
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**Background**
People using HIV pre-exposure prophylaxis (PrEP) are at risk for sexually transmitted infections (STI). Regular STI screening for PrEP users is recommended, but debate around the optimal STI testing frequency is ongoing. To inform STI screening guidelines, we examined STI testing rates among PrEP users randomized to 6-monthly or 3-monthly STI screening within the EZI-PrEP study.

**Methods**
EZI-PrEP is an ongoing four-arm randomized controlled trial on the feasibility and non-inferiority of 6-monthly versus 3-monthly, and online versus in-clinic PrEP monitoring. Monitoring included STI screening; free-of-charge STI testing in-between visits was optional. Sexual health centers of four public health services in the Netherlands implement EzI-PrEP: Amsterdam, Haaglanden, Rotterdam-Rijnmond and Gelderland-Zuid. This preliminary analysis included data from Amsterdam and Haaglanden, from participants with ≥1 monitoring visit between September 21st 2021 and August 1st 2023. We compared overall visit rates (i.e., total number of PrEP visits and additional STI visits per person-year (py)), and additional STI visit rates (i.e., number of additional STI visits per py) between 6-monthly and 3-monthly monitoring using visit rate ratios and 95% confidence intervals (CI). We compared positivity of any chlamydia, gonorrhea, or infectious syphilis ('any STI') between 6-monthly and 3-monthly monitoring by visit type, using $\chi 2$ test.

**Results**
321 participants (n=161 in 6-monthly arm; n=160 in 3-monthly arm) contributed 376 person-years of follow-up. The overall visit rate in the 6-monthly arm was lower compared to the 3-monthly arm (6-monthly arm: 3.3/py (95% CI: 3.1-3.6); 3-monthly arm: 4.8/py (95%CI: 4.5-5.1); visit rate ratio=0.69 (95% CI:0.62-0.76), p<0.0001). The additional STI visit rate in the 6-monthly arm was higher compared to the 3-monthly arm (6-monthly arm: 1.1/py (95% CI: 1.0-1.3; 3-monthly arm: 0.8/py (95% CI 0.7-0.9)); visit rate ratio=1.45 (95% CI:1.17-1.80)). Any STI positivity at PrEP visits was comparable across groups: 20.6% (n=114/554) and 18.0% (n=173/962) in the 6-monthly and 3-monthly arm, respectively (p=0.21). Any STI positivity at additional STI visits was 28.8% (n=59/205) and 32.3% (n=51/158) in the 6-monthly and 3-monthly arm, respectively (p=0.47).

**Conclusion**
Compared to PrEP users randomized to 3-monthly monitoring, PrEP users randomized to 6-monthly monitoring attended more additional STI visits, but fewer visits overall. STI positivity did not differ between 3-monthly and 6-monthly arms. These preliminary findings tentatively suggest that implementing 6-monthly PrEP follow-up as standard-of-care could reduce the total number of visits without resulting in major increases in STI positivity. Further research on the impact of 6-monthly monitoring on STI transmission is needed.

## 0.08

### SEX-BASED DIFFERENCES IN AUTOLOGOUS NEUTRALISING ANTIBODY RESPONSES INDUCED BY A NATIVE-LIKE HIV-1 ENVELOPE TRIMER VACCINE

**Emma Reiss**[1,2], Karlijn van der Straten[1,2], Marinus Liesdek[1,2], Annelou van der Veen[1], Marloes Grobben[1,2], Hongmei Gao[3], Kelli Greene[3], David Montefiori[3], Maarten Soeters[1], Michelle Klouwens[1], Jan Prins[1], Marit van Gils[1,2], Rogier Sanders[1,2,4], Godelieve de Bree[1]

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**Background**
A protective vaccine would be the most powerful instrument to reduce HIV-1 infections worldwide and help bring about a sustainable end to the AIDS epidemic as a public health threat. We assessed the safety and immunogenicity of ConM SOSIP.v7, a native-like envelope glycoprotein (Env) trimer based on an HIV-1 group M consensus sequence, in HIV-negative adults.

**Methods**
24 individuals were enrolled in the phase 1 ACTHIVE-001 clinical trial to receive three dosages of adjuvanted ConM SOSIP.v7 (baseline, eight and 24 weeks) and followed-up for one year thereafter. Out of 23 per-protocol participants, 10 received a one-fifth fractional third dose, aimed to increase B cell somatic hypermutation. Immunogenicity outcomes included Env-specific total immunoglobulin G (IgG) and IgG subclasses, ConM-pseudovirus neutralisation and single cell RNA sequencing of the B cell repertoire. Plasma levels of sex-steroid hormones were measured over time.

**Results**
The majority of adverse events were mild to moderate, self-limiting and similar between dosage groups and sexes. No serious adverse events were reported. Adjuvanted ConM SOSIP.v7 was reliably capable of inducing a potent binding antibody response to the immunogen, as well as modest binding to a panel of heterologous Env proteins in the majority of participants. Furthermore, the vaccine elicited strong autologous neutralising antibody responses in nearly all participants (96%) after three vaccinations, which remained detectable in half of the participants six months after the final boost. Neutralisation of the related ConS virus, but not other heterologous viruses, was detected. No differences in serological outcomes could be attributed to the fractional dose. Female born participants had an earlier increase in neutralising antibodies than males and had a 6.3-fold higher neutralisation titer post third vaccination. Sex-based differences in IgG1 and IgG4 subtype responses were also observed, with higher IgG1 but lower IgG4 in females. Subtle correlations, both positive and negative, were seen between autologous neutralisation, IgG2 and IgG3 levels on one hand, and oestradiol and testosterone on the other hand, but the small sample size limited drawing strong conclusions. Single B cell sequencing should reveal whether the fractional dose and/or sex influence B cell affinity maturation.

**Conclusion**
The adjuvanted ConM SOSIP.v7 native-like trimer vaccine is safe and elicits a robust strain-specific neutralising response in nearly all recipients. Females responded more rapidly and had a striking 6.3-fold higher neutralisation titer after the final vaccination. This study highlights that sex-based differences should be taken into consideration when assessing HIV-1 vaccine candidates and adjuvants.

*0.08 (Figure 1) Pseudovirus serum neutralisation over time*

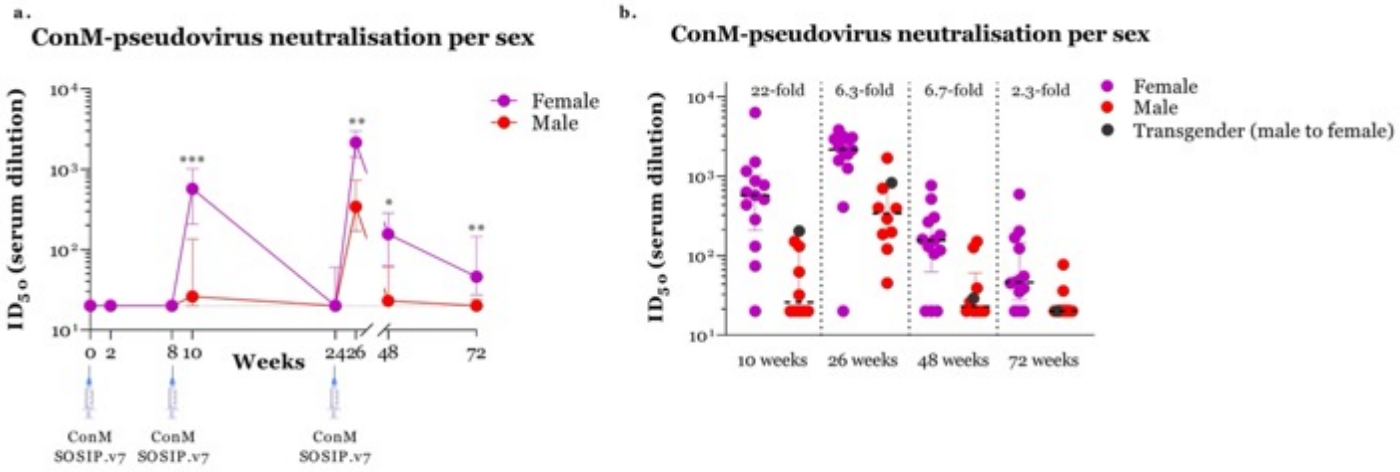


**Figure 1. Pseudovirus serum neutralisation over time. a.** ConM-pseudovirus serum neutralisation $ID_{50}$ values per sex at birth over time. Female n=13. Male n=10. **b.** ConM-pseudovirus serum neutralisation $ID_{50}$ values per sex at birth at 10, 26, 48 and 72 weeks. Respective fold changes are indicated. Transgender individual indicated in grey. Figures represent the per-protocol cohort (n=23). Differences between sexes were calculated by Mann-Whitney U-test. * $p < 0.05$,** $p < 0.01$, *** $p < 0.001$.

## 0.09

### BG505 SOSIP.GT1.1 GP140 VACCINE, ADJUVANTED IS WELL-TOLERATED, HAS ACCEPTABLE SAFETY PROFILE AND ELICITS A POTENT AUTOLOGOUS SERUM ANTIBODY RESPONSE IN HIV-UNINFECTED ADULTS IN GOOD GENERAL HEALTH

**Karlijn van der Straten**[1], Tom Caniels[1], Emma Reiss[1], Annelou van der Veen[1], Marinus Liesdek[1], Katrina Millard[2], Ronald van Leersum[1], Nicole Yates[3], Hongmei Gao[3], Kelly Greene[3], David Montefiori[3], Georgia Tomaras[3], Dagna Laufer[4], Vincent Philiponis[4], Michelle Klouwens[1], Marit van Gils[1], Rogier Sanders[1], David Diemert[5], Godelieve de Bree[1], Marina Caskey[2]

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**Background**
It is widely appreciated that an effective HIV-vaccine should induce broadly neutralizing antibodies (bNAbs) targeting the viral envelope glycoprotein. However, generating bNAb responses through vaccination is challenging, partly because they derive from rare naïve B cells with unusual properties and require multiple rounds of somatic hypermutation in germinal centers. Pre-clinical studies have shown the ability of the BG505 SOSIP.GT1.1 gp140 (GT1.1) vaccine to prime bNAb precursor B cells, including those targeting the CD4-binding site. Here, we report the first safety, tolerability and immunogenicity data from a first in-human clinical trial using GT1.1.

**Methods**
This phase 1, double-blinded, placebo-controlled, dose-escalating multicenter trial was conducted at two US sites and one in the Netherlands. Participants received intramuscular injections of either 30µg (low-dose) or 300µg (high-dose) of the GT1.1 vaccine with AS01B adjuvant, or saline placebo at zero, eight, and 24 weeks. Reactogenicities were reported during the 15 days post-vaccinations, Serious AEs for the entire study period. Serum antibody binding and neutralization responses were quantified using a BAMA and TZM-bl pseudovirus neutralization assay, respectively.

**Results**
We enrolled 47 HIV-uninfected adults (low-dose: n=20, high-dose: n=19, placebo: n=8), with an average age of 30 years and an equal sex distribution between groups. Ninety-four percent of participants reported at least one solicited Adverse Event (AE). Most AEs were graded mild (59.2%) or moderate (37.7%). There were no significant differences in number of solicited AEs between the vaccine administrations (Chi-Squared test, p=0.17), or dose groups (p=0.13). No vaccine-related Serious AEs were reported.
All vaccinated participants developed detectable GT1.1-binding serum antibodies at weeks 10 and 26, with the high-dose recipients showing a higher response rate after the first vaccination (10.5% low-dose vs. 31.5% high-dose) and significantly higher responses at week 10 (p=0.008) (Fig. 1A). GT1.1 neutralizing antibodies (NAb) were more prevalent in the high-dose compared to the low-dose recipients after the second (68% vs. 28%, respectively) and third vaccination (100% vs. 89%, respectively)(Fig. 1B), but titers among responders did not differ significantly between groups. Serum NAb activity was at least in part directed against the CD4-binding site.

**Conclusion**
The GT1.1 vaccine, adjuvanted with AS01B, has an acceptable safety profile, is well-tolerated and induced a strong vaccine-specific serum antibody response. Here, a higher GT1.1 dose induced a more rapid and robust serum antibody binding response without compromising safety. Thus, germline-targeting trimer GT1.1 may represent a promising vaccine candidate for priming bNAb responses in humans.

*0.09 (Table 1) Serum antibody responses against BG505 SOSIP.GT1.1 gp140 following GT1.1 vaccination*

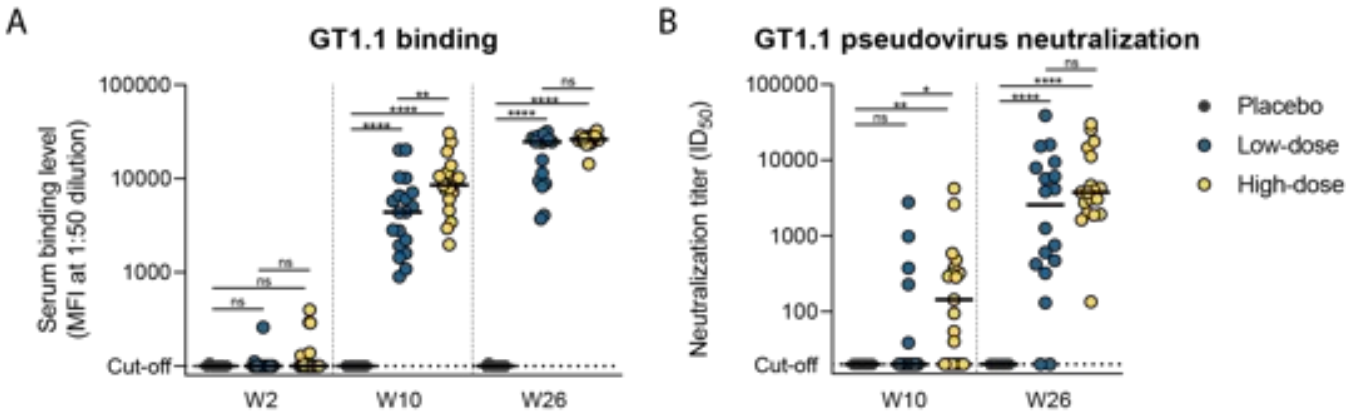


**Figure 1. Serum antibody responses against BG505 SOSIP.GT1.1 gp140 following GT1.1 vaccination.** **A)** Serum IgG binding antibody responses against BG505 SOSIP.GT1.1 gp140 using a BAMA-assay. Cut-off value (100 Median Fluorescent Intensity-MFI) marks the lower limit of detection. **B)** Serum neutralization responses against BG505 SOSIP.GT1.1 gp140 pseudovirus using a TZM-bl neutralization assay to quantify the 50% inhibitory dilution ($ID_{50}$). Cut-off value marks the lower limit of detection (<10 $ID_{50}$). Serum responses of the dose groups were compared using a Mann-Whitney U test. P>0.05: ns, p<0.05:* p<0.01:**, p<0.0001: ****

## O.10

### BG505 SOSIP.GT1.1 GP140 EXPANDS B CELLS WITH BROADLY NEUTRALIZING ANTIBODY SIGNATURES: PRELIMINARY RESULTS FROM A PHASE 1 HUMAN CLINICAL TRIAL

Madhu Prabhakaran[1], Rogier Sanders[2], Karlijn van der Straten[2], Weiwei Wu[1], Supra Gajjala[1], Jonne Snitselaar[2], Joey Bouhuijs[2], Tom Bijl[2], Isabel Baken[2], Vincent Philiphonis[3], Marit van Gils[2], David Diemert[4], Godelieve de Bree[2], Marina Caskey[5]

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**Background**
Eliciting a potent and broad neutralizing antibody (bNAb) response is a major goal in HIV-1 vaccine development. However, the generation of such a bNAb response has been challenging, in part due to the scarcity of bNAb-precursor B cells. We designed BG505 SOSIP.GT1.1 gp140 (GT1.1) to activate bNAb-precursor B cells, specifically those that target the conserved CD4 binding site epitope as well as the apex epitope on HIV-1 envelope (Env). In preclinical studies, GT1.1 was shown to activate CD4bs-specific B cells that share genetic features with bNAbs of the VRC01-class, which are among the broadest and most potent of bNAbs. Here, we report on the ability of GT1.1 to activate CD4bs-specific B cells in a first-in-human clinical trial.

**Methods**
Participants in this phase 1, double-blinded, placebo-controlled, dose-escalating multicenter trial received intramuscular injections of either 30 µg or 300 µg of the GT1.1 vaccine adjuvanted with AS01B, or a saline placebo at 0, 8 and 24 weeks. Epitope-specific B cells from week 10 from a subset of participants were analyzed by flow cytometry, single cell-sorted. B cell receptor sequences were determined by Sanger sequencing. Monoclonal antibodies (MAbs) were generated from BCR sequences and tested for their binding and neutralization capacities.

**Results**
47 adults were enrolled and randomly assigned to low dose (LD, n=20), high dose (HD, n=19) and placebo (n=8) groups. At week 10, we observed a >1000-fold increase in GT1.1-specific memory B cells versus pre-vaccination as detected by flow cytometry. All vaccine recipients had IgG memory B cells against CD4bs and apex epitopes. Preliminary sequence analysis revealed that 5/9 (56%) participants in the LD group and 6/9 (67%) participants in the HD group developed CD4bs-specific B cells that share the genetic signature of a well-defined class of CD4bs-targeting bNAbs (VRC01-class). These VRC01-class MAbs bind to the conserved CD4bs and occasionally neutralize circulating strains of HIV-1. Finally, cryo-electron microscopy revealed high similarity between MAbs from this study and VRC01-class bNAbs on a structural level.

**Conclusion**
GT1.1 induces a strong vaccine-specific memory B cell response. The majority of participants analyzed thus far demonstrated a VRC01-class bNAb signature as well as other bNAb signatures. Selected MAbs expressed from memory B cells derived from vaccine recipients bind in a CD4bs-specific fashion and highly similar to bNAb VRC01. This work suggests a possibility of bNAb induction through vaccination as a means to combat the global health threat of HIV/AIDS.

## O.11

### MEMBRANE-BOUND GERMLINE-TARGETING HIV-1 ENV IMMUNOGENS FOR MRNA VACCINATION

**Iván Del Moral-Sánchez**[1], Jahyun Koo[2], Yoann Aldon[1], Jonne Snitselaar[1], Thomas Ketas[3], Jelle van Schooten[1], Marit van Gils[1], Tom Caniels[1], Ronald Derking[1], Edward Lamperti[2], David Montefiori[4], John Moore[3], Francois Villinger[5], Sunny Himansu[6], Facundo Batista[2], Rogier Sanders[1]

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**Background**
An effective HIV-1 vaccine will likely require germline-targeting envelope glycoprotein (Env) immunogens that efficiently activate broadly neutralizing antibodies (bNAbs) B cell precursors. Germline-targeting proteins formulated with adjuvant have shown great promise in both preclinical and clinical studies. These include GT1.1, a BG505 SOSIP-derived germline-targeting Env trimer developed at Amsterdam UMC. The mRNA vaccine platform offers a number of advantages that should be exploited. Here, we designed novel GT1.1-based immunogens that, when delivered through mRNA, activated bNAb B cell precursors in knock-in mouse models and non-human primates.

**Methods**
We generated a panel of membrane-displayed BG505 GT1.1 constructs. The panel included single-chain (SC) constructs, with flexible linkers between gp120 and gp41 for furin independence, as well as Triple Tandem Trimer (TTT) constructs, which encode three genetically-fused SC protomers. Some constructs incorporated glycosylation motifs to mask the BG505-specific 241/289 glycan hole and/or avoid artificial glycan holes. We used both homologous (BG505) and heterologous transmembrane domains. We assessed the expression and antigenicity of the constructs by flow cytometry of transiently transfected 293T cells.
To test the immunogenicity, we vaccinated germline bNAb knock-in mice with mRNAs encoding a set of downselected constructs, as well as protein controls. We assessed germinal center formation and antigen-specific responses by flow cytometry. We also tested GT1.1 mRNA in non-human primates and evaluated the serum antibody responses.

**Results**
All GT1.1 designs were efficiently expressed on the membrane of transfected cells, with subtle differences. Most constructs presented favorable antigenic profiles, with high binding to bNAbs, including the quaternary-dependent PGT145 and PGT151. They efficiently bound to bNAb precursors targeting the CD4-binding site (CD4bs).
mRNAs encoding both soluble and membrane-bound GT1.1 immunogens induced antigen-specific responses in the low bar AG2 mouse model for VRC01-class bNAb precursors. However, only mRNAs encoding membrane-bound GT1.1 induced potent antigen-specific responses in high bar AG3 mice and in adoptive transfer experiments where the numbers of target B cells approach physiologically relevant frequencies. In non-human primates, GT1.1 mRNA induced a potent GT1.1-specific serum antibody response.

**Conclusion**
In summary, mRNA-delivered BG505 GT1.1 immunogens are promising candidates for the initiation of bNAb responses by vaccination. These results justify evaluating GT1.1 mRNA in humans.

## O.12

### ONE-YEAR EVALUATION: LOW ACCEPTANCE AND INCREASING COSTS FOLLOWING A HEALTH INSURER-MANDATED SPLIT FROM BRANDED SINGLE-TABLET REGIMEN TO GENERIC-BASED TWO-TABLET REGIMEN.

