# The Amsterdam Cohort Studies on HIV infection: annual report 2016

## Amy Matser and Maria Prins for the ACS

**Introduction**

The Amsterdam Cohort Studies (ACS) on HIV infection and AIDS were started shortly after the first cases of AIDS were diagnosed in the Netherlands. Since October 1984, men who have sex with men (MSM) have been enrolled in a prospective cohort study. A second cohort involving people who use drugs (PWUD) was initiated in 1985. In 2016, the cohorts reached 32 years of follow up. The initial aim of the ACS was to investigate the prevalence and incidence of HIV-1 infection and AIDS, the associated risk factors, the natural history and pathogenesis of HIV-1 infection, and the effects of interventions. During the past 32 years, these aims have remained primarily the same, although the emphasis of the studies has changed. Early on, the primary focus was to elucidate the epidemiology of HIV-1 infection, whereas later more in-depth studies were performed to investigate the pathogenesis of HIV-1 infection. In the past decade, research on the epidemiology of other blood-borne and sexually transmitted infections (STI) and their interaction with HIV has become an important component of the ACS research programme.

From the beginning, research in the ACS has taken a multidisciplinary approach (epidemiology, social science, virology, immunology and clinical medicine). This unique collaboration has been very productive, significantly contributing to the knowledge and understanding of many different aspects of HIV-1 infection. This expertise, in turn, has contributed directly to advances in prevention, diagnosis, and management of HIV infection.

**Collaborating institutes and funding**

Within the ACS, different institutes collaborate to bring together the data and biological sample collections and to conduct research. These include the Public Health Service of Amsterdam (*Gemeentelijke Gezondheidsdienst Amsterdam*; GGD Amsterdam) (Department of Infectious Diseases, Research and Prevention), the Academic Medical Center (AMC) of the University of Amsterdam (Departments of Medical Microbiology, Experimental Immunology, and Internal Medicine, Division of Infectious Diseases, HIV treatment centre, Emma Kinderziekenhuis), Stichting HIV Monitoring (SHM), the Jan van Goyen Medical Centre (Department of Internal Medicine) and the HIV Focus Centre (DC Klinieken) Amsterdam. From the start, Sanquin Blood Supply Foundation has been involved in the ACS and, until 2007, research in the ACS was conducted by the Department of Clinical Viro-Immunology at Sanquin Research. Sanquin financially supports the maintenance of the biobank of viable peripheral blood mononuclear cells (PBMC) at the AMC's Department of Experimental Immunology. In addition, there are numerous collaborations between the ACS and other research groups both within and outside the Netherlands. The ACS is financially supported by the Centre for Infectious Disease Control of the National Institute for Public Health and the Environment (*Centrum voor Infectieziektenbestrijding-Rijksinstituut voor Volksgezondheid en Milieu,* RIVM-CIb).

**Ethics statement**

The ACS have been conducted in accordance with the ethical principles set out in the declaration of Helsinki. Participation in the ACS is voluntary and written informed consent is obtained from each participant. The most recent version was approved by the AMC Medical Ethics Committee in 2007 for the MSM cohort and in 2009 for the PWUD cohort.

## The ACS in 2016

**The cohort of men who have sex with men**

As of 31 December 2016, 2,736 MSM were included in the ACS. Every three to six months, participants complete a standardised questionnaire designed to obtain information regarding

medical history, sexual and drug use behaviour, underlying psychosocial determinants, healthcare use, depression, psychological disorders, and demographics. Blood is collected for diagnostic tests and storage. Of the 2,736 MSM, 607 were HIV-positive at entry into the study, and 251 seroconverted during follow up. In total, the GGD Amsterdam was visited 57,467 times by MSM.

Until 1995, HIV-negative men of all age groups were eligible to participate if they lived in or around Amsterdam and had had at least two male sexual partners in the previous six months. During the period 1995–2004, only HIV-negative men aged ≤30 years with at least one male sexual partner in the previous six months could enter the study. Since 2005, recruitment has been open to HIV-negative MSM of all ages with at least one sexual partner in the preceding six months. In line with the advice issued by the international scientific advisory committee in 2013, the cohort made additional efforts to recruit young HIV-negative MSM. HIV-seroconverters within the ACS remained in the cohort until 1999, when follow up of a selection of HIV-positive MSM was transferred to the Jan van Goyen Medical Centre. In 2003, the 'HIV Onderzoek onder Positieven' (HOP) protocol (*HIV Research in Positive Individuals*) was initiated. Individuals with a recent HIV infection at study entry at the GGD Amsterdam and those who seroconverted for HIV during follow-up within the cohort continue to return for study visits at the GGD Amsterdam or at an HIV treatment centre. All behavioural data are collected on a six-monthly basis by questionnaires, coordinated by the GGD Amsterdam, and clinical data are provided by SHM.