**Piter Oosterhof**[1,2], Matthijs van Luin[3,4], Kees Brinkman[1], David Burger[2]

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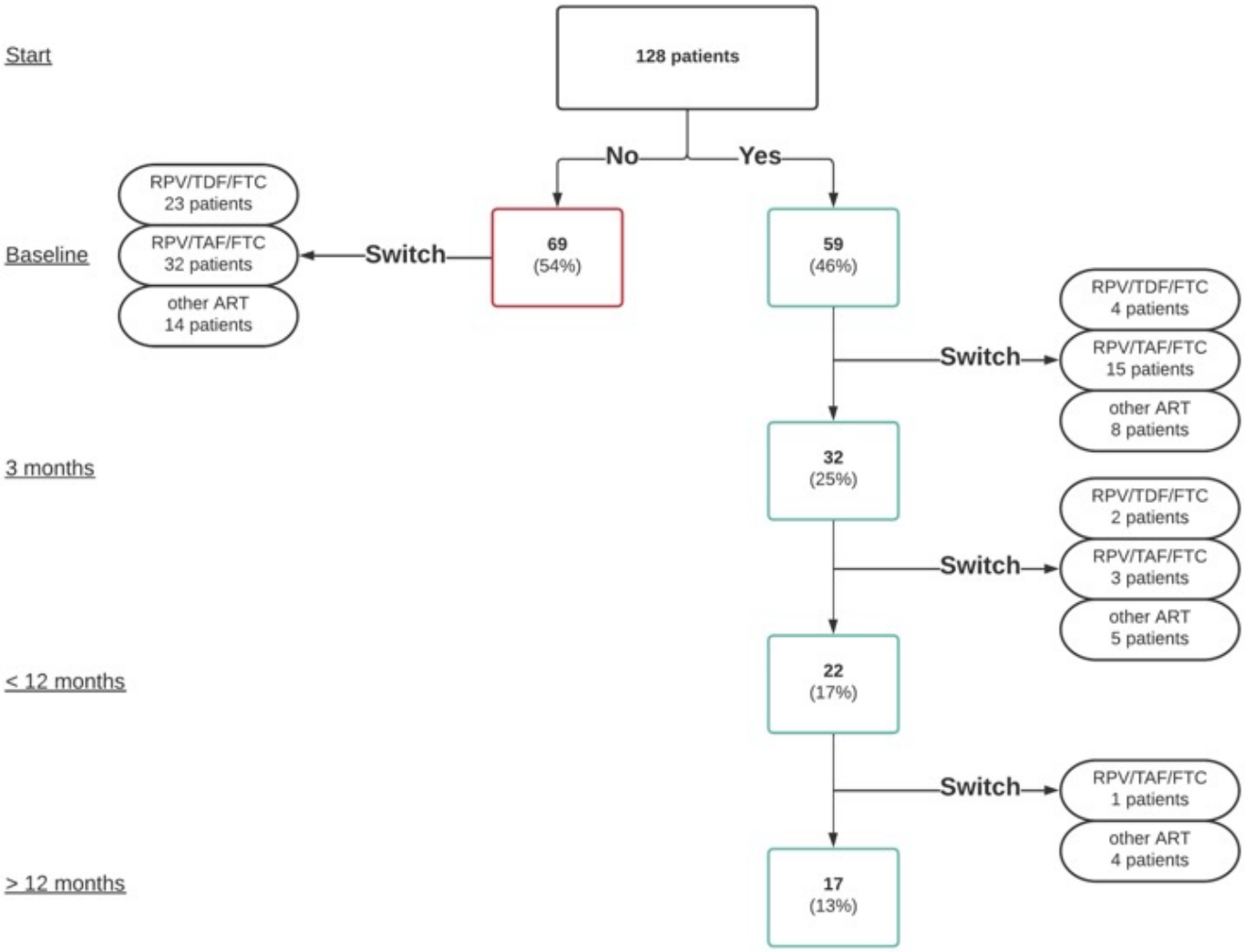
**Background**
Antiretroviral therapy (ART) accounts for a significant proportion of HIV care expenses. Previous studies have demonstrated that de-simplification of a single-tablet regimen (STR) to a generic-based two-tablet regimen (TTR) can result in substantial cost reduction. In June 2021, VGZ, a Dutch healthcare insurer, implemented a mandatory policy to split branded RPV/TDF/FTC (Eviplera®) into a TTR containing branded rilpivirine (Edurant®) plus generic TDF/FTC as part of cost-saving measures. The objectives of this study were (1) to assess patient and prescriber acceptance of this mandatory policy and (2) to evaluate the cost savings achieved by this mandatory switch.

**Methods**
This was a retrospective database study in which medication dispensation data were obtained from the Dutch Pharmaceutical Key Figures Foundation (SFK). This dataset covers all people with HIV who received ART from Dutch pharmacies, covering 98% of all medication dispensations in the Netherlands. We received pseudonymized data exclusively from individuals insured by VGZ for the years 2020, 2021, and 2022. Cost savings were calculated using the Dutch drug prices for each year.

**Results**
A total of 128 people with HIV insured by VGZ used branded RPV/TDF/FTC as an STR before June 1, 2021, in the Netherlands (figure 1). After June 1, 2021, 59 people (46%) received a split combination of RPV + generic TDF/FTC (further described as “split-compliant people”), while 69 people (54%) did not split. People not splitting either received a ‘medical necessity’ on the prescription to continue with branded RPV/TDF/FTC (Eviplera®; n=23), switched to RPV/TAF/FTC (Odefsey®; n=32), or changed their ART (n=14). Within one year, 42 patients (71% of the split-compliant group) either reverted to other ART or returned to branded Eviplera®, resulting in 17 subjects (13% of the original 128 patients) successfully maintaining the split regimen after 12 months. Most people eventually received treatment with Odefsey® (n=51) or remained/returned on Eviplera® (n=29). In May 2021, the cumulative medication costs for all 128 patients prescribed Eviplera® amounted to €72,988. By May 2022, the split-compliant group had incurred costs totaling €4,613, while the remaining 111 patients had expenses amounting to €71,035. Consequently, the total expenditure in May 2022 reached €75,649, representing an increase of €2,661 compared to the previous year.

**Conclusions**
A mandatory switch from an STR to a TTR in people with HIV proved unsuccessful, marked by low acceptance and increased costs after one year. This underscores the ineffectiveness of insurer-driven mandatory switches as cost-saving strategies.

*0.12 (Figure 1)*




ART: antiretroviral therapy, RPV: rilpivirine, TAF/FTC: tenofovir alafenamide / emtricitabine, TDF/FTC: tenofovir disoproxil / emtricitabine

## O.13

### MAJORITY OF INFECTED CELLS FROM PERIPHERAL BLOOD OF ART-TREATED INDIVIDUALS TRANSCRIBE HIV-1 CELL-ASSOCIATED GAG RNA

**Alexander Pasternak**[1], Kevin Groen[1], Maria Feuchert[1], Aurelija Cicilionytė[1], Yara Verschoor[1], Laura DeMaster[2], Marilia Pinzone[2], Stephen Migueles[3], Ben Berkhout[1], Una O'Doherty[2]

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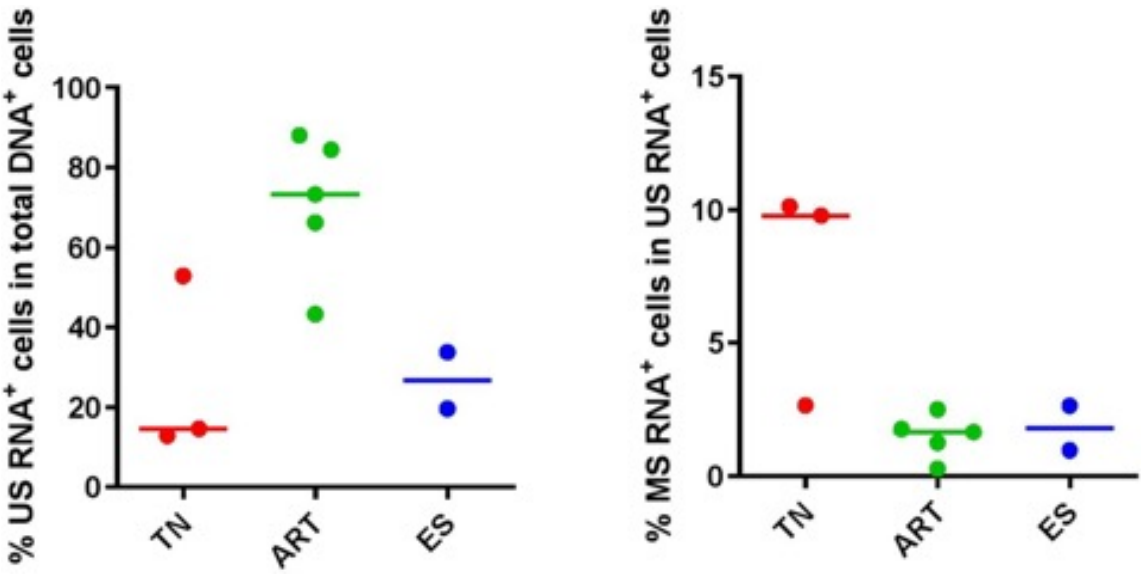
Although previous studies have detected HIV-1 RNA in ART-treated people with HIV (PWH), the prevailing dogma is that this "residual transcription" represents a rare exception rather than the rule and the reservoir is thought to be generally silent. For the most part, this stems from the absence of sufficiently accurate and sensitive assays to enumerate the reservoir cells that transcribe HIV-1 RNA. We developed AREA (Active Reservoir Evaluation Assay) – a novel sensitive and precise assay based on limiting dilution-multiplex seminested RT-qPCR that measures frequencies of cells transcribing HIV-1 cell-associated unspliced (US, gag) and multiply spliced (MS, tat/rev/nef) RNA, as well as US and MS RNA copy numbers per cell. We applied this assay to evaluate the active reservoir in peripheral blood of three therapy-naïve (TN), five ART-treated, and two elite suppressor (ES) PWH without ex vivo cellular stimulation. In total, 834 PBMC samples were processed. Both US RNA+ and MS RNA+ cells were detectable in all PWH, with the highest frequencies measured in TN, intermediate in ART-treated, and the lowest in ES (medians of 883–324–19 US RNA+ cells and 86–5–0.3 MS RNA+ cells per million PBMC, respectively). Surprisingly, in ART-treated PWH, majority (median, 73.3%) of HIV-1 DNA-positive cells transcribed US RNA. However, only a median of 1.7% of these US RNA+ cells transcribed MS RNA, due to post-transcriptional latency blocks and/or proviral genetic defects that prevented HIV-1 splicing. In contrast, in TN only 14.6% of HIV-1 DNA-positive cells transcribed US RNA, but of the latter, 9.8% transcribed MS RNA. No difference was observed between the groups in the US RNA copies per expressing cell, however MS RNA copies per expressing cell were higher in TN compared to ART-treated. For all participants, HIV-1 RNA copies per expressing cell were higher for US than for MS RNA. In summary, AREA revealed a large, previously underestimated, HIV-1 US RNA+ reservoir in ART-treated PWH, questioning transcriptional latency as the main mechanism of HIV-1 persistence on ART. However, the low percentages of MS RNA+ cells in all groups implies that with or without ART, most US RNA+ cells are still not productively infected. Our results argue for the shift of HIV-1 latency reversal strategies from stimulating HIV-1 transcription initiation and proximal elongation to the downstream steps such as distal elongation, splicing, or nuclear export of HIV-1 RNA. AREA can serve as a robust tool for the measurement of HIV-1 reservoir in the curative interventions.

*0.13 (Figure 1)*




Percentages of HIV-1 unspliced RNA+ cells among total infected cells and of multiply spliced RNA+ cells among unspliced RNA+ cells

## O.14

### IMPLEMENTING HIV TEAMS SUSTAINABLY IMPROVES HIV TESTING RATES IN PATIENTS WITH HIV INDICATOR CONDITIONS: A MULTICENTER STUDY

Carlijn Jordans[1], Jaap Hanssen[2], Kara Osbak[1], Marion Vriesde[1], Jan van Beek[1], Natasja van Holten[2], Willemien Dorama[2], Dorien van der Sluis[2], **Klaske Vliegenthart-Jongbloed**[1], Jan van Kampen[1], Annelies Verbon[3], Anna Roukens[2], Casper Rokx[1]

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[2] *Leiden University Medical Center, Leiden, Netherlands*
[3] *UMC Utrecht, Utrecht, Netherlands*

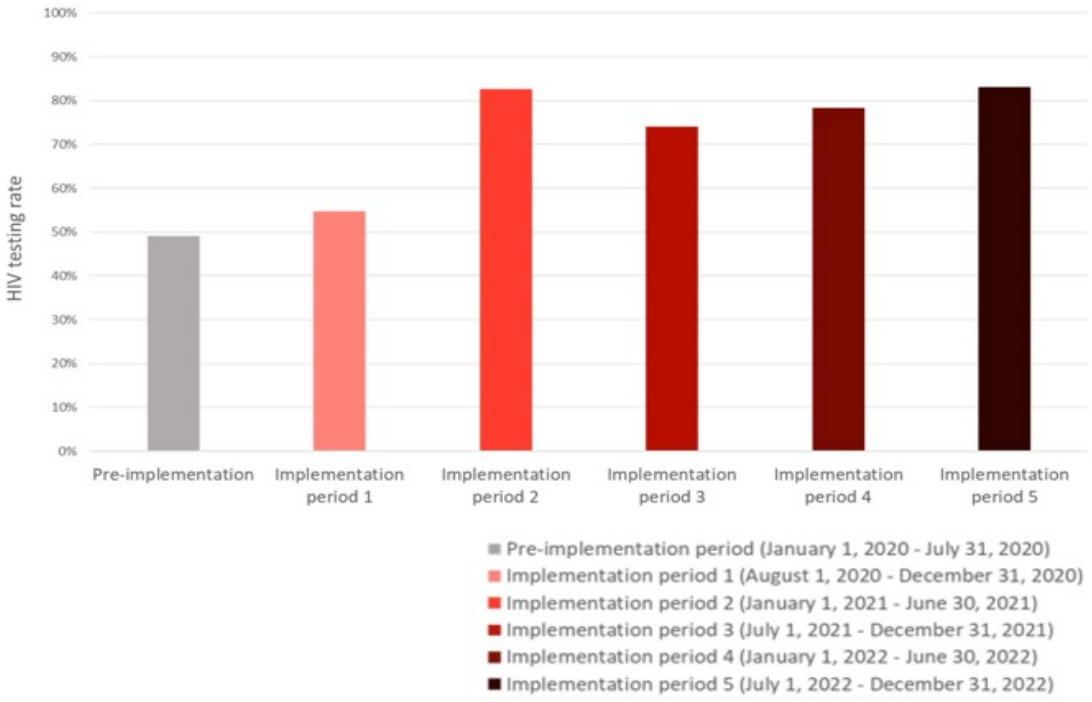
**Background**
Still over half of the newly diagnosed HIV cases in the Netherlands show late-stage disease and multiple missed HIV testing opportunities. HIV indicator condition-guided testing helps identifying individuals unaware of their HIV infection. This study evaluated the effect of HIV teams on hospital-based HIV indicator condition-guided testing and sought to confirm its durable effect across multiple hospitals.

**Methods**
This prospective implementation project was setup at Erasmus University Medical Center, Rotterdam. Data were collected registered diagnoses of patients ≥18 years. Potential HIV indicator conditions were flagged after automated ICD-10 and standardized health insurance codes screening. Flagged HIV indicator conditions were manually reviewed. The HIV team intervened in patients with confirmed HIV indicator conditions by proactive HIV testing recommendations to treating physicians, starting August 1st, 2020. For external validation, HIV teams were implemented at Leiden University Medical Center at October 1st, 2022. We evaluated HIV testing rates (number of tested HIV indicator conditions/total number of identified HIV indicator conditions) overall, over time and by medical specialty, HIV positivity rate and reasons to withhold testing. Lastly, we compared HIV testing rates between hospitals.

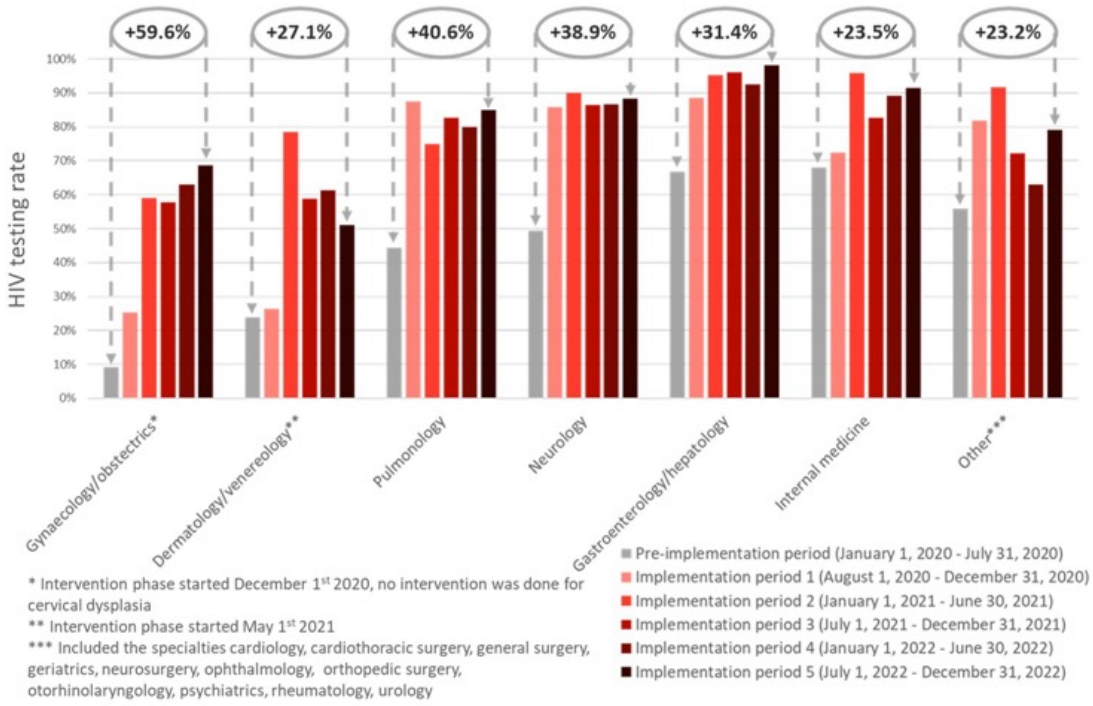
**Results**
Of 273,052 newly registered diagnoses at Erasmus University Medical Center, 23,311 (8.5%) were flagged as potential HIV indicator conditions. After manual review, 2,588 diagnoses were confirmed as HIV indicator conditions. Overall HIV testing rate was 69.7% (1,804/2,588), with an HIV testing rate of 49.1% pre-implementation (265/540) versus 75.1% (1,539/2,048) post-implementation (Figure 1). HIV testing rates showed a sustained increase at 2 years after implementation compared to pre-implementation across all medical specialties (range +23.2% to +59.6%) (Figure 2). Overall HIV positivity rate was 0.6% (10/1,804), including 9 diagnoses that tested positive after the implementation of HIV teams. Main reasons for not testing were that test execution is pending future appointments (n=51, 18.6%), unperformed HIV test despite uptake of testing advice in diagnostic plans (n=24, 8.7%), diagnostic plan for external HIV test (n=11, 4.2%) and treating physician rejects the possibility of HIV (n=11, 4.2%). No reason was identified in 49% of the cases. After implementation of the HIV teams in both hospitals, comparable HIV testing rates were found (68.1% [92/135] versus 75.1%).

**Conclusion**
Implementing HIV teams in hospitals showed a sustained increase in HIV indicator condition-guided testing and can be successfully expanded across hospitals. These results support the further roll-out of HIV teams to other hospitals and different settings.

*0.14 (Figure 1) Overall HIV testing rate at Erasmus MC over time*




*0.014 (Figure 1) Overall HIV testing rate at Erasmus MC over time*




* Intervention phase started December 1st 2020, no intervention was done for cervical dysplasia

** Intervention phase started May 1st 2021

*** Included the specialties cardiology, cardiothoracic surgery, general surgery, geriatrics, neurosurgery, ophthalmology, orthopedic surgery, otorhinolaryngology, psychiatrics, rheumatology, urology

# POSTER PRESENTATIONS

## P.01

### EFFECTS OF PRE-EXPOSURE PROPHYLAXIS PROGRAMS ON HIV AND GONORRHEA AMONG MSM IN THE NETHERLANDS: A MODELLING STUDY

Maarten Reitsema[1,2], **Maria Xiridou**[1], Jacco Wallinga[1,2], Ard van Sighem[3], Daniela Bezemer[3], Marc van der Valk[3,4], Fleur van Aar[1], Silke David[1], Janneke Heijne[5], Elske Hoornenborg[5], Ganna Rozhnova[6,7,8], Birgit van Benthem[1]

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[8] *Utrecht University, Utrecht, Netherlands*

**Background**
Pre-exposure prophylaxis (PrEP) is highly effective in reducing HIV acquisition. In 2019, a five-year PrEP pilot program started in the Netherlands, providing PrEP medication and care to men who have sex with men (MSM) and transgender persons at high risk of acquiring HIV. Since 2021, The pilot had a maximum capacity of 8,500 individuals. We investigated the impact on HIV transmission of this pilot program, and the prospects of its continuation, or expansion over the subsequent 10 years after 2024.

**Methods**
We developed a stochastic agent-based model that describes the transmission of HIV and N. gonorrhoeae (NG) via sexual partnerships among MSM. We evaluated the impact of the PrEP program on averted HIV and NG infections in the following scenarios: 1) Baseline scenario without PrEP: assuming PrEP was not introduced; 2) continued PrEP: starting in 2019 and continuing to 2034 with a maximum capacity of 8,500 individuals; 3) expanded PrEP: starting in 2019 and expanding to 12,000 individuals in 2024. We assumed a PrEP efficacy of 86%.

**Results**
From the model, we calculated that the PrEP pilot from 2019 to 2024 could lead to an average of 500 (95%CrI -200 – 1100) averted HIV infections and 1100 (95%CrI -3300 – 7400) averted NG infections, compared to the scenario without PrEP. A continuation of the PrEP pilot could lead to 3400 (95%CrI 1700 – 5000) and 30400 (95%CrI 13000 – 49500) averted HIV and NG infections respectively over the period 2019 to 2034, compared to the scenario without PrEP. With the expanded PrEP scenario 3900 (95%CrI 2000 – 5200) HIV infections and 29900 (95%CrI 15200 – 49400) NG infections could be averted by 2034, compared to the scenario without PrEP. When comparing the expanded PrEP scenario to the continued PrEP scenario, 300 (95%CrI -900 – 1300) HIV and 1300 (95%CrI -12700 – 10000) NG infections extra could be averted respectively by 2034.

**Conclusion**
The PrEP pilot of 2019-2024 could have resulted in a considerable reduction in the number of new HIV and NG infections. The reduction will be substantially higher if PrEP provision will be continued for another ten years. Expanding the PrEP provision in 2024 might result in a further decrease in the number of new infections by 2034, compared to the continued PrEP provision with the current capacity, however, a health-economic evaluation will be needed to further support the implementation of these scenarios.

P.02

## LOSS TO FOLLOW-UP IN THE DUTCH PREP PILOT PROGRAM

**Danja Sarink**[1], Daphne van Wees[1], Birgit van Benthem[1], Karlijn Kampman[2], Colette van Bokhoven[3], Fleur van Aar[1]

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

**Background**
HIV pre-exposure prophylaxis (PrEP) care has been offered through a Dutch national pilot program at Sexual Health Centers (SHC) since mid-2019. The program, intended for those at high risk for HIV as determined at program entry, is currently at capacity (8.500 places). Lowered risk for HIV is the most commonly cited reason among those who registered their participation stop with the SHC. However, three quarters of participants who leave the program are lost to follow-up (LTFU) and their reasons for exiting the program are unknown. To better understand if additional efforts should be made to retain those who are LTFU in PrEP care, it is key to gain insight into the reasons they exit the program. Therefore, we analyzed associations of demographic and behavioral factors with LTFU.

**Methods**
We used data from all three-monthly PrEP program consultations in men who have sex with men (MSM) aged ≥18 years who had at least two consultations (i.e. started PrEP use through the program) between July 2019 and December 2022. LTFU was defined as having no PrEP consultation for ≥7 months (i.e. two missed consultations). We used mutually adjusted, multivariable, multi-state, time-homogenous Markov models to analyze associations of demographics and sexual behavior with LTFU.

**Results**
A total of 68,423 consultations in 9,051 MSM were included; 2,046 participants (22%) were LTFU. At program entry, demographic and behavioral characteristics were similar between those who continue participation and those who were eventually LTFU. Not having (vs having) condomless anal sex and non-daily (vs daily) PrEP use at the current visit were predictors of LTFU the next visit, and those with ≥6 partners (vs 0-2) and age ≥25 years (vs <25) were less likely to be LTFU at the next visit (table 1).

**Conclusions**
Our results indicate MSM who are LTFU from PrEP care may engage in fewer behaviors associated with HIV risk than those who continue to participate. However, the increased risk of LTFU in younger MSM is not explained by concurrently analyzed behavioral factors. In addition, on-demand PrEP use may point towards fewer occasions of behavior associated with HIV risk when compared to daily use. Yet, those diagnosed with HIV in the PrEP program more frequently reported using on-demand than daily use, indicating that regular PrEP care remains important for some of those who use PrEP on-demand. Further work is needed to better understand LTFU in those who are younger or use on-demand PrEP.

*P.02 (Table 1) Mutually adjusted associations between demographic and behavioral characteristics and LTFU.*

**Table 1.** Mutually adjusted associations between demographic and behavioral characteristics and LTFU.

| | Hazard ratio | 95% confidence interval |
|---|---|---|
| **Age** | | |
| 18 - 24 years (ref.) | 1.00 | |
| 25 - 34 years | **0.68** | **0.53, 0.88** |
| 35 - 44 years | **0.45** | **0.34, 0.59** |
| = 45 years | **0.33** | **0.25, 0.43** |
| **Region of origin** | | |
| Dutch (ref.) | 1.00 | |
| Non-Dutch Western | 1.14 | 0.95, 1.38 |
| Non-Western | 1.15 | 0.97, 1.37 |
| **Education[1]** | | |
| High (ref.) | 1.00 | |
| Low/medium | 1.03 | 0.89, 1.21 |
| **Number of partners in the past 6 months** | | |
| <3 (ref.) | 1.00 | |
| 3-5 | 0.84 | 0.69, 1.02 |
| 6-9 | **0.76** | **0.59, 0.97** |
| =10 | **0.72** | **0.60, 0.87** |
| **Chemsex in the past 6 months[2]** | | |
| No (ref.) | 1.00 | |
| Yes | 1.11 | 0.93, 1.33 |
| **STI[3] diagnosis in PrEP consultation** | | |
| No (ref.) | 1.00 | |
| Yes | 0.96 | 0.70, 1.30 |
| **STI[3] diagnosis in past year** | | |
| No (ref.) | 1.00 | |
| Yes | 1.00 | 0.86, 1.17 |
| **Anal sex** | | |
| Yes, not always with condom (ref.) | 1.00 | |
| No or yes, always with condom | **1.21** | **1.00, 1.48** |
| **PrEP use in past 3 months** | | |
| Daily (ref.) | 1.00 | |
| On-demand | **1.58** | **1.32, 1.88** |
| Both | **1.48** | **1.02, 2.16** |
| No recent PrEP use | **2.15** | **1.79, 2.57** |

[1] Education levels (highest attained or currently studying): Low/medium: no education, elementary school, high school, mbo 1-4; high: university of applied sciences, university.
[2] Chemsex: use of crystal meth, mephedrone, or GHB/GBL before or during sex.
[3] STI: anorectal gonorrhea, anorectal chlamydia, or infectious syphilis.

## P.03

### LONGITUDINAL TRAJECTORIES OF SEXUAL BEHAVIOR AND INCIDENT HCV RE-INFECTION AMONG MEN WHO HAVE SEX WITH MEN WITH HIV IN THE NETHERLANDS: FINDINGS FROM AN OBSERVATIONAL COHORT STUDY

**Kris Hage**[1,2], Kalongo Hamusonde[3,4], Anders Boyd[1,5], Daniela van Santen[1], Astrid Newsum[1], Marc van der Valk[2,5], Kees Brinkman[6], Joop Arends[7], Fanny Lauw[8], Bart Rijnders[9], Arne van Eeden[10], Luisa Salazar-Viscaya[3], Janke Schinkel[11], Maria Prins[1,2]

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[2] *Amsterdam UMC, Infectious Diseases, Amsterdam, Netherlands*
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[7] *Maastricht University, Department of Health, Medicine and Life Sciences, Maastricht, Netherlands*
[8] *MC Jan van Goyen, Department of Internal Medicine, Amsterdam, Netherlands*
[9] *Erasmus MC, Department of Internal Medicine and Infectious Diseases, Rotterdam, Netherlands*
[10] *DC Klinieken Oud Zuid, Department of Internal Medicine, Amsterdam, Netherlands*
[11] *Amsterdam UMC, Department of Medical Microbiology and Infection Prevention, Amsterdam, Netherlands*

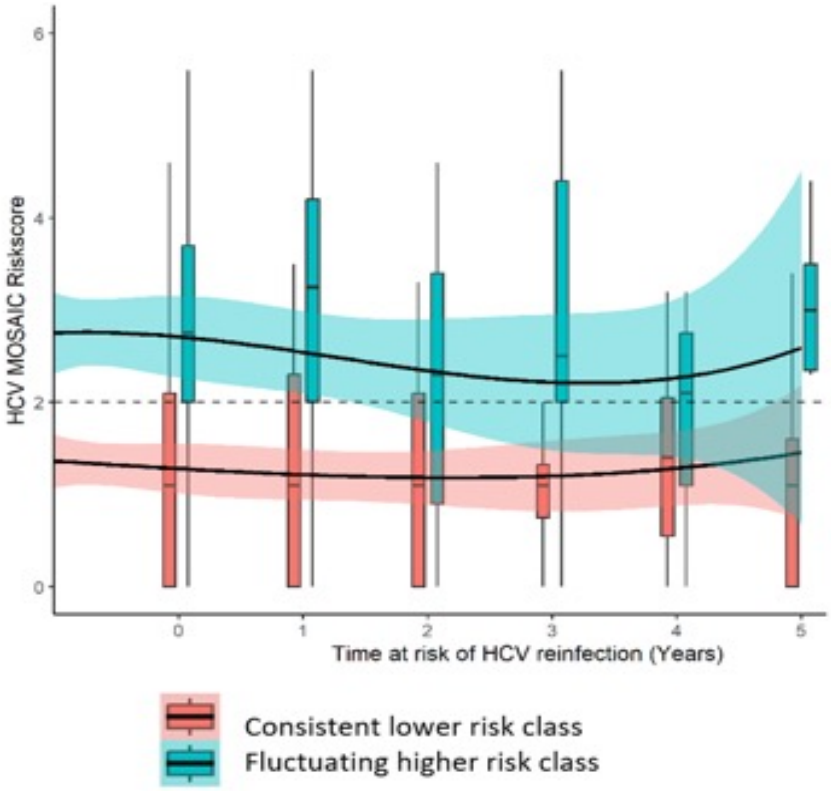
**Background**
Men who have sex with men (MSM) remain a key population for hepatitis C virus (HCV) re-infection owing to sexual practices associated with HCV transmission. Little is known on how these behaviors evolve over time and whether they are more closely associated with HCV re-infection. We aimed to identify subgroups of MSM with HIV with different patterns of HCV-related sexual behavior over time and assess re-infection risk within subgroups.

**Methods**
We included MSM at risk for HCV re-infection following successful HCV treatment or spontaneous clearance using data from the Dutch observational MOSAIC study (2009-2018). HCV risk behavior was assessed using the validated HCV-MOSAIC score (range=0.0–7.0), with a score ≥2 indicating high risk of re-infection. Classes were inferred from the mean HCV-MOSAIC score over time using a latent process mixed-effects model with the covariates age, group sex and casual partnership. The association between classes and HCV re-infection risk was assessed using a joint survival model.

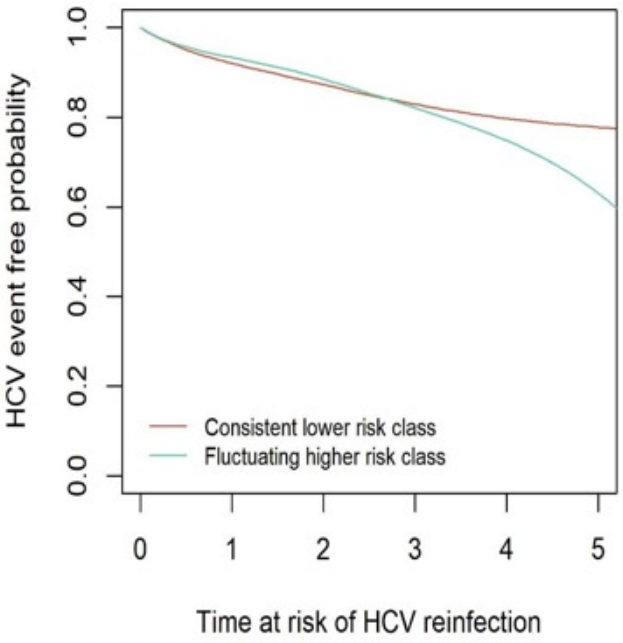
**Results**
Among the 123 MSM included, median age was 45 years (IQR=41-50). Median follow-up was 2.7 years (IQR=1.2-4.7). We identified two classes: one with consistent lower risk throughout follow-up (C1, n=67), and one with fluctuating higher risk during follow-up (C2, n=56). During follow-up, the median HCV-MOCAIC scores were higher in C2 than C1 (3.0, IQR=2.0-3.5 and 1.1, IQR=0.0-2.1, respectively) (Figure 1). The probability of HCV re-infection was similar at year 3 (C2: 18%, 95%CI=15-47% and C1: 17%, 95%CI=11-35%), but became higher in C2 than C1 at year 5 (37%, 95%CI=28-69% and 22%, 95%CI=13-39%, respectively) (Figure 2).

**Conclusions**
In this study population, there were two longitudinal patterns of high and low risk while the rates of HCV re-infection only increased in the high-risk group at later time points. The substantial variation in risk over time implies that behavioral assessment is continually needed during care to ensure timely testing.

*P.03 (Figure 1) HCV-MOSAIC risk score over time (in years since at risk for HCV re-infection) per class with 95% confidence intervals.*




*P.03 (Figure 2) Event-free probability for HCV re-infection over time (in years) per class.*



## P.04

### ASSESSING THE RISK-BASED APPROACH TO INTRA-MUSCULAR NEEDLESTICK INJURIES: IS BLOOD BY THE INJECTION SITE ASSOCIATED WITH BLOOD ON THE NEEDLE?

**Daniel Franken**[1,2], Vita Jongen[1,3], Olivier Abdelhamid[1], Maria Prins[1,2], Brigitte van Cleef[1]

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[3] *Stichting hiv monitoring, Amsterdam, Netherlands*

In the Netherlands, 15,000 needlestick injury's (NSIs) occur every year. According to the Dutch national guidelines, intra-muscular (i.m.) NSIs are categorized as high or low-risk, based on the observation of blood on the needle or at the injection site, as a proxy for blood on the needle. If blood is observed, NSIs are classified as high-risk and preventive measures against hepatitis B, hepatitis C, and HIV are needed. However, classifying blood at the injection site as high-risk may overestimate the number of high-risk events, resulting in possible overtreatment. Therefore, we aimed to determine how often blood was observed on the needle or injection site after i.m. injections, as well as the diagnostic accuracy of blood at the injection site.
I.m. injections were observed at the Public Health Service of Amsterdam, between February 2021 and January 2023. Patient and injection data, as well as the presence of blood on the needle and injection site, were registered. The sensitivity, specificity, positive and negative predictive values for the presence of blood at the injection site as a predictor for blood on the needle were calculated. The diagnostic gain of blood at the injection site as a predictor for blood on the needle was visualized using Fagan's nomogram.

Blood on the needle was observed after 25/616 (4.1%) injections; blood at the injection site was observed after 439/616 (71.3%) injections. Observing blood at the injection site ≤20 seconds after withdrawal of the needle, as well as the presence of a blood drop flowing from the injection site were both associated with the presence of blood on the needle (P-values<0.01). With increasing observation duration for blood at the injection site as indicator for blood on the needle, sensitivity increased from 52% at 2 seconds to 72% at 20 seconds. However, specificity decreased from 86% to 57%, respectively (Figure1). The probability of blood on the needle was 4.6% when blood was observed at the injection site, compared to 2.8% in the absence of blood at the injection site (Figure2).
Blood on the needle was seen in 4% of i.m. injections. The specificity for blood at the injection site as proxy for blood at the needle decreased with increasing observation time, resulting in possible over-classification of high-risk events. Therefore, the presence of blood at the injection site as an indicator for blood on the needle when distinguishing between high and low-risk i.m. NSIs may need to be re-evaluated.

*P.04 (Figure 1)*

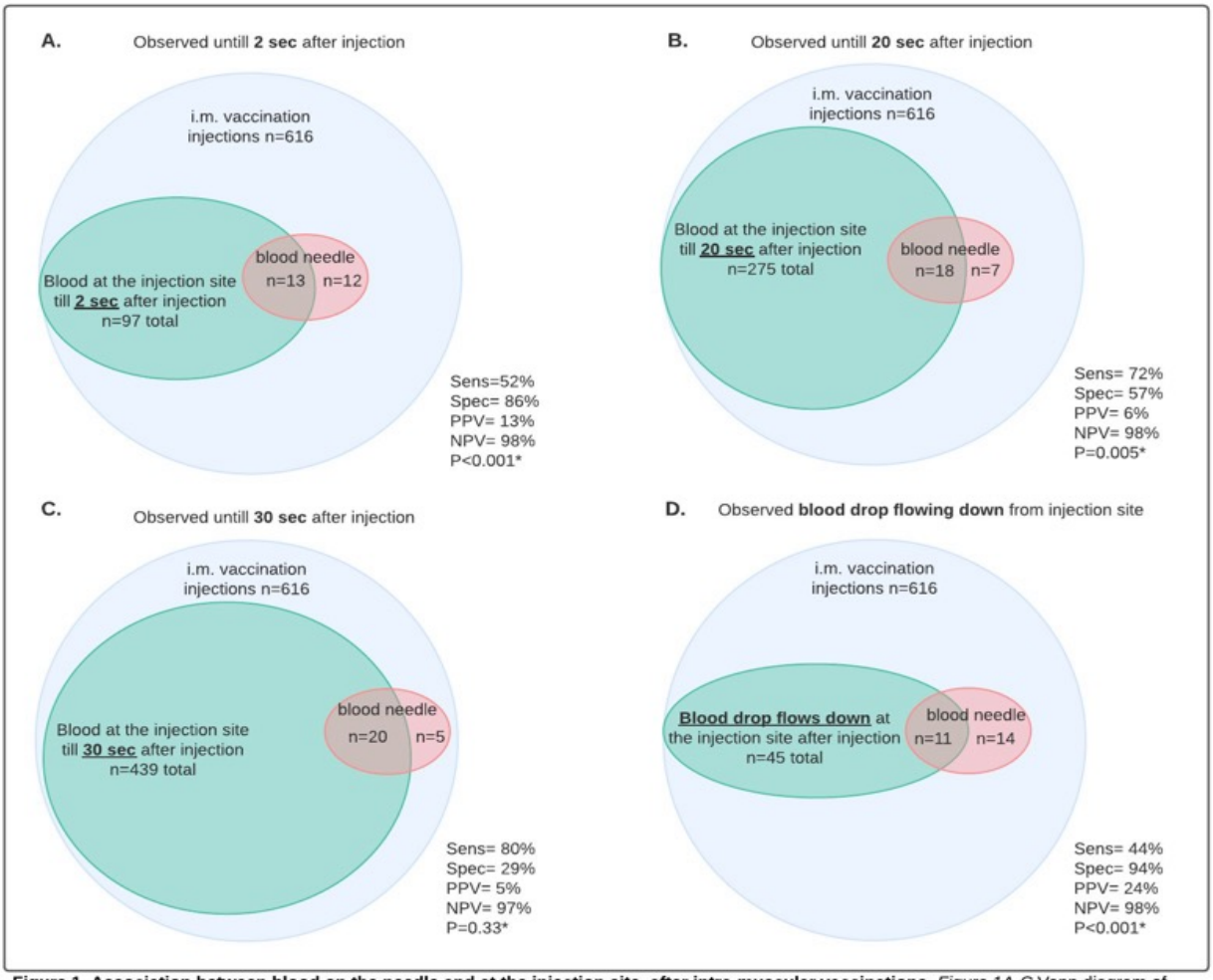


**Figure 1. Association between blood on the needle and at the injection site, after intra-muscular vaccinations**. *Figure 1A-C* Venn diagram of vaccinations demonstrating the relation between blood on the needle and blood at the injection site, after 2, 20 and 30 sec of observation after injection, respectively. *Figure 1D* Venn diagram demonstrating the relation between blood on the needle and a blood drop flowing down from the injection site. Abbreviations: I.M.= intra-muscular, Sens= sensitivity, Spec= specificity, PPV= positive predictive value, NPV= negative predictive value, sec= seconds. *P-values are based on the Pearson two-sided chi-square test or Fisher exact test for categorical variables.

*P.04 (Figure 2)*

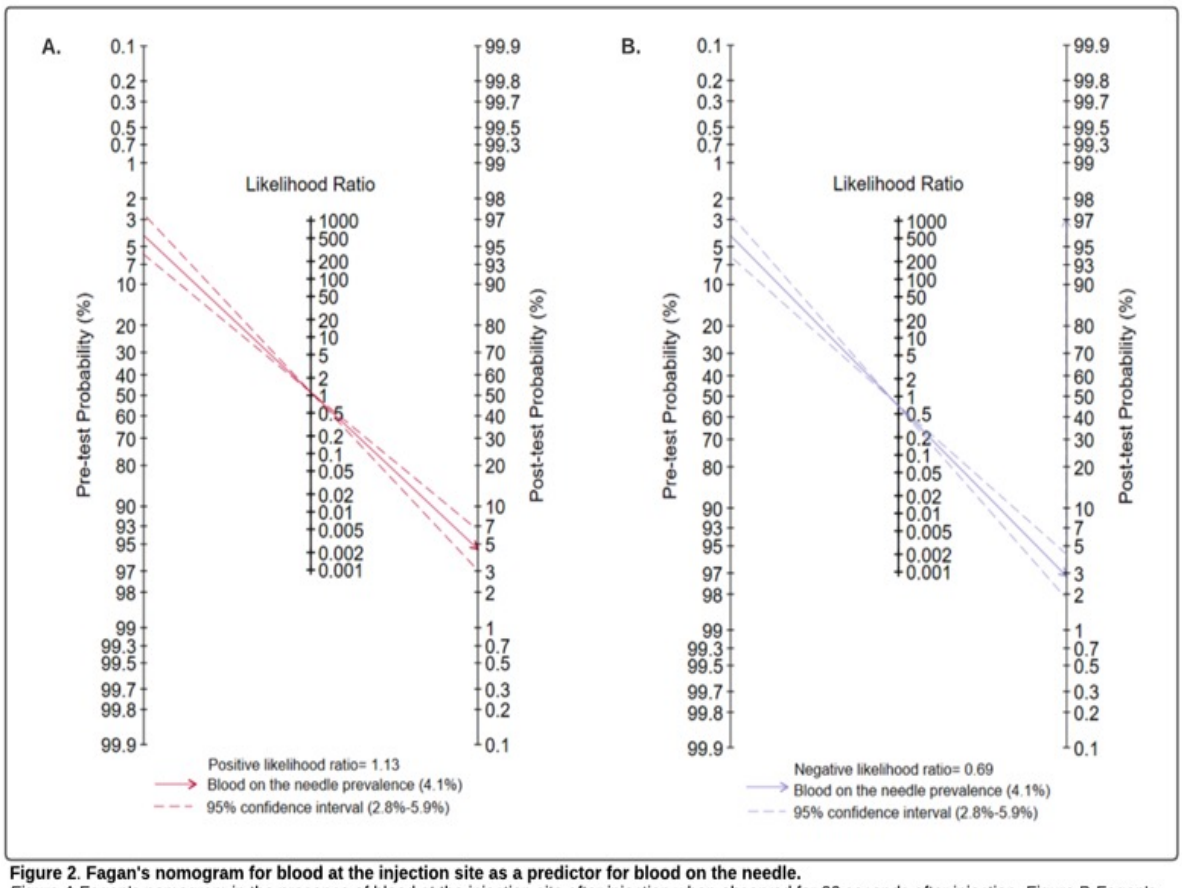


**Figure 2. Fagan's nomogram for blood at the injection site as a predictor for blood on the needle.**
*Figure A* Fagan's nomogram in the presence of blood at the injection site after injection when observed for 30 seconds after injection. Figure B Fagan's nomogram in the absence of blood at the injection site after injection when observed for 30 seconds after injection.

## P.05

### SELF-SAMPLING AND SELF-TESTING FOR HIV AT A COMMERCIAL AND COMMUNITY-BASED TEST PROVIDER IN THE NETHERLANDS: USABILITY AND USER PREFERENCES

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**Background**
At-home HIV testing (self-sampling and self-testing) reduces testing barriers and potentially reaches populations who may not test otherwise. In the Netherlands, at-home HIV tests became commercially available in 2019, but data on user experiences are limited. Aim of this study was to explore characteristics of end users and their experiences with HIV self-sampling (HIVSS) or -testing (HIVST).

**Methods**
From April 2022 to June 2023 a survey link was distributed among end users who ordered a commercial HIVSS/HIVST online or a free-of-charge HIVST via a community-based provider (AHF checkpoint Amsterdam), in the Netherlands. Questions included usability, preferences, and barriers of testing. In descriptive analyses, we compared characteristics of end users and their experiences with HIVSS or HIVST from a commercial and community-based test provider.

**Results**
Of 133 end users completing the questionnaire, 89 participated via the online commercial provider (88 HIVSS with lab results and 1 HIVST with self-read result) and 44 via the community-based provider (HIVST). Survey participants recruited through the commercial provider were more often men having sex with men (MSM), 35 years and older, born in the Netherlands and living outside the city compared to survey participants at the community-based provider.
MSM were more often repeat HIVSS/HIVST users compared to women and heterosexual men.
None of the participants reported a reactive test, but 36% were worried about having HIV. The majority of participants had tested for HIV before (67%) of whom 44% had tested in the past 6 months. Free-of-charge testing (96%) and immediate test results (66%) were the most often reported reasons to take a HIVST via the community-based provider. Not having to talk to a GP about HIV tests (38%), saving time (36%) and waiting lists at the Sexual Health Center (30%) were the most often reported reasons to take a HIVSS/HIVST via the commercial provider. For both providers anonymity was also often reported as reason for choosing HIVSS/HIVST (36%).
23 (26%) study participants at the commercial provider reported some problems with the test performance, compared to 5 (12%) at the community-based provider, mostly finger prick and obtaining enough blood aspects: 16 (70%) and 4 (80%) at respectively commercial and community-based provider.