In 2016, 630 HIV-negative, and 64 HIV-positive MSM were in active follow up within the ACS (6-monthly visits to the GGD Amsterdam for STI testing, including HIV). Of these 64 HIV-positive MSM, 62 filled in behavioural questionnaires. Apart from the HIV-positive MSM visiting the GGD Amsterdam, 267 HIV-positive MSM were followed outside the GGD Amsterdam at the Jan van Goyen Medical Centre or the HIV Focus Centre in Amsterdam. Behavioural questionnaires were filled in by 20 of these men. The median age of the total group of MSM was 44.5 years (interquartile range [IQR] 37.3-52.1), 8.2% were non-Dutch, and 72.8% had attained a high level of education. The majority of the participants (84.6%) were residents of Amsterdam. In 2016, 23

new HIV-negative MSM were recruited. The median age in this group was 23.9 years (IQR 23.2-26.6).

**The cohort of drug users**

As of 31 December 2016, 1,680 people who use drugs (PWUD) were included in the ACS and contributed 28,194 visits. Before 2014, participants visited the GGD Amsterdam every four to six months. They completed a standardised questionnaire designed to obtain information regarding medical history, sexual and drug use behaviour, underlying psychosocial determinants, healthcare use, depression, psychological disorders, and demographics. In addition, HIV-positive participants, and in the past also HIV-negative participants, underwent a medical examination. Blood was collected for diagnostic tests and storage.

In 2014, the cohort was closed for new participants and PWUD included in the ACS were divided into two groups in line with the advice of the international scientific advisory committee in 2013. Group 1 consisted of PWUD who visited the GGD Amsterdam once a year to complete questionnaires with no testing and blood sampling. Group 2, the focus group, consisted of PWUD who were 1) HIV positive; 2) hepatitis C virus (HCV) seroconverters; 3) multiple-exposed, non-infected with HIV and HCV, and 4) a random control group. This group visited the GGD Amsterdam twice a year for testing and blood sampling and to fill out questionnaires, as in previous years. Regular follow-up of drug users continued until February 2016. Finally, all drug users who had ever participated in the ACS were invited for an end-of-study interview. A total of 182 end-of-study interviews were held between February and July 2016, after which the follow up of drug users was successfully ended.

Of the 1,680 PWUD, 323 were HIV-positive at entry, and 99 seroconverted during follow up. The last HIV seroconversion was seen in 2012. By 31 December 2016, 576 deaths had been confirmed among PWUD. The median age of the PWUD who visited the ACS in 2016 was 55 (IQR 49-59), 8.1% had attained a high level of education, and 63.4% were born in the Netherlands.

## ACS Biobank

The ACS visits, together with data collection from several subgroup studies and affiliated studies embedded in the ACS, have resulted in a large collection of stored samples. The ACS biobank includes plasma/serum and PBMC samples collected within the context of the Primo-SHM study (a national randomised study on the effects of early temporary antiviral therapy as compared to no therapy among patients who presented with primary HIV-1 infection at the AMC outpatient clinic and ACS seroconverters). These samples are stored at the AMC. At present, the biological samples are still being collected prospectively for Primo-SHM participants visiting the AMC clinic until one year after they have recommenced therapy. The ACS biobank also includes plasma and PBMC samples that were collected from HIV-positive and HIV-exposed children at the Emma Kinderziekenhuis in the AMC until 2008. All stored samples are available for ACS research.

## Subgroup studies and affiliated studies

### $AGE_hIV$ cohort study

The $AGE_hIV$ cohort study, a collaboration between the AMC Department of Infectious Diseases, Department of Global Health, Amsterdam Institute of Global Health and Development, the GGD Amsterdam, and SHM, was started in October 2010. The aim of the study is to assess the prevalence and incidence of a broad range of comorbidities and known risk factors for these comorbidities in HIV-infected patients aged ≥45 years, and to determine the extent to which comorbidities, their risk factors and their relation to quality of life differ between HIV-infected and uninfected groups. Participants undergo a comprehensive assessment for comorbidities and complete a questionnaire at intake and follow-up questionnaires every 2 years afterwards. In total, 598 HIV-1-infected participants and 550 HIV-uninfected individuals completed a baseline visit between October 2010 and September 2012. HIV-1-infected participants were included through the AMC HIV outpatient clinic and HIV-uninfected participants from similar risk groups through the STI clinic of the GGD Amsterdam (n=486) or the ACS (n=64). All participants were

aged ≥45 years and were as comparable as possible with respect to age, gender, ethnicity, and risk behaviour. By the end of 2016, 437 HIV-1-infected participants and 457 HIV-uninfected individuals had completed the third follow-up visit. In October 2016 the fourth round of study visits started, which is expected to continue until summer 2019.