**Conclusion**
End users experience HIVSS/HIVST as private, anonymous and timesaving. Yet difficulties with performing the finger prick were reported and recommendations to improve services were made. More research into the role of HIVSS/HIVST for accessibility of HIV testing in the Netherlands is needed.

## P.06

### SUSTAINED HIV-SPECIFIC T-CELL RESPONSES ARE PREDICTIVE OF INTACT VIRAL RESERVOIR DECLINE IN INDIVIDUALS TREATED DURING ACUTE HIV INFECTION

**Pien van Paassen**[1], Alexander Pasternak[2], Ninee Buchholtz[3], Karel van Dort[1], Michelle Klouwens[4], Annelou van der Veen[4], Liffert Vogt[5], Jori Symons[3], Monique Nijhuis[3], Jan Prins[4], Neeltje Kootstra[1], Godelieve de Bree[4]

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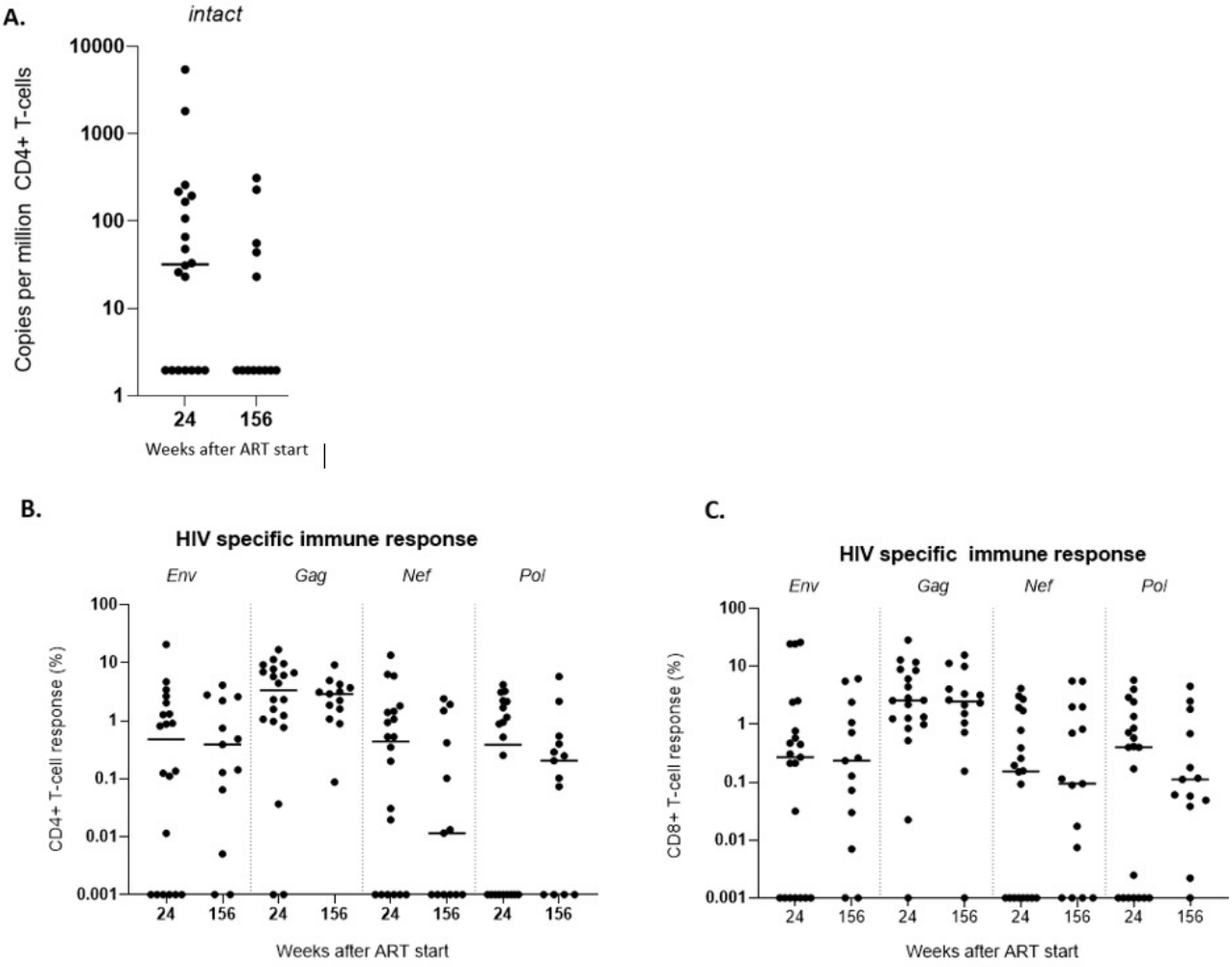
**Background**
Starting antiretroviral treatment (ART) during acute HIV infection (AHI) is known to limit damage to the immune system and lower the size of the viral reservoir. In light of cure interventions, understanding the longitudinal dynamics of the early host immune responses in relation to viral reservoir size is important. Therefore, we investigated the viral reservoir size and HIV specific immune responses in participants of the Netherlands Cohort Study on Acute HIV Infection (NOVA study), who initiated antiretroviral therapy (ART) immediately after diagnosis of acute HIV infection (AHI).

**Methods**
Participants of the NOVA study (n=22) diagnosed during Fiebig II-VI were included in the analysis. PBMC at 24 weeks and 156 weeks after start ART were analyzed. Viral reservoir size was assessed by Intact Proviral DNA Assay (IPDA). HIV specific T-cell responses upon HIV peptide pool stimulation (Env, Gag, Nef, Pol) were determined by flowcytometry. Correlations were determined using Pearson's correlations ($p<0,05$).

**Results**
Overall, a decline was observed of intact proviral DNA between 24 weeks and 156 weeks after ART start (Fig.1A). We observed broad HIV-specific CD4+ and CD8+ T-cell responses in the majority of individuals at both time points (Fig.1 B+C). At 24 weeks, intact proviral DNA load was associated to CD4+ T-cell responses to Env ($p<0,001$, $R2=0,96$), Gag ($p=0,005$, $R2=0,6$), Nef ($p<0,001$, $R2=0,9$) and Pol ($p=0,002$, $R2=0,6$). At 156 weeks, intact proviral DNA load was correlated to CD8+ T-cell response to Gag ($p=0,034$, $R2=0,59$) and Pol ($p<0,001$, $R2=0,77$). The observed decay in intact proviruses at 156 weeks between the two time points was positively correlated to CD4+ T-cell responses to Env ($p=0,034$, $R2=0,64$) and Nef ($p=0,007$, $R2=0,76$).

**Conclusion**
Our data show a positive correlation between HIV-specific T-cell responses and the decay in intact proviral DNA load in individuals treated during AHI. This implies that early ART in acute infection, in addition to a decline in intact proviral DNA load, also leads to potent HIV-specific T-cell responses. This may provide a promising avenue for cure interventions aiming at reservoir induction in combination with T-cell activating strategies.

*P.06 (Figure 1)*


A.
intact
Copies per million CD4+ T-cells
10000
1000
100
10
1
24
156
Weeks after ART start
B.
HIV specific immune response
Env
Gag
Nef
Pol
CD4+ T-cell response (%)
100
10
1
0.1
0.01
0.001
24
156
Weeks after ART start
C.
HIV specific immune response
Env
Gag
Nef
Pol
CD8+ T-cell response (%)
100
10
1
0.1
0.01
0.001
24
156
Weeks after ART start

P.07

## THE EXPECTED IMPACT OF AN HIV CURE ON SEXUAL AND PREVENTIVE BEHAVIORS OF MEN WHO HAVE SEX WITH MEN IN THE NETHERLANDS

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**Background**
The advancements in biomedical interventions such as antiretroviral therapy (ART) and pre-exposure prophylaxis (PrEP) have made HIV manageable. A potential future HIV cure may further reduce fear related to HIV and increase sexual freedom, leading to changes in sexual and preventive behaviors. This quantitative study explored the expected impact of two hypothetical HIV cure scenarios on sexual and preventive behaviors of men who have sex with men (MSM) in the Netherlands.

**Methods**
A cross-sectional survey was conducted among MSM with and without HIV in the Netherlands from October 2021 till June 2022. The survey assessed the number of casual partners, condom use with casual partners, PrEP use, and intention of PrEP use for participants' current situation (section I) and for two hypothetical HIV cure scenarios: HIV post-treatment control (PTC) (section II), where HIV is suppressed without the need for ongoing ART, but the viral reservoir is expected to persist, and HIV elimination (section III), where HIV is completely eliminated from the body. Expected changes in sexual and preventive behaviors after both PTC and elimination were analyzed using the McNemar test, dependent t-test for paired samples, and the generalized estimating equations.

**Results**
Of 893 participants starting the survey, 586 MSM completed questions about the current situation (section I) and PTC (section II), and 526 MSM completed all three survey sections. Included in the analyses were the 586 MSM (n = 182 with HIV; n = 404 without HIV) who completed at least sections I and II. MSM with HIV expected an increase in the number of casual partners after both PTC and elimination. MSM without HIV expected an increase in the number of casual partners and PrEP use, as well as a decrease in condom use with casual partners and intention of PrEP use after both PTC and elimination.

**Conclusions**
MSM with and without HIV expect that an HIV cure may have an impact on their sexual and preventive behaviors. This impact is expected not only for complete HIV elimination but also for HIV PTC, the development of which on a global scale seems much more likely. These findings provide insights for future public health policies on HIV prevention and control in the context of an HIV cure.

## P.08

### ENHANCING HIV CURE RESEARCH THROUGH SOCIAL ENGAGEMENT: PERSPECTIVES FROM PEOPLE WITH HIV AND KEY POPULATIONS IN THE NETHERLANDS

**Maaike Noorman**[1], John de Wit[1], Tamika Marcos[2], Sarah Stutterheim[2], Kai Jonas[2], Chantal den Daas[3]

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[2] *Maastricht University, Maastricht, Netherlands*
[3] *University of Aberdeen, Aberdeen, United Kingdom*

**Background**
Judith Auerbach's plenary session at NCHIV 2023 emphasizes the pivotal role of community engagement and the integration of social sciences in HIV research. This recognition aligns with the Dutch NL4cure initiative. Funded by Aidsfonds, the present social science study aims to contribute to a better understanding of the social engagement of people with HIV (PHIV) and key populations (KP) in the Netherlands in advancing (basic) HIV cure research. We do this by assessing the awareness, perceived importance, and ascribed meaning of HIV cure (research) of these diverse communities.

**Methods**
Between April 2021 and January 2023, we conducted, in the Netherlands, semi-structured interviews with 30 PHIV, 16 partners of PHIV, and 19 MSM not in a relationship with a partner with HIV. Participants were recruited through the Dutch Association of People with HIV, HIV specialist nurses, and snowball sampling. Thematic analysis was undertaken.

**Results**
Almost all participants had some engagement with HIV cure research. Most PHIV and KP indicated an awareness of significant HIV cure developments and acknowledged their importance. However, engagement was mostly passive. Most PHIV felt that they did not personally need an HIV cure as they reported a high quality of life. Similarly, most KP did not consider a cure important for themselves due to their low perceived susceptibility to HIV, which was derived from their experiences with condoms, PrEP, and U=U. KP defined HIV cure broadly, seeing sustained HIV suppression as a type of cure. Given their overall high quality of life, PHIV had high expectations for an HIV cure, and considered viral eradication to be the only true cure. Sustained viral suppression without medication was not considered a cure, but rather improved treatment, and was met with concerns. These concerns reflected limited awareness of HIV cure strategies and techniques, which also affected PHIV's attitudes toward participating in HIV cure-related clinical trials.

**Conclusion**
Addressing the limited awareness PHIV and KP had of HIV cure strategies and techniques is imperative, as this contributes to uncertainty and concerns. Effective communication about specific and realistic cure strategies is needed. Presently, the development of sustained HIV suppression appears more plausible than complete viral eradication. However, it is important to recognize that PHIV may not view this as a true cure. To ensure an acceptable HIV cure strategy, proactive communication, addressing misconceptions, and engagement of PHIV and KP in all phases of HIV cure research remains paramount.

## P.09

### TRANSCRIPTOMIC PROFILING OF THE HIV RESERVOIR REVEALS A ROLE FOR MITOCHONDRIAL FUNCTIONALITY IN VIRAL LATENCY

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[2] *Amsterdam Institute for Infection and Immunity, Amsterdam, Netherlands*

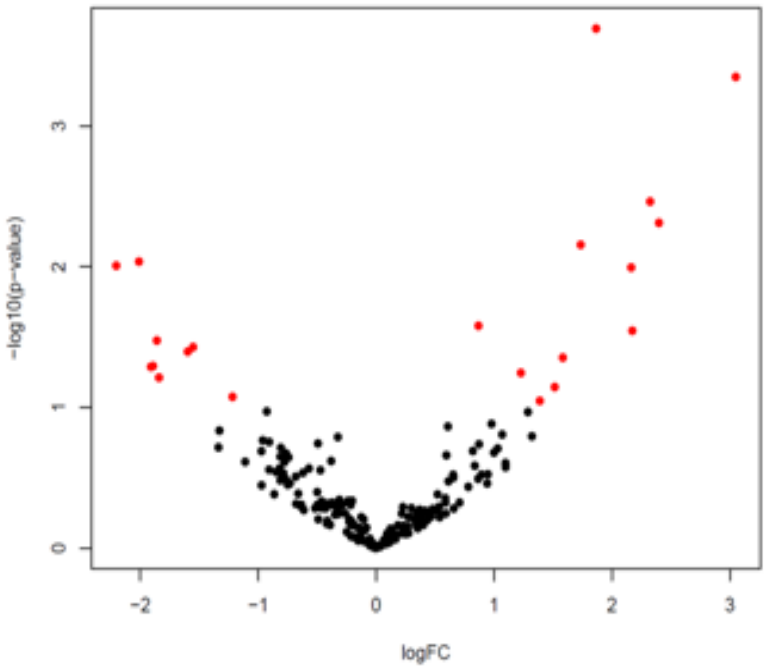
**Background**
Improved characterization of the HIV reservoir is crucial for devising effective cure strategies. Here we developed a strategy for isolating and characterizing the viral reservoir in peripheral blood from people with HIV (PWH). Based on our hypothesis that short abortive HIV transcripts are present in latently infected cells, we used our prior developed flow cytometry-fluorescent in situ hybridization (flow-FISH) method to directly sort HIV-infected cells, without ex vivo reactivation, for transcriptomic analysis of the viral reservoir.

**Methods**
Peripheral blood mononuclear cells (PBMCs) from 5 ART-naïve PWH from the Amsterdam Cohort Studies were used for this study. Flow-FISH was performed with probes targeting either abortive (TAR+Gag-) or elongated HIV transcripts (TAR+Gag+), representing latently and productively infected cells, respectively. Flow cytometry sorting was used to isolate three distinct cell populations (i.e. TAR+Gag-, TAR+Gag+, and probe-negative) from CD4 T cells. The transcriptomic profile was determined by 3' RNA sequencing (RNAseq). The role of mitochondrial functions on HIV transcriptional activity was assessed with antioxidant compounds in HIV-infected cells.

**Results**
Without the need for reactivation, our flow-FISH method distinguished between HIV-infected CD4 T cells harboring transcriptionally latent or active HIV. Supervised RNAseq analysis allowed for the identification of transcriptomic signatures that separate the isolated populations independently of individual-related characteristics. Notably, we identified several differentially expressed mitochondrial genes in latently infected (TAR+Gag-) compared to productively infected (TAR+Gag+) CD4 T cells. Interestingly, enhancing mitochondrial function increased HIV transcriptional activity in latently infected CD4 T cells from PWH.

**Conclusion**
Our transcriptomic profiling data shows an association between diminished mitochondrial functioning and the transcriptional activity of the viral reservoir. These findings underline the relevance of altered cellular metabolism in HIV infection, and support the development of therapeutics that take this into consideration.

*P.09 (Figure 1)*




Supervised differential gene expression analysis of transcriptionally latent and active HIV-infected CD4 T cells.

## P.10

### DEVELOPMENT AND CHARACTERIZATION OF BIVALENT AND TETRAVALENT BISPECIFIC ANTIBODIES TARGETING CD16 AND HIV-1 ENV

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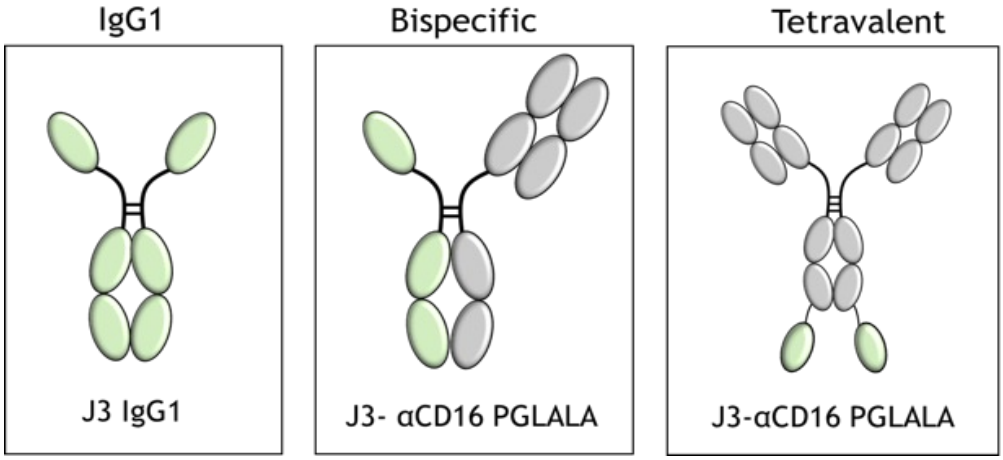
**Background**
HIV-1 remains a global health problem with no cure currently available. The “shock and kill” strategy has emerged as a promising approach to reduce the viral reservoir, through viral reactivation and subsequent elimination of HIV-1 infected cells. We engineered bispecific antibodies targeting CD16 (FcγRIIIa) and HIV-1 Env, that represent a potential strategy for achieving the elimination of HIV-1-infected cells via antibody-dependent cellular cytotoxicity (ADCC).

**Methods**
In this study, we designed and produced bivalent and tetravalent bispecific antibodies specific for the CD4 binding site (CD4bs) of HIV-1 Env and CD16. CD16 is expressed on NK cells and facilitates ADCC upon interaction with oligomerized antibodies. The bispecific IgG1 antibodies contain the PGLALA mutations to prevent killing of CD16 expressing cells by the bispecific constructs. Parental antibodies (anti-CD16 / anti-CD4bs) were produced in HEK 293F cells and purified using protein G affinity chromatography, followed by fab arm exchange to obtain bispecific antibodies. The tetravalent antibody was made by fusing the nanobody J3, targeting the CD4bs, via a GS-linker directly to the Fc domain of the anti-CD16 IgG1. The interaction with HIV-1 Env and CD16 was assessed using ELISA and an octet-based assay. The ability to activate natural killer (NK) cells and induce ADCC was determined with an NK cell degranulation assay.

**Results**
Bispecific antibodies lacking a functional Fc domain exhibited reduced potency in NK activation in comparison to the parental anti-HIV-1 IgG1. This could be attributed to a decrease in the number of binding domains/sites specific for the CD4bs and CD16. Interestingly, the tetravalent bispecific antibody showed a slight increase in potency compared to the parental anti-HIV-1 IgG1.

**Conclusion**
Our study highlights the effect and contribution of a functional Fc domain in mediating NK activation. Additionally, we demonstrate the potential of tetravalent bispecific antibodies to achieve enhanced NK activation. Further investigations into different anti-CD16 clones will allow us to optimize the bispecific antibody design for future HIV-1 therapeutic strategies.

*P.10 (Figure 1)*




Visual representation of the bispecific constructs

## P.11

### HOW WE RECRUIT MATTERS: DIFFERENT INTAKE AND ACCESS MODALITIES FOR FREE HIV TESTING YIELD DIFFERENT LEVELS OF INTEREST, UPTAKE, AND OUTCOMES

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**Background**
We offered free HIV testing to people unaware of their HIV-status in the cross-border EuRegio Meuse-Rhine (EMR). We recruited people who were never or not tested in the past year for a free HIV test through various channels (long vs. short intake survey, in-clinic vs. outreach). We compare differences in interest, uptake and test outcomes across channels, as well as demographic characteristic.

**Methods**
First, we recruited through an online cross-sectional survey (May-July 2022) that offered participants who had never tested or tested more than a year ago a free in-clinic HIV test. Then, we shortened the survey (August 2022) so that it only identified individuals eligible for a test. Lastly, we organized two in-person HIV test-events (May and September 2023) where tests were conducted by the same clinic, but via outreach at a central and student-focused location.

**Results**
We included 344 participants (long-intake: n=164, 48%; short-intake: n=130, 38%; test-events: n=50, 14%). More participants were never-tested in the short-intake (n=76, 61%) or attended test-events (n=35, 70%) than in the long-intake (n=46, 29%, p<0.001). 41% of those never-tested in the long-intake, 63% in the short survey and 72% at test-events were unaware where to test (p<0.001). Test-events were fully booked, while free-test interest among those eligible varied between the long (16%, n=12/73) and short (75%, n=79/105) intake. The interest-uptake gap was high in both long and short-intake offering in-clinic testing (17/91, 19%), while 38/50 (76%) participants tested at test-events. 1/55 test was HIV-positive (1.8%). In terms of demographics, we reached younger and more gender-diverse participants with the short-intake and test-events (median 23 years, 49% men) than with the long-intake (median 26 years, 70% men, p<0.001). The long-intake reached more people identifying as gay (n=99, 60%); the short-intake and test-events more people identifying as straight (N=65, 50%; N=30, 60%, respectively) or bisexual (n=32, 18% for both, p<0.001). We reached 156 people (45%) with a migration background (37% long-intake; 50% short-intake; 62% test-events, p=0.003), of whom 71% were born outside the EMR (did not differ between channels, p=0.779)

**Discussion**
Recruitment and access modalities matter. By using multiple channels, we reached a young, gender, sexuality and migration diverse sample who were never tested before and often unaware of testing options. The high interest-uptake gap in the survey for in-clinic HIV-testing but high uptake of outreach test-events demonstrates that we need testing options that are anonymous, easily accessible and offered at low or no cost.

## P.12

### INNOVATIVE PROTOCOLS ENABLE LINKAGE OF PHYLOGENETIC AND GEOSPATIAL DATA AND CHARACTERISE HIV TRANSMISSION HOTSPOTS AMONG MSM WITH A MIGRATION BACKGROUND IN AMSTERDAM

**Alexandra Blenkinsop**[1], Ard van Sighem[2], Daniela Bezemer[2], Peter Reiss[3,4], Godelieve de Bree[3,4], Oliver Ratmann[1], - on behalf of the H-TEAM[3]

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[2] *Stitchting hiv monitoring, Amsterdam, Netherlands*
[3] *Amsterdam Institute for Global Health and Development, Amsterdam, Netherlands*
[4] *Amsterdam UMC, Amsterdam, Netherlands*

**Background**
Meeting UNAIDS' 95-95-95 targets has contributed to falling incidence among Amsterdam MSM. However, MSM with a migration background have experienced a slower decline in new diagnoses than their native counterparts and account for an estimated 43% of all locally acquired transmissions in Amsterdam (Blenkinsop, 2022). Using high resolution geospatial and viral sequence data, we investigate whether locally acquired incident cases among foreign-born MSM occur within localised transmission hotspots among all Amsterdam MSM.

**Methods**
We aligned sequences from MSM enrolled into ATHENA with an Amsterdam postcode and reconstructed phylogenetic trees in the context of sequences from other ATHENA participants and international background. We identified phylogenetically observed transmission chains circulating among Amsterdam MSM in 2014-2021 with more than one individual. Using an innovative protocol, an independent SHM data manager linked participant postcodes of residence (PC4) and provided aggregated data for further analysis, destroying all other data.

Among circulating transmission chains, we mapped observed incident cases and identified PC4 areas with the highest number of locally acquired cases among foreign-born MSM. Next, we identified transmission hotspots as PC4 areas with the highest numbers of concentrated phylogenetic transmission chains, in which over half of observed members resided in the same area. We then evaluated whether incident locally acquired cases among foreign-born MSM occurred within the same transmission hotspots among all MSM. Since transmission networks are unlikely to remain highly localised, we aggregated incident cases and members in phylogenetic networks to a larger spatial area, identifying hotspots at district level.

**Results**
Among Amsterdam MSM, 86 phylogenetically observed transmission chains grew or emerged in 2014-2021 with more than one member. Figure 1 shows the incidence of locally acquired infections acquired in circulating transmission chains among Dutch-born and foreign-born MSM, by PC4 and district of residence. Centrum, West and Oost had the highest number of locally acquired cases among foreign-born MSM (134/229). 18 (21%) of the 86 phylogenetically identified growing or emerging transmission chains were concentrated in one of Amsterdam's districts, of which 15 were in Centrum, West and Nieuw-West (Figure 2B).

**Conclusion**
Phylogenetic and residential postcode data indicate the large majority of growing or emerging Amsterdam MSM transmission chains in 2014-2021 were not concentrated in a particular district in Amsterdam. However, the majority of locally acquired infections among Dutch-born and foreign-born Amsterdam MSM were concentrated in residents of three Amsterdam districts. Targeting interventions towards these hotspots may reach both subgroups, reducing incidence among foreign-born MSM.

*P.12 (Figure 1)*

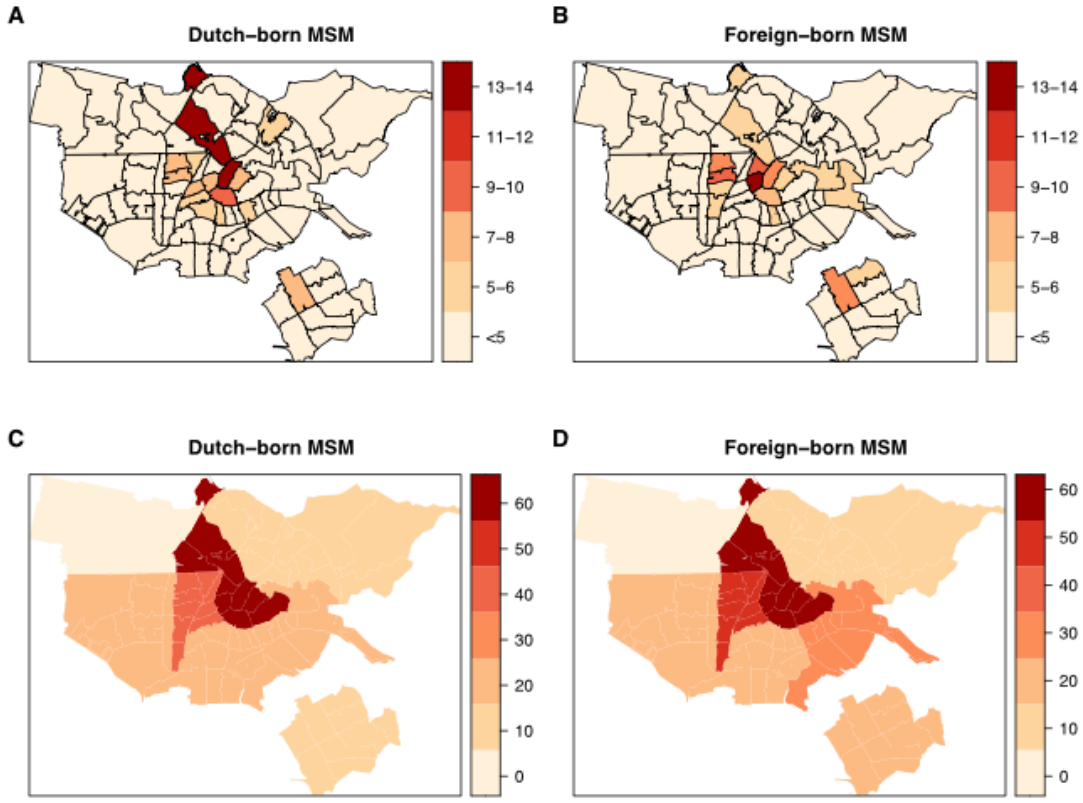


**Figure 1:** ***Number of locally acquired incident cases among Amsterdam MSM, estimated to have been acquired in 2014-2021 in circulating Amsterdam transmission chains.*** *A) Dutch-born MSM (PC4-level); B) Foreign-born MSM (PC4-level); C) Dutch-born MSM (district-level); D) Foreign-born MSM (district-level).*

*P.012 (Figure 2)*

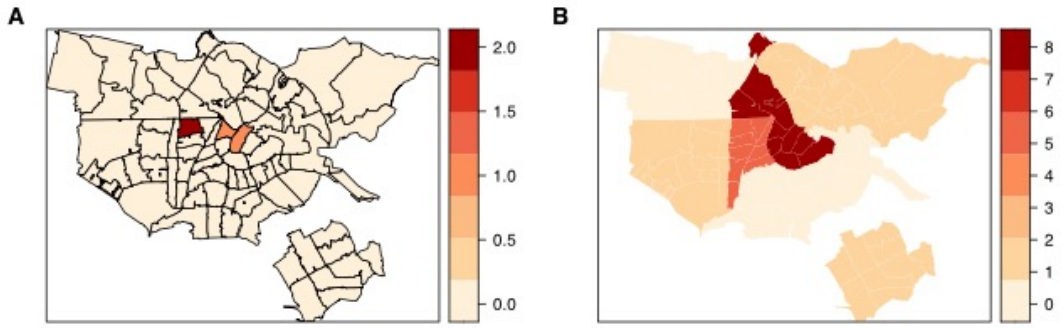


**Figure 2:** ***Inferred transmission hotspots for Amsterdam MSM who acquired HIV in 2014-2021 by PC4 area and district.*** *A) Number of circulating transmission chains in which at least half of members reside in the same PC4 area; B) Number of circulating transmission chains in which at least half of members reside in the same district.*

## P.13

### PROBLEMATIC SUBSTANCE USE AMONG MEN WHO HAVE SEX WITH MEN IN AMSTERDAM IN THE CONTEXT OF THE COVID-19 PANDEMIC

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[2] *AMC Medical Research, Amsterdam, Netherlands*
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[4] *Amsterdam UMC, Infectious Diseases, Amsterdam, Netherlands*
[5] *Amsterdam Institute for Infection and Immunity, Infectious Diseases, Amsterdam, Netherlands*
[6] *Amsterdam Institute for Infection and Immunity (AII), Amsterdam, Netherlands*
[7] *Amsterdam UMC, Department of Internal Medicine, Amsterdam, Netherlands*
[8] *Stichting hiv monitoring, Amsterdam, Netherlands*

**Background**
Higher frequency of substance use has been observed among men who have sex with men (MSM). National COVID-19 restrictions have likely affected mental and social health, which could potentially contribute to changes in substance use. We therefore assessed the frequency and determinants of transitioning between unproblematic and problematic substance use among Amsterdam MSM before, during and after the COVID-19 pandemic.

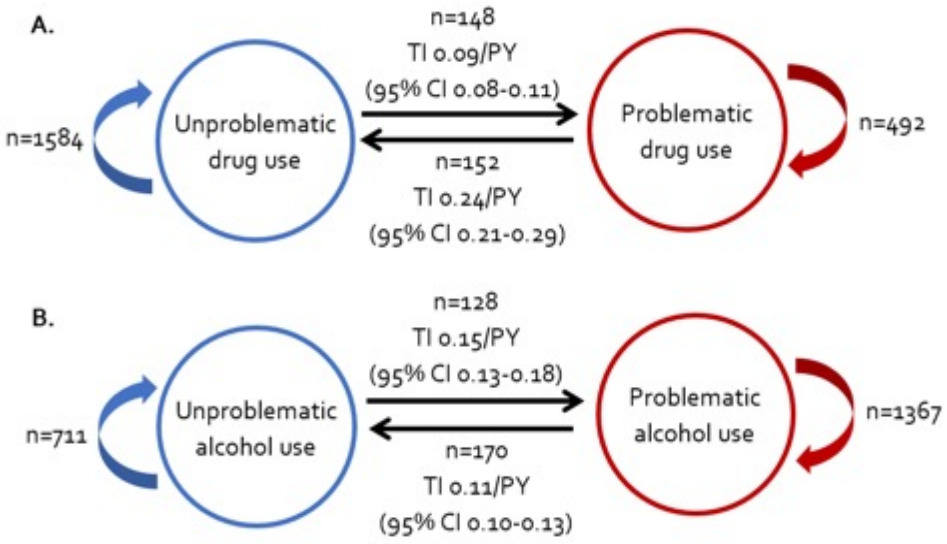
**Methods**
We included participants of the Amsterdam Cohort Studies who completed ≥2 questionnaires between 2017 and mid-2023. Problematic alcohol and drug use was assessed using the Alcohol Use Disorder Identification Test-Consumption (AUDIT-C) and Drug Use Disorders Identification Test (DUDIT), respectively. Transition intensities (TI) between unproblematic and problematic use were estimated using multistate Markov models. Multivariable Hazard ratios (HRs) were estimated by including time period (i.e., before, during and after COVID-19 restrictions) and other covariates to the model.

**Results**
Of 667 MSM, 510 (76.5%) and 281 (42.1%) exhibited problematic AUDIT-C and DUDIT scores, respectively, at least once during follow-up. During a median follow-up of 4.9 years (IQR=3.4-5.3), there were 148 transitions to problematic drug use (TI=0.09/PY, 95%CI=0.08-0.11) and 152 to unproblematic use (TI=0.24/PY, 95%CI=0.21-0.29). In multivariable analysis, decreases in problematic drug-use TI occurred during COVID-19 restrictions period (HR=0.51, 95%CI=0.28-0.95), but not after restrictions (HR=0.99, 95%CI=0.55-1.76), compared to pre-lockdown. Higher loneliness was associated with less frequent transitions to unproblematic drug use, and generalized anxiety disorder with frequent transitions between drug use states.
During follow-up, there were 128 transitions to problematic alcohol use (TI=0.15/PY, 95%CI=0.13-0.18) and 170 to unproblematic alcohol use (TI=0.11/PY, 95%CI=0.10-0.13). COVID-19 period was not associated with TI from unproblematic to problematic alcohol use and the reverse. Higher loneliness was associated with more frequent transitions to problematic use, and depression with more frequent transitions to unproblematic use.

**Conclusions**
COVID-19 restrictions did not substantially affect substance use of Amsterdam MSM, though age, mental health and social factors emerged as significant determinants of progression to and from problematic drug and alcohol use.

*P.13 (Figure 1)*

**Figure 1. Switches between problematic and unproblematic drug (A) and alcohol (B) use between January 2017 and June 2023, among 667 MSM participating in the Amsterdam Cohort Studies, Amsterdam, the Netherlands**




Non-black arrows represent no change in (un)problematic substance use.
Abbreviations: TI, transition intensity; PY, person-year; CI, confidence interval.

Switches between problematic and unproblematic drug (A) and alcohol (B) use between January 2017 and June 2023, among 667 Amsterdam MSM

*P.13 (Table 1)*

**Table 1. Determinants of switching to and from unproblematic and problematic substance use among 667 MSM participating in the Amsterdam Cohort Studies, Amsterdam, the Netherlands (January 2017 – June 2023).**

| | Multivariable, drug use | | Multivariable, alcohol | |
|---|---|---|---|---|
| | Unproblematic → Problematic aHR (95% CI) | Problematic → Unproblematic aHR (95% CI) | Unproblematic → Problematic aHR (95% CI) | Problematic → Unproblematic aHR (95% CI) |
| **COVID-19 period** | | | | |
| Before | ref. | ref. | ref. | ref. |
| During | **0.51 (0.28-0.95)** | 1.18 (0.72-1.93) | 0.86 (0.54-1.37) | 0.92 (0.61-1.39) |
| After | 0.99 (0.55-1.76) | 1.26 (0.67-2.35) | 1.13 (0.67-1.90) | 1.10 (0.68-1.78) |
| **Socio-demographic characteristics** | | | | |
| Age (per year increase) | **0.98 (0.96-1.00)** | 1.01 (0.99-1.03) | **0.97 (0.95-0.99)** | 1.01 (0.99-1.02) |
| Western European | NA | NA | 1.05 (0.53-2.07) | **2.17 (1.23-3.82)** |
| **Sexual behaviour** | | | | |
| Participation in group sex before lockdown | 0.85 (0.55-1.30) | **2.09 (1.35-3.23)** | NA | NA |
| **Mental health characteristics during lockdown** | | | | |
| Generalized anxiety disorder (GAD-7) | **2.11 (1.23-3.62)** | **2.63 (1.42-4.88)** | NA | NA |
| Depression (PHQ-9) | NA | NA | 0.84 (0.53-1.33) | **1.93 (1.30-2.87)** |
| Loneliness score ≥ 5 | 1.02 (0.65-1.59) | **0.56 (0.35-0.91)** | **1.57 (1.04-2.37)** | 0.74 (0.51-1.06) |

Variables that were not significant in the univariable model included: education level, living situation, relationship status, sexual satisfaction and COVID-19 effect score.

Abbreviations: MSM, men who have sex with men; GAD, generalized anxiety disorder; PHQ, patient health questionnaire.

Determinants of switching to and from unproblematic and problematic substance use among 667 Amsterdam MSM

## P.14

### BARRIERS AND ENABLERS THAT INFLUENCE THE UPTAKE OF HIV TESTING AMONG HETEROSEXUAL MIGRANTS IN THE NETHERLANDS: UNDERSTANDING LATE-STAGE HIV DIAGNOSIS

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

**Background**
Heterosexual migrant men and women in the Netherlands often face barriers to accessing health services (including HIV testing), with a lesser willingness or awareness among men to test for HIV. This study explored factors of influence in the usage of HIV testing among heterosexual migrants to understand late-stage HIV diagnosis.

**Methods**
Exploratory qualitative evaluation with semi-structured interviews at the AIDS Healthcare Foundation (AHF) Checkpoint and one focus group discussion (FGD) conducted during June-July 2023 with 12 heterosexual migrants and seven key informants from the (public) health sector, respectively. Recorded interviews were transcribed and thematically analyzed, taking into account the Andersen's Expanded Behavioral Model of Health Services Use framework.

**Results**
Participants were from various ethnic backgrounds. Analysis of interviews revealed that insufficient availability of information on HIV and testing services, and difficulty in accessing these services are barriers. Most participants perceived their overall health status to be good and were thus less likely to seek any type of health service, including HIV testing. The majority of participants expressed free, rapid testing, no appointment required, and a positive experience during their HIV test as enablers to test in the future. Analysis of the focus group discussion (FGD) showed that poor health literacy and lack of clarity on the healthcare system's guidelines were barriers for heterosexual migrants in accessing information on HIV and testing services. The FGD also revealed past initiatives and interventions that were successful in reaching at-risk groups such as the integration of HIV testing into STI testing, but subsequently encountered financial issues. The Andersen framework appeared useful in helping to assess inequalities in accessing these services.

**Conclusion**
Various factors that contributed to a low uptake of HIV testing were identified, namely participants' low knowledge of HIV (including transmission routes, when to test (window period), and where to test), and the Dutch healthcare system, perception of limited accessibility of municipal health service (GGD) facilities, insufficient available information on HIV (testing) services, and low perception of HIV risk. Unclear policies and guidelines on accessing HIV/STI testing services at GGDs as well as potential missed opportunities for HIV testing with general practitioners (GPs) were also contributing factors as illustrated by key informants. Past successful initiatives in Amsterdam such as the H-TEAM (HIV Transmission Elimination Amsterdam) or other Fast Track Cities initiatives could be optimized by also focusing on HIV testing towards heterosexual migrants to reduce late-stage HIV diagnosis.

## P.15

### DEVELOPING INTRACELLULAR ANTIBODIES THAT HARNESS INNATE ANTIVIRAL MECHANISMS TO PREVENT HIV-1 INFECTION

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HIV-1 has been a global health problem for decades, and finding a cure still remains a challenge. Recent studies have explored antibodies targeting various parts of the HIV virus as alternative therapies. These antibodies bind the virus and subsequently enter the cell, where the complex is sensed by the E3 ubiquitin ligase and antibody receptor TRIM21. This protein is part of an intracellular defence mechanism that targets incoming pathogens with attached antibodies for degradation. Here we investigated the potential of this TRIM21 technology to develop intracellular antibodies against HIV-1 infection. We designed nanobodies, based on llama antibodies, targeting the HIV-1 capsid protein p24, and fused these to the human IgG1 Fc domain. The p24 nanobody-Fc constructs were synthesized, and produced in a mammalian expression system. Next, they were characterized by flow cytometry and tested for their functionality to bind p24 using an ELISA-based binding assay. Our data suggests that these Fc-modified nanobodies recognized intact HIV-1 capsid and had a functional Fc domain. Next, the p24 nanobodies-Fc constructs were stably expressed in the U87-CD4-CCR5 cell line. Interestingly, upon HIV-1 infection, intracellular p24 production was decreased in cells expressing the p24 nanobody, and no HIV-1 p24 production was observed in the culture medium. In contrast, control cells efficiently produced p24 upon infection.
To conclude, we have developed a cloning cassette that allows for easy generation of nanobodies. We constructed a Fc-modified p24 nanobodies that interacts with the intact HIV-1 capsid. Overexpression of the p24 nanobody in U87-CD4-CCR5 cells, completely blocked of p24 production in the culture supernatant upon HIV-1 infection. This indicates the potential of these nanobodies in HIV prevention or therapy. Lastly, this technology has a wide variety of potential applications in providing TRIM21-mediated intracellular immunity against viruses like HIV-1, directly or through targeting of host factors and signaling pathways that are important during infection.

## P.16

### DEVELOPMENT OF METHODS TO QUANTIFY THE HIV-2 RESERVOIR

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**Background**
HIV-2 infection remains relatively understudied. In the absence of treatment, the pathogenicity of HIV-2 is notably lower than that of HIV-1, with approximately 50% of individuals with HIV-2 never progressing to AIDS. The higher prevalence of individuals who naturally control HIV-2 offers a unique opportunity to better understand the mechanisms of control and assess whether these mechanisms are transferable to people with HIV-1. However, there is a lack of tools designed to specifically study the HIV-2 reservoir.

**Study objective**
The aim of this study was to create a novel quantitative tool to quantify the HIV-2 reservoir.

**Methods**
In this study, we used sequence alignments to design oligonucleotide primers and probes suitable for the detection of >85% HIV-2 viruses documented to date (both group A and B). Our focus was on two different regions of the HIV-2 genome: the capsid open reading frame and the rev-responsive element (RRE). The choice of these regions, positioned at opposite ends of the HIV-2 genome, was strategically selected to facilitate the development of an intact proviral DNA assay (IPDA) for HIV-2, mirroring the approach used to study HIV-1 reservoirs. Initially, we assessed the primers and probes independently on plasmid proviral DNA and subsequently in a multiplex configuration. Digital PCR experiments are scheduled.

**Results**
We report the successful detection of HIV-2 DNA at a 1 copy threshold for both sets of primers and probe. When optimized individually (n=3), we observed a Cp value of 35±3 for the capsid-specific set and 33±4 for the RRE-specific set for one copy. In multiplex, the Cp values were 35±1 and 37±1 for capsid- and RRE-specific sets again at the one-copy level (n=3). No signal was detected in the no-template controls across all experiments.

**Conclusions**
We describe the development and validation of two quantitative PCR assays specifically designed for quantifying the HIV-2 reservoir. Through careful selection and optimization of our primers-probe sets, we have made them compatible for use in a digital PCR configuration, where they exhibit a narrow yet meaningful target cycle range, spanning from 36 to beyond 40 cycles. These novel analytical tools will facilitate the understanding of HIV-2 reservoir dynamics. Further, their utility may extend to cure-related investigations involving people with HIV, irrespective of the main type of virus.

P.**17**

## GENOTYPIC AND PHENOTYPIC CHARACTERIZATION OF REPLICATION COMPETENT HIV-2 ISOLATED FROM CONTROLLERS AND PROGRESSORS

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**Background**
Although some individuals with HIV-2 develop severe immunodeficiency and AIDS, many never progress to AIDS. Both immunological and viral factors may contribute to these differences in progression. To investigate possible viral factors, replication-competent HIV-2 viruses were isolated from asymptomatic long-term non-progressors (controllers) and from individuals who progress to AIDS (progressors). Viruses from controllers have lower replication rates than viruses progressors in vitro. We sequenced and analysed the entire genomes from both groups and tested Tat- long terminal repeat (LTR) transactivation in vitro.

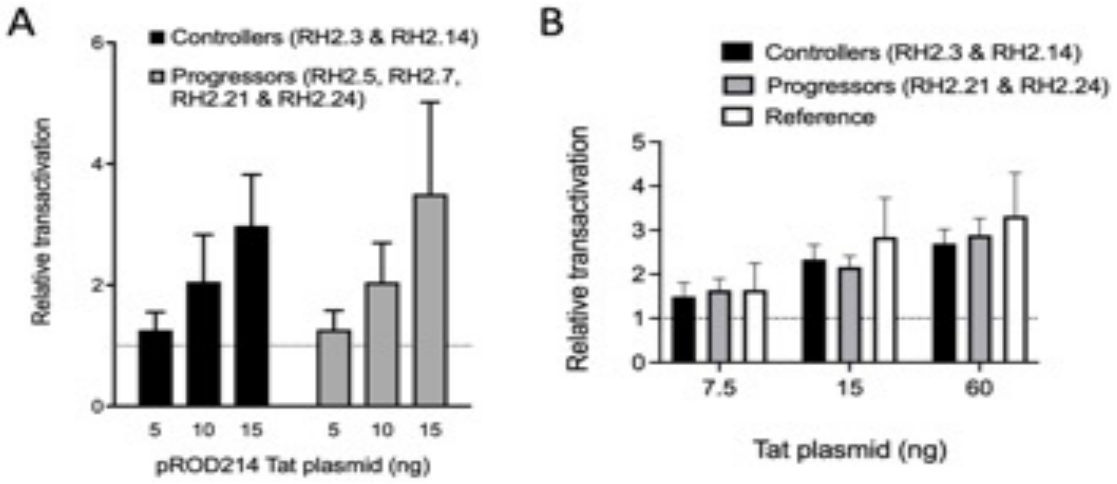
**Study objective**
To investigate potential retroviral factors that correlate with disease progression in HIV-2.

**Methods**
We sequenced the complete genomes of replication-competent viruses from controllers and progressors, using Sanger sequencing on purified overlapping PCR products. Contiguous sequences were assembled, visually inspected and manually edited. Maximum-likelihood phylogenetic trees were constructed using PhyML 3.0. We used phylogeny to seek genotypic correlates of disease progression. We used cell-based assays to study the retroviral transcriptional activity of autologous sets of LTRs and Tat proteins from controllers and progressors.

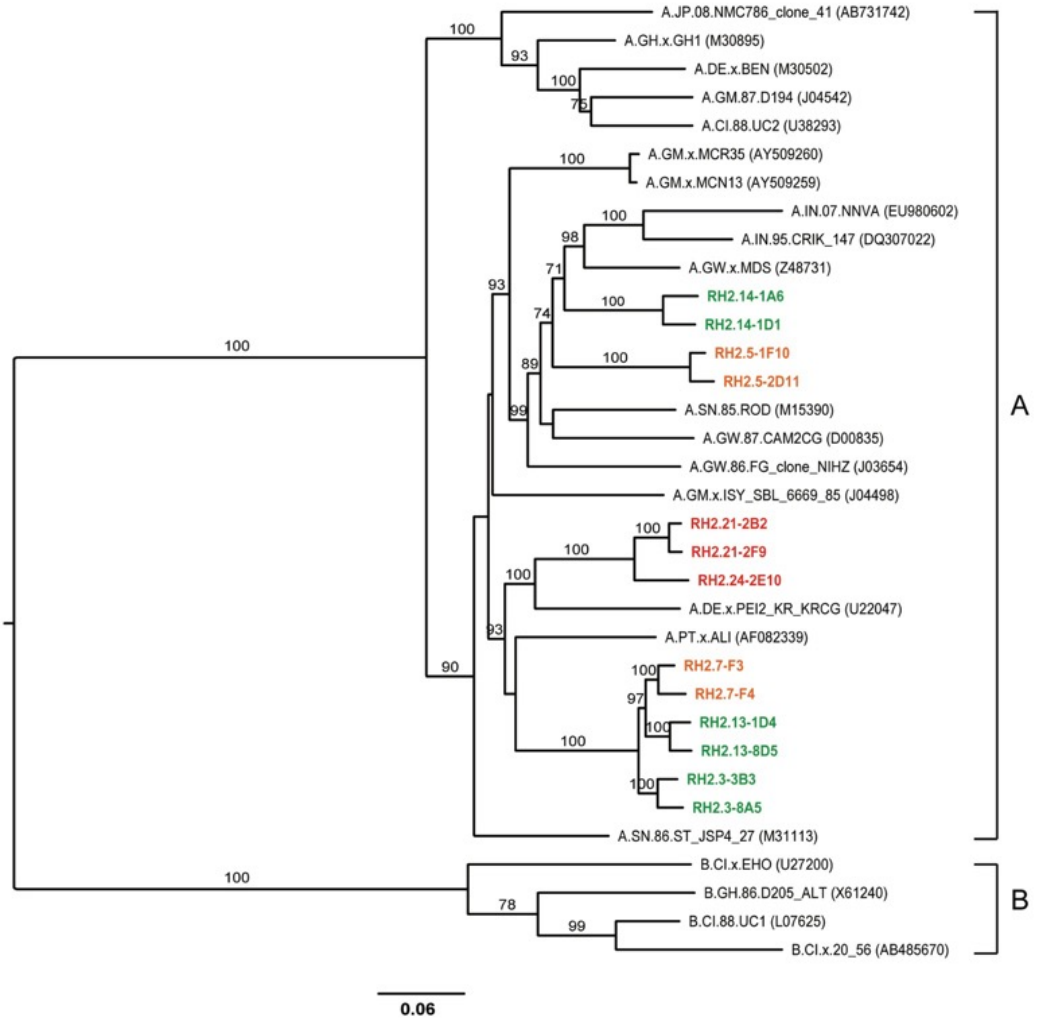
**Results**
Complete genome sequences of viruses from controllers did not cluster together (figure 1). We also reconstructed trees based on individual open reading frames (ORFs: gag, pol, env, vif, vpx, vpr, tat, rev and nef) as well as the LTRs. These additional analyses yielded a similar distribution over the subtype A tree without clustering of the controllers' sequences. As expected from replication-competent viruses, none of the sequence was found to be hypermutated and no premature stop codons were found in individual ORFs. Thus, no obvious haplotype contributed to HIV-2 control. We assessed the basal transcriptional activity and Tat-mediated activation of cloned LTRs from controllers and progressors. We considered that Tat transactivation potential may have co-evolved with the LTRs. Thus, we performed a similar assay with paired autologous Tat-LTRs. This work confirmed the absence of transcriptional differences between controllers and progressors (Figure 2).

**Conclusions**
Overall, the full genome sequences of this limited set of HIV-2 biological clones did not reveal unique features that explain the differences in cell-based replication capacity or in vivo progression. Given that we did not uncover significant variations in transcription between the two groups in in vitro transactivation assays, and the consistent integrated DNA quantities between matched individuals, we hypothesize that the quality of integrants rather than their quantities may differ between controllers and progressors. Our future work will focus on the characterization of HIV-2 integration in controllers and progressors.

*P.17 (Figure 1) Maximum-likelihood phylogenetic tree of complete genome sequences of replication-competent HIV-2 viruses isolated from donors and HIV-2 subt*




*P.17 (Figure 1) Conservation of transcriptional transactivation between HIV-2 controllers and progressors. A) Relative transactivation of LTRs from controll*



## P.18

### IMPACT OF CRISPR-CAS GENE CASSETTES ON THE PACKAGING EFFICIENCY AND TRANSDUCTION TITER OF LENTIVIRAL VECTORS

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CRISPR-Cas technology has revolutionised the use of genome-editing in studies on diverse biological topics. Lentiviral vectors (LVs) have been widely utilised for the generation of transduced cells that durably express the Cas nuclease and guide RNA (gRNA), the key components of the CRISPR-Cas editing system. The LV delivery system allows sustainable gene expression in vitro and in vivo, both in dividing and non-dividing cells. A major challenge for the use of LVs is the requirement to obtain sufficiently high titres for in vivo applications. This work aimed to assess the impact of the CRISPR-Cas transgenes, which differ in size, nucleotide composition and RNA structure, on the production of LVs and their ability to transduce cells. LV particles were produced by co-transfection of the packaging plasmids with an equimolar amount of LV plasmid, containing the transgene, in Human Embryonic Kidney 293 T (HEK293T) cells. Two days post-transfection, the LV containing supernatant was collected, filtered and concentrated. The impact of the transgene length on RNA packaging was determined by quantifying viral RNA levels via cDNA production and PCR. The effect of the LV transgene length on virion production was assessed by measuring the CA-p24 protein level before and after concentration of the LV particles with an in-house developed CA-p24 ELISA assay. The correlation between the vector titre and the size of the LV transgene was evaluated by transduction of the SupT1 T cell line with concentrated LV particles. Three days post-transduction, the LV titre was ascertained by quantitating GFP expression using flow cytometry. This study demonstrates that the transfer efficiency inversely correlates to the CRISPR-Cas transgene size, thus confirming the general rule about RNA size restriction. Remarkably, the LV transduction efficiency measured on the SupT1 cell line dropped dramatically for RNA transcripts approaching 8 Kb, as a further increase of 1 Kb reduced the transduction efficiency by more than 5-fold. As the number of produced virus particles was not affected, the use of larger transgenes most probably caused the production of empty virions. Even though we observed a striking inverse correlation between gene transfer efficiency and the insert size, this will most likely not represent a perfect correlation, as other properties of the packaged RNA may still exhibit a modulatory effect.

## P.19

### CONTEXT, COLLABORATION AND CURE: THE VALUE OF ETHNOGRAPHY FOR GLOBAL HIV CURE RESEARCH

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**Background**
Developing safe, affordable, and accessible HIV cure strategies is urgent for global health, yet this pursuit encounters major challenges. Among these is a need for biomedical research collaborations across geographic boundaries, which can drive the development of a globally equitable cure. Whilst most HIV cure research is based in the global North, the majority of people with HIV reside in Africa. It is imperative to understand how global partnerships and collaboration in HIV cure research between high-, low- and middle-income countries currently occurs and might be further fostered.

**Methods**
In a review of ethnographic work about biomedical research collaborations, we highlight the value(s) of this kind of research for globalising HIV cure. In the works reviewed, ethnographers have immersed themselves in the everyday laboratory lives of research institutions in sub-Saharan Africa and Europe. In doing so, they have relied on ethnography, a combination of qualitative research methods, including observation fieldnotes and interviews based on long-term relationships of trust between the ethnographer, biomedical scientists and affected communities. Ethnography typically allows to explore complex phenomena in their natural setting with a focus on explanation, rather than measurement.

**Results**
Firstly, ethnography allows for the contextualization of scientific knowledge by revealing how knowledge is influenced by the values, practices and assumptions of scientists and the broader societal and cultural milieu in which they work. Secondly, ethnography provides an in-depth understanding of power dynamics within collaborations and how these might shape the ability of developing equitable and accessible HIV cure interventions. Thirdly, embedded ethnographic research is valuable through providing real-time insights based on emerging findings which can be used to make adaptations of research strategies and finetune interventions to different cultural settings.

**Conclusion**
Through making contextual and power dynamics of collaborative practices explicit, ethnography can help global HIV cure partnerships to critically reflect on their practices and underlying ideologies. This is imperative for designing more effective, ethical, and community-centred HIV cure interventions, and for building trust and collaboration between researchers and affected communities across different contexts. Existing and future ethnographic work on research collaboration for HIV cure can be used to draw overarching lessons and identify good collaboration practices that can further globalise HIV cure research.

## P.20

### PROSPECTS OF HIV ELIMINATION AMONG MEN WHO HAVE SEX WITH MEN: A SYSTEMATIC REVIEW OF MODELLING STUDIES

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**Background**
The Joint United Nations Programme on HIV/AIDS (UNAIDS) formulated the goal of ending the HIV epidemic globally and the specific targets (known as '95-95-95') to be reached by 2030. Although this goal is far from being achieved on a global scale, reports for reaching the UNAIDS targets and HIV elimination exist for key populations, such as men who have sex with men (MSM). We systematically reviewed recent modelling studies that assess the impact of interventions on the prospects of HIV elimination among MSM to provide a comprehensive overview of (i) MSM population subgroups and geographical settings where HIV elimination may or may not be achieved, (ii) interventions required, and (iii) HIV elimination definition/criteria used in different studies.

**Methods**
Articles were searched for on EMBASE and MEDLINE (PubMed) from 1 January 2021 until 7 August 2023 using permutations of the following terms: HIV, MSM, transgender, bisexual, gay, model, framework, simulation, treatment, prevention, mathematical, transmission and computational. Studies assessing the population-level impact of HIV interventions among MSM using a dynamic mathematical transmission model were eligible for inclusion. Data extraction focused on the demographic characteristics of the MSM population, interventions evaluated, public health guidance, elimination criteria, elimination prospects, model structure.

**Results**
Out of 604 articles screened, 37 were eligible and included in the review (Figure 1). Studies focused on MSM populations in Northern America (28 studies), Western Europe (1), East Asia (2), Africa (4) and Central America (2). 8 studies focused on the general MSM population in the country, and 29 considered smaller geographical settings such as cities or regions.
10 studies considered population subgroups such as young MSM, and 18 considered different ethnic groups.
Interventions evaluated in the models were pre-exposure prophylaxis (25 studies), improved antiretroviral treatment (34), condoms (25), circumcision (11) and other (14).
We identified 8 different definitions of HIV elimination, with 15 studies including some definition of elimination. 9 of these studies were able to model a scenario in which HIV elimination was possible.

**Conclusions**
There is an underrepresentation of modelling studies that address HIV elimination among MSM outside Northern America or in specific population subgroups (e.g, young MSM, ethnic minorities, etc.). The development of a common definition of HIV elimination is needed for transmission models to provide meaningful guidance to policymakers on the prospects of HIV elimination and interventions needed t o reach it across various settings.

*P.20 (Figure 1)*

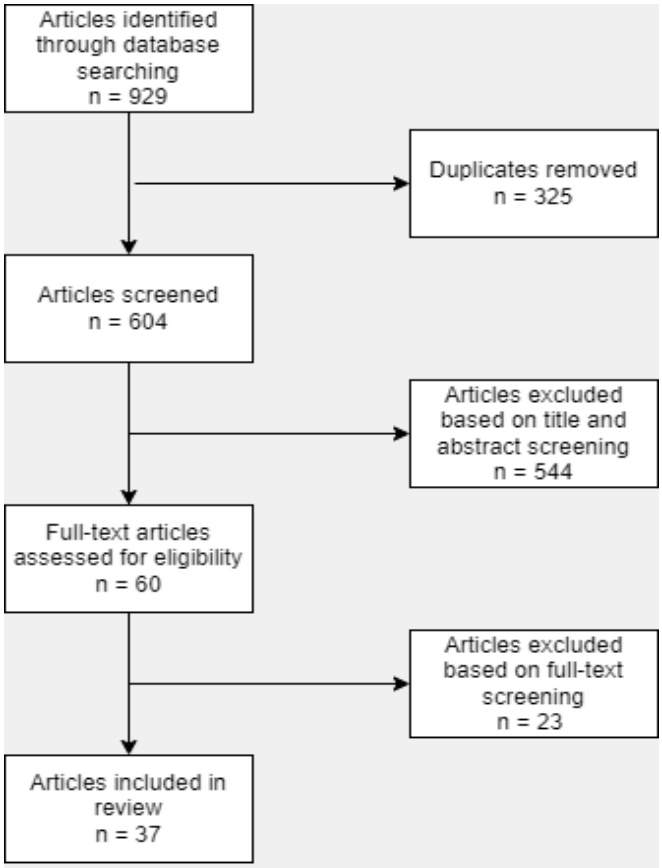


Figure 1. PRISMA flow diagram

## P.21

### THE ROLE OF GGD AND NON-GGD STAKEHOLDERS: EPIDEMIOLOGICAL IMPACT AND COST-EFFECTIVENESS ANALYSIS OF EXPANDING PREP PROVISION TO MSM WHO ARE PREP-ELIGIBLE IN THE NETHERLANDS

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**Background**
The Dutch PrEP program, administered through public health services (GGD), has reached its maximum capacity of 8,500 slots, leaving 3,000 MSM on the waiting-list and approximately 4,500 PrEP prescriptions from non-GGD sources. Approximately 15,000 PrEP-eligible/intending MSM are still waiting for access. Despite multiple avenues for PrEP access, GGD offers a comprehensive package (i.e., free tests, and a cheaper and stable medication supply for PrEP users) compared to non-GGD sources. To inform decision-making, we modelled the epidemiological impact, cost-effectiveness, and budget implications of extending PrEP provision to all eligible/intending MSM, considering both GGD and non-GGD sources.

**Methods**
We utilised a calibrated mathematical model of HIV transmission among MSM in the Netherlands. In our model, PrEP provision was expanded in 2022 to cover an additional 3,000 waiting-list MSM, one-third (5,000), two-thirds (10,000), and all (15,000) PrEP-eligible/intending MSM by 2024. The epidemiological impact of expanding was evaluated by 2030 in comparison to a non-extension scenario. Costs were calculated from a payer's perspective, differentiating between GGD and non-GGD providers over a 40-year period. Short-term budget impact over five-years were examined with increased GGD capacity.

**Results**
Additionally covering 3,000 waiting-list MSM, one-third, two-thirds, and all of PrEP eligible/intending MSM by 2024 will reduce the number of new HIV infections to 4, 2, 0 and 0 in 2030, averting 17 (5.7%), 46 (15.2%), 88 (29.1%), and 115 (37.9%) cumulative new HIV infections by 2030, respectively. Assuming non-GGD stakeholders provide additional PrEP beyond GGD's capacity, all extension scenarios were cost-saving from a payer's perspective, as significant costs (PrEP-medications and PrEP-related tests) were co-paid by PrEP users via non-GGD sources. Increasing GGD's capacity resulted in reduced cost-effectiveness and higher short-term costs. Enlarging GGD's capacity to 10,000, 15,000, 20,000, 25,000, and 30,000 slots would incur additional costs of €3.72 million, €16.07 million, €28.42 million, €40.01 million, and €45.86 million over five-years, respectively.

**Conclusion**
Expanding PrEP coverage is crucial and can potentially achieve zero HIV infections among Dutch MSM by 2030. Encouraging non-GGD stakeholders to play a more significant role in expanding PrEP provision will enhance cost-effectiveness from a payer's perspective, and ensure greater availability of PrEP to MSM. Simultaneously, increasing GGD's capacity is also vital for ensuring affordable and reliable access for PrEP users. Therefore, achieving a balance between payer costs and individual costs is essential. In summary, we emphasize that PrEP should be accessible and available to all eligible/intending MSM in the Netherlands, regardless of the provider.

## P.22

### PREVOTELLA TIMONENSIS ENHANCES HIV-1 TRANSMISSION IN PRIMARY HUMAN BLOOD DENDRITIC CELLS

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HIV-1 remains a serious global health problem with many newly acquired infections affecting young women and girls in sub-Saharan Africa. The main route of HIV-1 infection is via mucosal surfaces in the genital tract during sexual intercourse. Alterations in the vaginal microbiota enhance susceptibility to HIV-1 infection however, underlying molecular mechanisms remain largely unknown. Here, we investigated the role of vaginal dysbiosis associated bacteria in altering HIV-1 uptake and transmission in dendritic cell (DC) subsets. Prevotella timonensis, but not other microbiota, enhanced uptake of different HIV-1 strains in monocyte-derived DCs. Notably, P. timonensis-enhanced uptake seems specific for viruses as P. timonensis enhanced cellular uptake of different viruses, but not other antigens or pathogens, such as fungi or bacteria. Strikingly, analysis of primary blood DC subsets showed that P. timonensis not only enhanced HIV-1 uptake, but this also resulted in increased HIV-1 transmission to T cells, which can contribute to the enhanced HIV-1 susceptibility observed in women with vaginal dysbiosis. Besides increasing HIV-1 uptake and transmission, we observed that P. timonensis enhanced clustering of DCs with CD4 T cells, providing an additional mechanism enhancing HIV-1 transmission. To conclude, our study provides new insights into the role DCs play in HIV-1 uptake and transmission after bacterial exposure, and underscores the importance of examining the role of the microbiome in viral pathogenesis. Identification of underlying mechanisms and potential targets could facilitate the design of therapies to reduce the risk of HIV-1 acquisition and AIDS.

## P.23

### EXPERIENCED BARRIERS AND FACILITATORS TO HEALTHCARE AMONG MIGRANT TRANSGENDER AND GENDER-DIVERSE (MTGD) PERSONS IN THE NETHERLANDS: RELEVANCE FOR IMPROVING HIV/STI SERVICE ACCESS AMONG MTGD

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**Background**
Transgender and gender-diverse (TGD) people, particularly those with migrant backgrounds (mTGD), face health inequalities and barriers to care globally. We evaluated experienced barriers and facilitators to finding and continuing healthcare for various health needs among mTGD in the Netherlands. We report findings relevant for accessible, inclusive, and sensitive sexual health care and prevention.

**Methods**
This community-based participatory research (CBPR) comprised in-depth interviews with mTGD individuals, conducted by TGD community members and close allies. Two researchers independently open-coded transcribed interviews and discussed themes with the research team.

**Results**
Results from 31 interviews (n=16 trans women; n=8 trans men; n=7 non-binary; twenty-seven nationalities from five continents) revealed gender-affirming care was deemed priority over other health needs. Four major themes (each with barriers and facilitators) arose: model of care, knowledge, trust, and syndemic circumstances. Regarding model of care, community-based care settings were preferred as they facilitated trust and building a peer network. Integrated care could address complex life circumstances, including syndemic circumstances. A knowledge barrier was providers' unfamiliarity with TGD-specific health and care, or with facilities that have such expertise (impeding linkage-to-care especially for those new to the Netherlands or not speaking Dutch). The main facilitator to client knowledge was having a peer network. Client-provider trust was deemed highly important in settings where sensitive topics are discussed and physical examination could occur, like sexual healthcare. Barriers to trust were a perceived distancing from clients' health needs (e.g., after providers expressed a lack of TGD health knowledge), misgendering or questioning clients' transition journey, and frequent rotation of providers (leading to clients having to continually disclose their trans identity). Facilitators to trust included demographic similarity of providers, kindness and empathy, validation of clients' gender identity, willingness to learn about TGD health, and shared decision-making. Syndemic circumstances formed competing concerns: interviewees prioritized their medical transition, and often dealt with mental health issues (relating to gender dysphoria or migration history), financial or housing instability, and gender- or ethnicity-based discrimination, harrassment or violence. These competing concerns left little mental room for non-acute or preventative care, like sexual health care and prevention.

**Conclusion**
Sexual healthcare for mTGD individuals in the Netherlands can be improved by promoting TGD representation and improving TGD-specific health knowledge and cultural competence among sexual health providers. Integrating sexual healthcare with gender-affirming care and social support can help mTGD persons initiate and continue healthcare whilst navigating syndemic circumstances.

## P.24

### PRIORITIZATION OF POPULATIONS WITH ANTICIPATED BARRIERS TO CARE FOR SUBSIDIZED PREP COULD ENGAGE INDIVIDUALS PREVIOUSLY NOT ATTENDING HIV/STI SERVICES, IN AMSTERDAM, THE NETHERLANDS

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**Background**
The Dutch national HIV pre-exposure prophylaxis (PrEP)pilot program (NPP) provides subsidized PrEP care to individuals at risk for HIV. At the Centre for Sexual Health Amsterdam (CSH-A), populations less likely to access PrEP elsewhere received priority access to the NPP: those <25 years, transgender or gender-diverse (TGD), sex workers, migrants from low- or middle-income countries (LMIC) and those uninsured. We determined to what extent individuals belonging to prioritized groups and requesting PrEP through the NPP had prior experience with HIV/STI services.

**Methods**
We used enrolment visit data from individuals starting PrEP at the CSH-A (July 2019-February 2023). Using latent class analysis (LCA), we identified classes of prior HIV/STI service experience using the following covariates, all pertaining to the 12 months before NPP enrolment: self-reported PrEP use (yes, formally in the Netherlands/yes, informally in the Netherlands or abroad/no), registered CSH-A visit (yes/no), and self-reported or registered STI test (yes/no). Individuals were assigned to a class based on the highest posterior probability. We assessed determinants of class membership using multinomial regression.

**Results**
Among 4,075 individuals starting PrEP, the best fitting LCA model comprised three classes. First, “newly engaged” individuals (n=551, 14%): all were new to the CSH-A, none used PrEP formally in the Netherlands, and 58% (n=289) self-reported recent STI testing. Second, “PrEP-initiators” (n=1,642, 40%): all previously used CSH-A services and 97% (n=1,590) previously tested for STI, but none used PrEP. Third, “PrEP experienced” individuals (n=1,882, 46%): all previously used PrEP, 95% (n=1,751) reported STI testing and 82% (n=1,545) visited the CSH-A. “Newly engaged” individuals were more often TGD, born in LMIC, uninsured and bisexual than individuals in both other groups. “PrEP-experienced” individuals were more often >25 years and college- or university-educated, and more often engaged in chemsex and condomless anal sex with casual partners than those in both other groups (Table). The majority of new HIV diagnoses at enrolment (n=10/14) was found among those “newly engaged”. Prevalence of any chlamydia, gonorrhoea or infectious syphilis did not differ between “newly engaged” and “PrEP-experienced” individuals, but was lower among “PrEP-initiators”.

**Conclusion**
NPP participants without prior experience with PrEP or other STI/HIV services more often belonged to priority populations, and accounted for most new HIV diagnoses at enrolment. Prioritization of populations with anticipated barriers to care can be used as strategy to include more individuals eligible for, but naïve to PrEP, into PrEP care.

*P.24 (Table 1) Determinants of latent class of prior HIV/STI service experience, among national PrEP pilot participants in Amsterdam, the Netherlands (July 2019-February 2023)*

| | Class 1 (versus Class 3) | | Class 2 (versus Class 3) | | Class 1 (versus Class 2) | |
|---|---|---|---|---|---|---|
| | aOR [95% CI] | p-value | aOR [95% CI] | p-value | aOR [95% CI] | p-value |
| **Sociodemographic determinants** | | | | | | |
| **Younger than 25** (vs ≥25 years) | 2.12 [1.65-2.72] | **<0.001** | 2.91 [2.43-3.47] | **<0.001** | 0.73 [0.58-0.92] | **0.0072** |
| **Transgender** (vs. cisgender) | 3.54 [2.29-5.47] | **<0.001** | 2.08 [1.39-3.09] | **<0.001** | 1.71 [1.21-2.41] | **0.0024** |
| **Born in non-Western country** (vs. NL or other Western country) | 1.57 [1.25-1.98] | **<0.001** | 1.31 [1.11-1.54] | **0.0015** | 1.21 [0.96-1.51] | 0.11 |
| **Practical schooling** (vs. college or university degree) | 1.26 [0.99-1.59] | **0.060** | 1.25 [1.06-1.46] | **0.0078** | 1.01 [0.8-1.28] | 0.94 |
| **No health insurance** (vs. insured) | 2.08 [1.33-3.24] | **0.0014** | 1.06 [0.70-1.60] | 0.78 | 1.96 [1.34-2.87] | **<0.001*** |
| **Bisexual** (vs. exclusively homosexual) | 3.12 [2.03-4.8] | **<0.001** | 2.12 [1.46-3.08] | **<0.001** | 1.48 [1.03-2.12] | 0.036 |
| **Behavioral determinants** | | | | | | |
| **HIV** (yes vs. no) | 8.95 [1.01-79.13] | **0.049** | 1.52 [0.15-15.75] | 0.73 | 5.90 [1.5-23.16] | **0.011** |
| **Any STI** (yes vs. no) | 1.14 [0.88-1.49] | 0.32 | 0.68 [0.56-0.84] | **<0.001** | 1.67 [1.27-2.2] | **<0.001** |
| **CAS with casual partners** (yes vs. no) | 0.38 [0.29-0.5] | **<0.001** | 0.43 [0.34-0.54] | **<0.001** | 0.89 [0.69-1.15] | 0.37 |
| **Number of sex partners** (>3 vs ≤3) | 1.09 [0.85-1.4] | 0.51 | 0.88 [0.74-1.05] | 0.16 | 1.23 [0.96-1.58] | 0.095 |
| **Chemsex** (yes vs. no) | 0.69 [0.55-0.86] | **0.001** | 0.64 [0.54-0.74] | **<0.001** | 1.08 [0.86-1.35] | 0.51 |

**Abbreviations**: PrEP: pre-exposure prophylaxis; OR: odds ratio; CI: confidence interval; aOR: adjusted odds ratio; NL: the Netherlands; HIV: human immunodeficiency virus; STI: sexually transmitted infections; CAS: receptive condomless anal sex;

[1]'Newly engaged': 11% used PrEP (all sourced it informally or abroad), 58% reported recent STI testing, but none visited the CSHA in the past 12 months.

[2]'PrEP initiators': none used PrEP, but 97% was recently STI tested and all visited the CSHA in the past 12 months.

[3]'PrEP-experienced': all used PrEP, 95% was recently STI tested and 82% visited the CSHA in the past 12 months.

[4]Sex work was removed from the multivariable model due to collinearity with the variables region of birth, gender identity, and insurance status.

## P.25

### STI INCIDENCE AND RETENTION IN CARE AMONG PRIORITY POPULATIONS PARTICIPATING IN THE NATIONAL HIV PRE-EXPOSURE PROPHYLAXIS (PREP) PILOT PROGRAM IN AMSTERDAM, THE NETHERLANDS

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**Background**
The Dutch national HIV pre-exposure prophylaxis (PrEP) pilot (NPP) provides subsidized PrEP care through Centers for Sexual Health (CSH). In Amsterdam, people less likely to access PrEP elsewhere were prioritized for inclusion in the NPP: those <25 years, transgender and gender-diverse (TGD) people, sex workers, migrants from low- and middle-income countries (LMIC) and those without healthcare insurance. We aimed to assess behavioral risk for HIV among these priority groups by comparing incidence of sexually transmitted infections (STI) by group. We furthermore compared NPP retention.

**Methods**
We used longitudinal data from PrEP visits and additional STI visits among individuals with >1 NPP visit at the CSH-Amsterdam (July 2019-February 2023). We compared incidence of any STI (i.e., chlamydia, gonorrhea or infectious syphilis) by priority group using incidence rate ratios (IRR), adjusted for STI testing frequency, other priority group memberships (if applicable), and sexual behavior. We used a Markov switch model to calculate transition intensities between attended visits, missed visits, and loss-to-follow-up (LTFU) (i.e., last PrEP visit was >6 months before February 2023). We calculated hazard ratios (HR) for each transition by demographic priority group, adjusted for other priority group memberships if applicable.

**Results**
Among 3,624 individuals (n=1,683 belonging to ≥1 priority group), STI incidence was 85.6/100 person-years.
STI incidence was higher among those <25 years (n=867, aIRR=1.34[95%CI=1.20-1.50]), or born in a LMIC (n=1198, aIRR=1.12[1.03-1.21]), and lower among TGD clients (n=228, aIRR=0.73[0.57-0.92]), compared to individuals not in the respective priority group (Table). 20% (727/3,624) of clients were LTFU. LTFU was more common among those <25 years (aHR=1.59[1.24-1.03]), doing sex work (aHR=1.94[1.39-2.70]), or belonging to a multitude of priority groups (HR=2.05[1.58-2.66]). These groups also more often missed a PrEP visit, which was predictive of LTFU (p<0.001).

**Conclusion**
STI incidence was higher in some, but not all populations prioritized for inclusion in the NPP. NPP retention was lower among prioritized populations. PrEP programs with limited capacity should continue prioritizing populations less likely to access PrEP elsewhere, but interventions to improve retention among these populations are needed.

*P.25 (Table 1) Incidence of any chlamydia, gonorrhea or infectious syphilis among populations prioritized for access to the National PrEP Pilot in Amsterdam*

| | Incidence rate | | Incidence rate ratio | | | |
|---|---|---|---|---|---|---|
| | Exposed | Unexposed | Crude | | Adjusted[1] | |
| | IR/100 py [95% CI] | IR/100 py [95% CI] | IRR [95% CI] | p-value | IRR [95% CI] | p-value |
| <25 years (vs ≥25 years) | 99.7 [94.0-105.8] | 82.9 [80.5-85.3] | 1.20 [1.13-1.29] | <0.0001 | 1.34 [1.20-1.50] | **<0.0001** |
| Transgender or gender-diverse (vs cisgender) | 70.1 [59.8-82.0] | 86.1 [83.9-88.4] | 0.81 [0.69-0.95] | 0.0094 | 0.73 [0.57-0.92] | **0.0073** |
| Sex worker (vs no sex worker) | 113.7 [103.8-124.4] | 83.9 [81.6-86.2] | 1.36 [1.23-1.49] | <0.0001 | 1.15 [0.98-1.34] | 0.092 |
| Uninsured (vs insured) | 113.8 [100.8-128.5] | 85.2 [82.6-87.8] | 1.34 [1.17-1.51] | <0.0001 | 1.09 [0.92-1.30] | 0.32 |
| Born in LMIC (vs high income country) | 98.7 [94.2-103.4] | 81.0 [78.5-83.5] | 1.22 [1.15-1.29] | <0.0001 | 1.12 [1.03-1.21] | **0.0060** |
| Multiple priority groups (vs no priority groups) | 111.3 [99.8-124.1] | 77.6 [74.9-80.4] | 1.43 [1,27-1.61] | <0.0001 | 1.05 [0.99-1.11] | 0.071 |

Abbrevations: IR: incidence rate; py: person-years; CI: confidence interval; LMIC: low- or middle income country; STI: sexually transmitted infection

[1]Adjusted for other priority group memberships (if applicable), individual yearly STI testing frequency, and sexual behavior (number of sex partners in quartiles (past 3 months), any condomless analysex with a casual partner (past 3 months), any chemsex (past 6 months)

## P.26

### WHAT DETERMINES MPOX VACCINATION UPTAKE? ASSESSING THE EFFECT OF INTENT-TO-VACCINATE VERSUS OTHER DETERMINANTS AMONG MEN WHO HAVE SEX WITH MEN

**Vita Jongen**[1,2], Marije Groot Bruinderink[1,3], Anders Boyd[1,2,4], Jeffrey Koole[1], Buhari Teker[1], Nicole Dukers-Muijrers[5,6], Ymke Evers[5,6], Maarten Schim van der Loess[1,4], Maria Prins[1,4], Henry de Vries[1,4], Amy Matser[1,4], Udi Davidovich[1,3]

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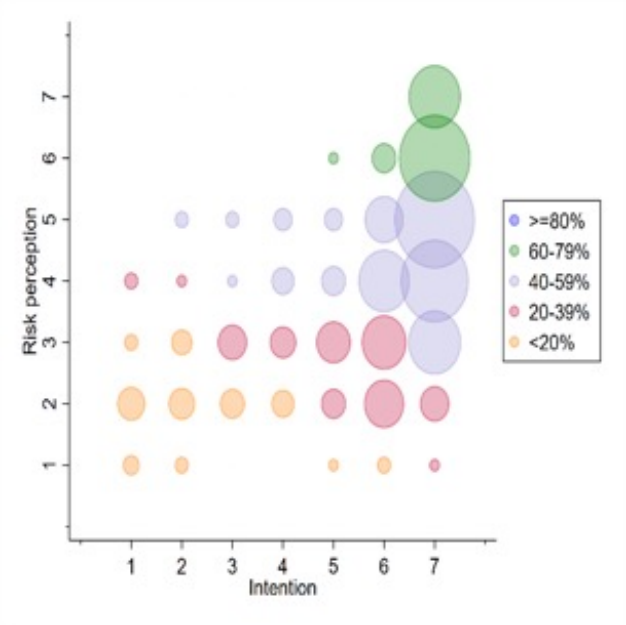
**Background**
In response to the mpox outbreak, vaccination was offered in the Netherlands to men who have sex with men (MSM) at increased risk for mpox. We assessed the impact of intent-to-vaccinate and other factors on vaccination uptake among participants of the Amsterdam Cohort Studies (ACS).

**Methods**
In July 2022, prior to the mpox vaccination campaign, we distributed a survey regarding mpox intent-to-vaccinate among ACS participants. Vaccination uptake was self-reported during study visits after August 2022. The association between high vaccination intent and uptake, and determinants of intent, was jointly assessed using a structural equation model (SEM) based on components of the Theory of Planned Behavior. In a second SEM, determinants of intent were allowed to have a direct effect on vaccination uptake.

**Results**
492 MSM (median age 46 years) were included in analyses. 380 (77%) had a high intent-to-vaccinate and 238 (48%) received at least one vaccine dose. In the first model, high intent-to-vaccinate was associated with getting vaccinated (β=1.1, 95%CI=0.6-1.5). 175/380 (46%) participants with high intent-to-vaccinate did not get vaccinated. The second model had an improved model fit compared to the first model. The effect of intent on uptake was non-significant, and only perceiving to be at higher risk of infection significantly increased vaccination uptake (β=0.42, 95%CI=0.26-0.59). Having a steady relationship decreased the probability of vaccination (β=-0.59, 95%CI=-1.0- -0.18). The probability of vaccination uptake was driven by risk perception, independently of intent-to-vaccinate; i.e., the marginal proportion of participants who received vaccination decreased among those with a risk perception <6, regardless of intent-to-vaccinate (Figure).

**Conclusions**
While intent-to-vaccinate for mpox was high among MSM, high intent did not necessarily result in vaccine uptake. Mpox risk perception played a more pivotal role in getting vaccinated.

*P.26 (Figure 1) Heatmap of the marginal proportion of mpox vaccination uptake corresponding to each combination of intention and risk perception*



## P.27

### CROSSTALK BETWEEN TOLL-LIKE RECEPTOR-8 AND RIG-I-LIKE RECEPTORS ENHANCED ANTIVIRAL IMMUNITY AGAINST HIV-1 IN ACUTE INFECTED INDIVIDUALS AND PEOPLE LIVING WITH HIV-1.

**Killian Vlaming**[1,2], John van Hamme[1,2], Tanja Kaptein[1,2], Neeltje Kootstra[1,2], Godelieve de Bree[1,2], Teunis Geijtenbeek[1,2]

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**Background**
An HIV-1 cure necessitates not only the reactivation of the viral reservoir but also robust antiviral immunity to eliminate this reactivated HIV-1 reservoir. We have recently shown that crosstalk between TLR-8 and RIG-I-like Receptors (RLRs) strongly enhances antiviral immunity by enhancing IL-12p70, IL-27 and Interferon (IFN) type I responses. These responses are essential for antiviral T helper (Th) type 1, follicular Th as well as boosting CD8+ cytotoxicity. Here we investigated whether this crosstalk between TLR8 and RLR persists in the context of HIV-1, by investigating crosstalks in acute infected, treated, individuals as well as people living with HIV (PWH).

**Methods**
We had four distinct categories of participants: time-matched HIV-negative and chronically infected HIV-positive participants from the ACS cohort (antiretroviral treatment (ART) initiated after CD4 <300), and two groups of participants from the NOVA, where ART was initiated directly after HIV-1 diagnosis, cohort (24-weeks post-treatment initiation and three years post-treatment initiation). Peripheral blood mononuclear cells (PBMCs) and isolated monocytes were treated with TLR-8 and RLR agonists alone or in combination for 24 hours. Subsequently, innate and adaptive immune responses, including cytokine levels, type I IFN responses, and co-stimulatory molecule expression, were assessed.

**Results**
TLR-8 agonist Selgantolimod (GS9866) triggered the release of various pro-inflammatory cytokines, including IL-6 and IL-12. Poly(I:C)-lyovec, a RLR agonist, predominantly induced the potent pro-inflammatory cytokine IL-27 in PBMCs across all four groups. Co-stimulation with the TLR-8 agonist and the RLR agonist resulted in a two fold increase of IL-12 and IL-27 in PBMCs, while IL-6 secretion was halved. We observed that TLR8/RLR crosstalk induced a x-fold increase of IL-12 and IL-27 in uninfected cohort compared to TLR8 stimulus alone as well as In the NOVA group of early treatment at 24 weeks and 3 year post treatment (x fold and x fold respectively). Notably, in PWH during chronic infection crosstalk was impaired; IL-12 and IL-27 increased 1.5 fold and Il-6 decreased to 1.2 fold.

**Conclusion**
Our data strongly suggest that quick initiation of therapy upon diagnosis is paramount to preserving crosstalk between TLR8 and RLR. TLR8 and RLR crosstalk induced strong antiviral responses in uninfected cohort as well as in early treatment cohort, suggesting that this combination might be important in HIV-1 reversal strategies. Moreover, our data suggest that the antiviral responses are less effective in chronic treated PWH .

## P.28

### PCID2 DYSREGULATES TRANSCRIPTION AND VIRAL RNA PROCESSING TO PROMOTE HIV-1 LATENCY

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HIV-1 latency results from tightly regulated molecular processes that act at distinct steps of HIV-1 gene expression. To elucidate the molecular players that govern latency, we previously performed a dCas9-chromatin immunoprecipitation coupled with mass spectrometry (Catchet-MS) and identified the interactome of the latent HIV-1 LTR. Here we characterize the Catchet-MS-identified PCI domain-containing 2 (PCID2) protein, a component of the TREX2 complex, to play a dual role in promoting HIV-1 latency by enforcing both transcriptional repression and post-transcriptional blocks to HIV-1 gene expression. PCID2 bound the latent HIV-1 LTR and repressed transcription initiation during latency. Depletion of PCID2 remodelled the chromatin landscape at the HIV-1 promoter and resulted in transcriptional activation and reversal of latency. Immunoprecipitation coupled to Mass Spectrometry identified PCID2-interacting proteins to include members of the spliceosome, including negative viral RNA (vRNA) alternative splicing regulators, and PCID2 depletion resulted in over-splicing of intron-containing vRNA and misregulated expression of vRNA splice variants.
We demonstrate that MCM3AP and DSS1, two other RNA-binding TREX2 complex subunits that comprise the dock of the complex also inhibit transcription initiation and viral RNA alternative splicing during latency and similarly to PCID2 function as prominent latency associated repressors of HIV-1 gene expression. Thus, PCID2 is a novel HIV-1 latency-promoting factor, which in context of the TREX2 sub-complex PCID2-DSS1-MCM3AP blocks transcription and dysregulates vRNA processing.

## P.29

### LOWER EXPOSURE TO BICTEGRAVIR IN THIRD TRIMESTER IN PREGNANT WOMEN LIVING WITH HIV

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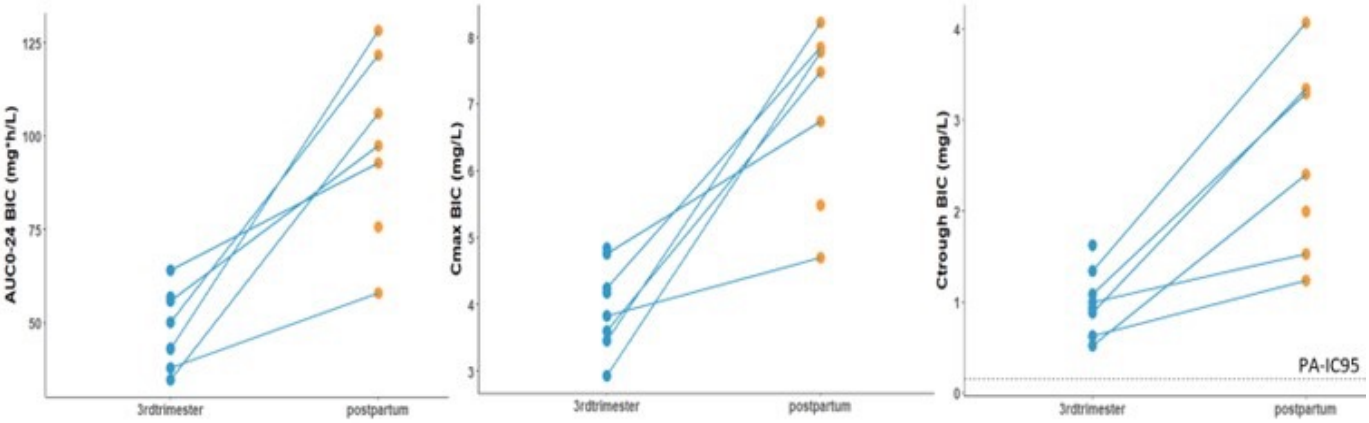
**Background**
Antiretroviral treatment in pregnant women living with HIV reduces the risk of mother to child transmission of the virus, but also to guarantee maternal health. Due to physiological changes during pregnancy, drug concentrations may be altered, whereby drug efficacy might be hampered. The aim of this study was to compare the pharmacokinetic profile of bictegravir during the third trimester of pregnancy and in a non-pregnant state.

**Methods**
In this multicentre, open-label, non-randomized trial pregnant women living with HIV and using a bictegravir containing regimen were included. Pharmacokinetic sampling was performed in the third trimester and 4-6 weeks postpartum. If possible, cord blood and maternal plasma at the delivery date were also collected. Plasma concentrations were determined with the use of LC-MS/MS. Pharmacokinetic parameters were determined with noncompartmental analysis. To evaluate the influence of pregnancy on the pharmacokinetics of bictegravir, a linear mixed-model (with pregnancy as fixed-effect and random effect for participant) was used on the log transformed pharmacokinetic parameters to calculate the geometric mean ratios and 90% confidence interval (CI). Bictegravir trough levels were compared to the protein-adjusted IC95 (PA-IC95) value of 0.162 mg/L. In addition, clinical efficacy and safety outcomes were collected.

**Results**
9 women were included. The median (IQR) age was 33.00 (30-34) years. The geometric mean (CV%) in third trimester for AUC0-24, Cmax, Ctrough, and T1/2 was 47.3 (21.5) h*mg/L, 3.9 (17) mg/L, 0.9 (38.4) mg/L and 12.2 (38.7) (h) respectively. The geometric mean ratio third trimester versus postpartum (90% CI) of AUC0-24, Cmax, Ctrough, and T1/2 were 0.50 (0.40-0.62), 0.59 (0.48-0.73), 0.38 (0.28-0.51) and 0.70 (0.53-0.91) respectively. None of the bictegravir trough levels were below the PA-IC95. No virologic failure or vertical transmission occurred in this cohort. Three cord blood concentrations were obtained, the cord blood:maternal plasma ratios were: 0.65, 1.42 and 1.49 respectively.
No congenital abnormalities were reported.

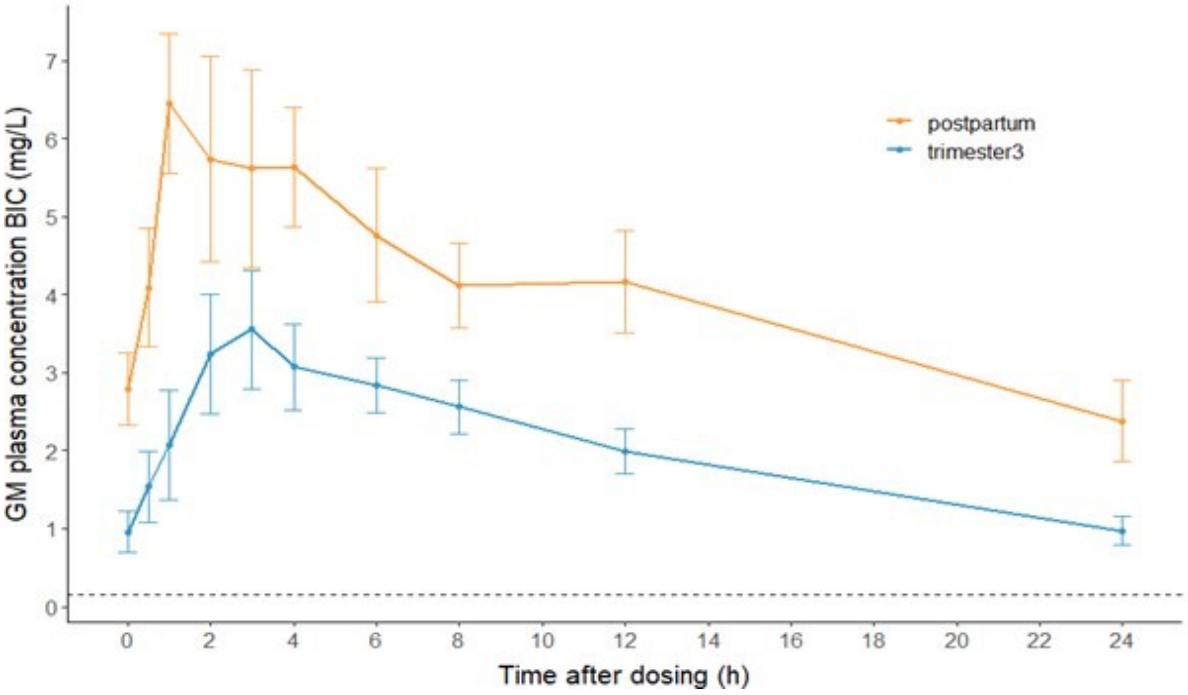
**Conclusion**
The lower exposure to bictegravir in third trimester compared to postpartum might be attributed to increased hepatic clearance trough CYP3A4 and UGT1A1. Despite the decrease, bictegravir trough levels remained above the PA-IC95 and no virological failure or vertical transmission occurred.
More data are needed to confirm our findings.

*P.29 (Figure 1)*




Geometric mean (CV%) of plasma concentrations of bictegravir (mg/L) in pregnancy (blue line) and post-partum (orange line). Dotted line indicates PA-I

*P.29 (Figure 2)*




Intrasubject comparison of AUC0-24, Cmax and Ctrough in pregnancy and postpartum

## P.30

### PHARMACOKINETIC DATA OF ATAZANAVIR/ RITONAVIR IN SECOND-LINE TREATMENT OF CHILDREN LIVING WITH HIV: RESULTS FROM THE CHAPAS4-TRIAL

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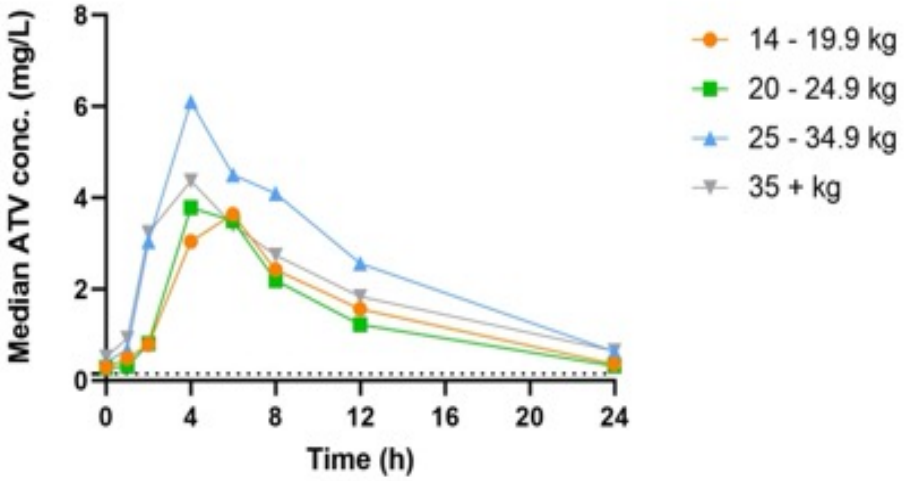
**Background**
In 2022, 1.5 million children were living with HIV worlwide. As children need life-long antiretroviral therapy, the question is raised whether the current second-line antiretroviral regimens are optimal with regard to maximizing children's health gains and minimizing toxicity long-term. Atazanavir/ ritonavir (ATV/r) is recommended by the World Health Organization for children living with HIV as a preferred boosted protease inhibitor for second-line treatment. ATV/r has been evaluated in African children enrolled in the CHAPAS4 trial (#ISRCTN22964075), where second-line treatment options for children with HIV were investigated. We did a pharmacokinetic (PK) sub-study within CHAPAS4 to evaluate the ATV/r exposure in children with HIV.

**Methods**
Children living with HIV aged 3-15 years failing first-line antiretroviral therapy were enrolled. Children in weight bands 14–19.9 and 20–24.9kg received 200/75mg ATV/r and children weighing 25–34.9 and ≥35kg received 300/100mg ATV/r. At steady-state, 8 ATV/r plasma PK samples were taken over 24hours after observed ATV/r intake. The primary pharmacokinetic parameters were the area under the concentration-time curve over 24h (AUC0-24h), maximum concentration (Cmax), and the concentration 24h after intake (Ctrough), calculated using non-compartmental analysis. Reference adult PK data were used for comparison. The individual target trough concentration (Ctrough) was defined as 0.15mg/L (EC90). Statistical analysis was performed using ANOVA on log-transformed values to check for differences in ATV/r AUC0-24 and Ctrough in the different weight-bands and NRTI backbones.

**Results**
A total of 61 children were included in this sub study. Seven children were excluded due to non-adherence, RTV dose deviation or dose taken at the wrong time, leaving 54 eligible PK profiles to evaluate. For the whole study population, the Geometric Mean (GM), (CV%) AUC0-24h was 44.3mg*h/L (47%) and GM (CV%) Cmax was 4.6mg/L (47%), which is comparable to the adult reference values. The AUC0-24h was significantly higher in children weighing 25–34.9 kg (61.1h*mg/L) compared to children in the 14–19.9kg and 20–24.9kg weight-bands (34.1 and 33.2h*mg/L, respectively); p-values <0.05. There was no difference in AUC0-24h when comparing the different backbones. The GM (CV%) Ctrough was 0.48mg/L (70%), which is below the adult reference Cmin (0.64mg/L), but the Ctrough target of 0.15mg/L was achieved in all subjects.

**Conclusions**
This PK sub-study shows that the exposure of ATV/r taken with food in children 3–15 years weighing ≥14kg on second-line treatment is comparable to adult reference data. This data supports the use of an ATV/r based regimen as a second-line treatment option for children in sub-Saharan Africa.

*P.30 (Figure 1)*




Median ATV plasma concentration versus time profiles of the CHAPAS4 sub study by weight band.

## P.31

### DEVELOPING CONTENTS FOR A DIGITAL ADHERENCE TOOL AMONG CHILDREN, ADOLESCENTS AND BREASTFEEDING WOMEN LIVING WITH HIV IN KILIMANJARO, TANZANIA: A MIXED-METHODS STUDY

**Marion Sumari-de Boer**[1,2,3], Iraseni Swai[2,4], Lyidia Masika[2,5], Kennedy Ngowi[2], Alan Mtenga[2], Perry Msoka[2], Benson Mtesha[2], Rob Aarnoutse[6], Tobias Rinke de Wit[4,1,7]

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**Background**
Antiretroviral treatment adherence is a challenge for people living with HIV (PLHIV), and support tools remain important to assist in adhering well. Digital adherence tools (DAT) that offer real-time intervention are promising due to their ability to detect non-adherence with the opportunity to send short messages service (SMS) texts in real-time and provide counselling. We aimed to understand the needs and contents for a customised DAT among children and adolescents (CALHIV) and breastfeeding women living with HIV (BWLHIV).

**Methods**
We conducted a mixed-methods study among CALHIV with their caregivers and BWLHIV. Participants completed a survey at study entry asking disease, treatment, and adherence background information. Then, 60 participants used the DAT for one month. The DAT included (1) using a pillbox that records lid opening, a proxy for medication intake, (2) receiving different types of reminder-SMS varying from asking about medication intake to more neutral one-word messages, and (3) receiving adherence feedback based on reports generated by the DAT. Feedback sessions of 30 minutes focused on identifying solutions to the non-adherence patterns. After that, we conducted exit-interviews, in-depth interviews and focus group discussions. We did descriptive and thematic content analyses. We used the Sekhon framework for acceptability to guide the analysis.

**Results**
We included 142 children (33%), 143 adolescents (33%) and 142 BLHIV (33%) in the survey. Their median ages (interquartile range) were 9(7-12), 18(16-18), and 31(27-36) years, respectively. Median adherence was 94% among breastfeeding women, 99% among children and 72% among adolescents. Nearly a quarter of the participants (22.3%) reported skipping medication over the past month, and 72 (78.5%) missed due to forgetting. Eighty percent (97/121) of children, 78% (94/121) of adolescents and 90% of BLHIV preferred to receive daily reminders with neutral wording. Themes from in-depth interviews were: positive attitude about and have good understanding of the device, perceived high effectiveness of the DAT, SMS to have neutral wording, stigmatization not being present, concerns about being monitored daily, reasons for forgetting to take medication and recommended topics for health education messages. Technical issues and challenges existed due to poor mobile networks, as reported by several participants.

**Conclusion**
This study shows that DAT is acceptable and provides insight into the needed SMS content for a customized DAT for CALHIV and BWLHIV. It is a promising intervention to improve counselling and disease management. Our ongoing randomized clinical trial will assess DATS effectiveness in improving adherence and reducing virological failure.

*P.31 (Table 1) Adolescents SMS Preference (N=20)*

| | | Preferred the SMS? | | |
|---|---|---|---|---|
| | SMS contents | **Yes (%)** | **No (%)** | **Do not remember the SMS (%)** |
| WEEK1 | "Hello, your time to take the medication is near, you are reminded to take your medication on time as directed by the health care workers" | **13(65%)** | 6(30%) | 1(5%) |
| WEEK2 | "Remember to observe your health." | 16(80%) | 3(15%) | 1(5%) |
| | "Remember to protect your health today." | 16(80%) | 3(15%) | 1(5%) |
| | "Don't stop caring for your health today" | 18(90%) | 1(5%) | 1(5%) |
| | "Your time is at hand"? | 15(75%) | 4(20%) | 1(5%) |
| | "You are reminded to protect your health" | 17(85%) | 2(10%) | 1(5%) |
| | "Remember to drink on time"? | 15(75%) | 4(20%) | 1(5%) |
| | "Your time to use is at hand" | 12(60%) | 6(30%) | 2(10%) |
| WEEK3 | "You are reminded to drink"? | 14(70%) | 4(20%) | 2(10%) |
| | "Do not forget to use"? | 16(80%) | 2(10%) | 2(10%) |
| | "The time is at hand"? | 19(95%) | 0(0%) | 1(5%) |
| | "Your health is important" | 18(90%) | 0(0%) | 2(10%) |
| | "Do not forget to protect yourself" | 18(90%) | 1(5%) | 1(5%) |
| | "Care for your health" | 19(95%) | 1(5%) | 0(0%) |
| | "Drinking is caring"! | 9(45%) | 4(20%) | 7(35%) |
| WEEK4 | "Remember"? | 13(65%) | 1(5%) | 6(30%) |
| | "Use"! | 13(65%) | 2(10%) | 5(25%) |
| | "Take care"? | 15(75%) | 1(5%) | 4(20%) |
| | "Drink"? | 15(75%) | 4(20%) | 1(5%) |
| | "Health" | 15(75%) | 1(5%) | 4(20%) |
| | "Care for your health" | 18(90%) | 1(5%) | 1(5%) |
| | "Value health"? | 15(75%) | 1(5%) | 4(20%) |

Preference of SMS for adolescents

*P.31 (Table 2) Children SMS Preference (N=20)*

(Questions were answered by caregivers/parent)

| | | Preferred the SMS? | | |
|---|---|---|---|---|
| | SMS contents | YES (%) | No (%) | Did not remember the SMS (%) |
| WEEK1 | "Hello, you are reminded that the time for your child to take medication is approaching. Kindly give the child the medication on time as instructed by the health care workers. Thank you. | 12(60%) | 8(40%) | 0(0%) |
| WEEK2 | "Remember to observe child's health" | 17(85%) | 1(5%) | 2(10%) |
| | "Kindly, remember to protect the child's health today" | 16(80%) | 1(5%) | 3(15%) |
| | "Don't stop to care for the child's health" | 16(80%) | 1(5%) | 3(15%) |
| | " The time for the child is approaching" | 16(80%) | 2(10%) | 2(10%) |
| | "You are reminded to protect child's health" | 16(80%) | 2(10%) | 2(10%) |
| | "Remember to give the child on time" | 16(80%) | 2(10%) | 2(10%) |
| | "The time for the child to use is at hand" | 18(90%) | 1(5%) | 1(5%) |
| WEEK3 | "You are reminded to feed the child" | 13(65%) | 3(15%) | 4(20%) |
| | "Don't forget to give the child" | 15(75%) | 3(15%) | 2(10%) |
| | "Child's time is approaching" | 16(80%) | 2(10%) | 2(10%) |
| | "Health of the child is important" | 18(90%) | 1(5%) | 1(5%) |
| | "Don't stop to protect the child" | 17(85%) | 1(5%) | 2(10%) |
| | "Care for child's health" | 17(85%) | 1(5%) | 2(10%) |
| | "Feeding the child is the act of caring" | 15(75%) | 2(10%) | 3(15%) |
| WEEK4 | "Remember the child" | 15(75%) | 1(5%) | 4(20%) |
| | "Give the child."? | 13(65%) | 3(15%) | 4(20%) |
| | "Protect the child" | 12(60%) | 4(20%) | 4(20%) |
| | "Feed the child"? | 16(80%) | 0(0%) | 4(20%) |
| | "Care for child's health"? | 16(80%) | 1(5%) | 3(15%) |
| | "Protect child's health" | 17(85%) | 1(5%) | 2(10%) |
| | " Child's health" | 16(80%) | 0(0%) | 4(20%) |

Preference of SMS for children

## P.32

### FACTORS ASSOCIATED WITH PERSISTENT LOW-LEVEL VIREMIA AFTER INITIAL VIROLOGICAL SUPPRESSION IN PEOPLE WITH HIV: AN OBSERVATIONAL COHORT STUDY

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**Background**
Persistent low-level viremia (PLLV) is a common occurrence in people with HIV (PWH) on antiretroviral therapy (ART), even after initially achieving virologic suppression. Its occurrence has been associated with adverse clinical outcomes and gives rise to additional diagnostic testing. This study assesses the odds of PLLV across various ART regimens and evaluates the clinical management after PLLV and its outcomes.

**Methods**
In this cohort study conducted in the University Medical Centre Utrecht, we included virologically suppressed PWH on ART from April 1, 2010, to April 1, 2020, to investigate the association between integrase strand transfer inhibitor (INSTI)-based, protease inhibitor (PI)-based, non-nucleoside reverse transcriptase inhibitor (NNRTI)-based and non-standard ART regimens (i.e. regimens not consisting of two nucleoside/nucleotide reverse transcriptase inhibitors and one anchor), and PLLV. All medical records were reviewed and regimens in which viral loads (VLs) ≥50 cop/mL were deemed to result from non-adherence were excluded. We specifically analyzed PLLV, defined as two or more consecutive VL measurements ≥50 cop/mL more than 30 days apart without meeting virologic failure criteria (i.e., two consecutive VLs ≥ 200 cop/mL or a single VL ≥500 cop/mL), in PWH after virologic suppression. Factors associated with PLLV were analyzed using generalized linear mixed models using a random intercept. Additionally, we evaluated the clinical management and outcomes of PLLV.

**Results**
In total, 1,762 PWH with 3,551 ART regimens were included. Participants were mostly male (80.9%), had a zenith VL ≥100,000 cop/mL (49.0%), and had a median lowest available CD4+ count of 237.0 cells/mm3. The 3,551 treatment courses consisted of 1,010 (28.4%) INSTI-based, 1,276 (35.9%) PI-based, 1,121 (31.6%) NNRTI-based and 144 (4.1%) non-standard regimens. PLLV occurred in 64 (3.6%) participants and 72 (2.0%) ART regimens. In multivariable analyses, a higher odds of PLLV was observed in PI-based (odds ratio 3.18; 95% confidence interval: 1.45-6.96) and non-standard regimens (odds ratio 5.86; 95% confidence interval: 1.26-27.32) compared with INSTI-based regimens (Table 1). Additionally, a higher zenith VL, older age at diagnosis, and shorter time since ART initiation were associated with higher odds of PLLV. Although PLLVs led to a significant clinical burden, the majority of PLLVs were managed without altering the ART regimen (Table 2).

**Conclusion**
In this cohort study, INSTI-based regimens were associated with the lowest odds of PLLV, with a substantial clinical burden of PLLV observed. Further research is needed to investigate underlying mechanisms and improve diagnostic efficacy and clinical management of PLLV.

*P.32 (Table 1) Factors associated with the odds of PLLV in univariable and multivariable generalized linear mixed model analyses*

| | *Univariable analysis* | | *Multivariable analysis* | |
|---|---|---|---|---|
| | ***OR (95% CI)*** | ***p-value*** | ***OR (95% CI)*** | ***p-value*** |
| Male sex (vs. female sex) | 1.47 (0.70 to 3.08) | 0.310 | 1.18 (0.53 to 2.61) | 0.704 |
| Age at diagnosis (per year) | 1.04 (1.02 to 1.06) | **<0.001** | 1.04 (1.02 to 1.06) | **0.005** |
| **ART regimens** | | | | |
| - INSTI-based | 1 | | 1 | |
| - PI-based | 4.13 (1.89 to 9.04) | **<0.001** | 3.18 (1.45 to 6.96) | **0.004** |
| - NNRTI-based | 1.61 (0.67 to 3.86) | 0.286 | 0.93 (0.36 to 2.34) | 0.876 |
| - Non-standard | 10.03 (2.97 to 33.94) | **<0.001** | 5.86 (1.26 to 27.32) | **0.024** |
| Time since ART initiation (per year) | 0.91 (0.86 to 0.97) | **0.003** | 0.90 (0.84 to 0.97) | **0.004** |
| **HIV transmission route** | | | | |
| - MSM | 1 | | - | |
| - Heterosexual | 0.83 (0.41 to 1.71) | 0.615 | | |
| - Intravenous drugs / blood products | 0.34 (0.04 to 2.84) | 0.319 | | |
| - Other / unknown | 1.49 (0.77 to 2.89) | 0.233 | | |
| $HBsAg^+$ at any point during FU individual | 1.14 (0.29 to 4.47) | 0.846 | - | |
| HCV $RNA^+$ at any point during FU individual | 1.60 (0.41 to 6.16) | 0.496 | - | |
| Lowest available $CD4^+$ count (cells/$mm^3$) | 0.97 (0.93 to 1.01) | 0.189 | 1.01 (0.96 to 1.06) | 0.765 |
| **Zenith VL (cop/mL)** | | | | |
| - <100,000 | 1 | | 1 | |
| - ≥100,000 | 2.72 (1.37 to 5.37) | **0.004** | 2.32 (1.15 to 4.67) | **0.018** |
| Follow-up duration of treatment course (per year) | 1.20 (1.09 to 1.32) | **<0.001** | 1.17 (1.06 to 1.30) | **0.002** |

*ART: antiretroviral therapy; cop: copies; HBsAg: hepatitis B surface antigen; HCV: hepatitis C virus; MSM: men who have sex with men; VL: viral load.*

*P.32 (Table 2) Clinical management of the 72 PLLV instances*

| | *72 PLLV instances (%)* |
|---|---|
| **Additional viral load measurement** | |
| - 1 measurement | 40 (55.5) |
| - 2 measurements | 15 (20.8) |
| - ≥3 measurements | 5 (6.9) |
| **Additional telephonic consultation** | |
| - 1 consultation | 27 (37.5) |
| - 2-4 consultations | 24 (33.3) |
| - ≥ 5 consultations | 12 (16.7) |
| **Additional outpatient visit** | |
| - 1 visit | 21 (29.2) |
| - 2-3 visits | 9 (12.5) |
| - ≥ 4 visits | 5 (6.9) |
| **Drug level measurement*** | 42 (58.3) |
| - Abnormal result | - 15/42 (35.7) |
| **Lumbar puncture*** | 9 (12.5) |
| - Abnormal result | - 1/9 (11.1) |
| **Pharmacokinetic curve** | 7 (9.7) |
| **Genotyping*** | 22 (30.6) |
| - Abnormal result | - 2/22 (9.1) |
| - Unclear | - 3/22 (13.6) |
| **Tropism determination** | 10 (13.9) |
| **ART regimen switch** | |
| - No switch | 44 (61.1) |
| - Switched ART regimen in absence of abnormal diagnostic findings | 14 (19.4) |
| - Switched ART regimen due to abnormal diagnostic findings | 14 (19.4) |

*ART: antiretroviral therapy; PLLV: persistent low-level viremia*

* Drug level measurements were considered abnormal in case of subtherapeutic levels, lumbar punctures were considered abnormal in case of cerebrospinal fluid viral RNA levels >200 cop/mL and genotyping was considered abnormal if discrepant from baseline or pre-ART results