**H2M cohort study**

From 2010 to 2013, the H2M (HIV and human papillomavirus [HPV] in MSM) cohort study was conducted in a subset of the HIV-negative (n=459) and HIV-positive (n=40) participants of the ACS who were in active follow up, and also among patients of the STI clinic of GGD Amsterdam and the Jan van Goyen Medical Centre. The aim of the study was to compare the prevalence, incidence, and clearance of high-risk (hr) HPV infections between HIV-negative and HIV-infected MSM.

In 2015, a study based on the H2M cohort was initiated to identify potential predictors for high-grade anal intra-epithelial neoplasia in the HIV-infected MSM population. This study, the H2M2, is an Aids Fonds-supported project and a collaboration between the GGD Amsterdam, AMC, DC Klinieken Oud-Zuid, the RIVM-CIb, DDL diagnostic laboratories and VUmc. The study includes a subset of the HIV-positive participants of the ACS (n=19). In 2016, initial analyses showed that among 193 HIV-infected MSM, neither persistence of anal HPV infection nor HPV viral load in the anal mucosa nor anti-HPV antibodies in serum were good predictors of anal high-grade dysplasia.

Since September 2014, collection of anal and genital swabs has been resumed in all consenting ACS participants. The key aim of this second new study (the H2M3 study), which builds on the H2M study, is to examine long-term incidence and clearance of anal and penile hrHPV infections. Between September 2014 and November 2015, 700 men provided samples for HPV testing during ACS cohort visits. Of these, 434 (62%) were already participating in the H2M study (recruited 2010-2011), and 266 (38%) were new participants who joined the ACS after inclusion in the H2M study had ended. Samples at two time points (6 months apart) have been tested in

the laboratory for HPV DNA, and initial analyses have been conducted. This study found that one-third of MSM had not cleared an anal HPV-16 infection after four years; thus, persistence of anal HPV is common. Twenty-two percent of men who were not infected with HPV-16 at baseline acquired an anal HPV-16 infection over a four-year period. So, even in highly pre-exposed men, the incidence rate of hrHPV infections is high. The H2M3 study is a collaboration between GGD Amsterdam, ACS, and Crucell.

**AMPrEP project in H-TEAM**

The Amsterdam pre-exposure prophylaxis (AMPrEP) project is a prospective, longitudinal, open-label demonstration study. The aim of the study is to assess the uptake and acceptibility of daily versus event-driven PrEP among MSM and transgender persons (TG) at increased risk for HIV infection, as part of a comprehensive HIV reduction package offered at a large STI clinic.

In total, 374 MSM and 2 TG were enrolled between August 2015 and May 2016 at the STI outpatient clinic of the GGD Amsterdam. In 2016, 35 ACS participants also participated in the AMPrEP project at their own initiative. Participants were asked to return for follow-up visits one month after the PrEP start visit and then every three months. At every visit participants fill in questionnaires on risk behaviour, adherence and general wellbeing and are screened for STI and HIV. Participants will be provided with PrEP until June 2018.

The AMPrEP project is part of the HIV Transmission Elimination Amsterdam (H-TEAM) initiative, a multidisciplinary and integrative approach to stop the epidemic (www.hteam.nl).

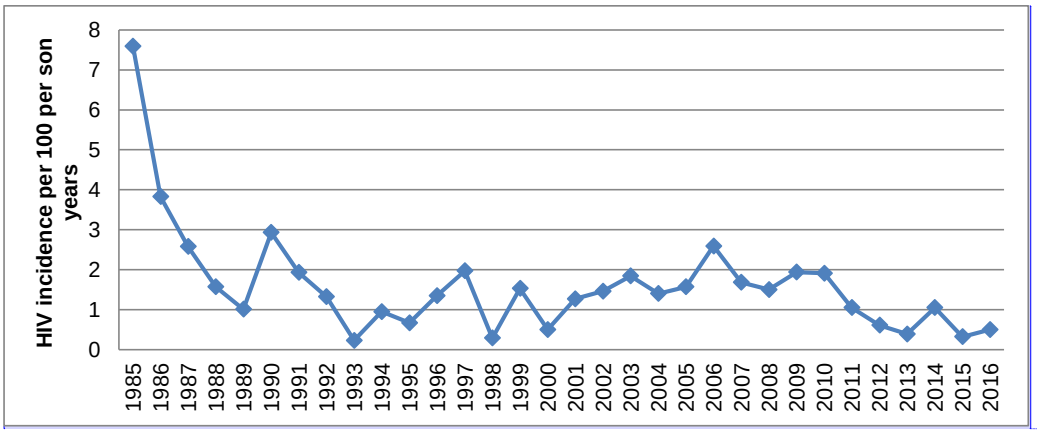
## The HIV epidemic

**HIV incidence**

In 2016, 3 MSM participating in the ACS seroconverted for HIV. The observed HIV incidence among MSM has remained relatively stable in recent years and was 0.5 per 100 person years in

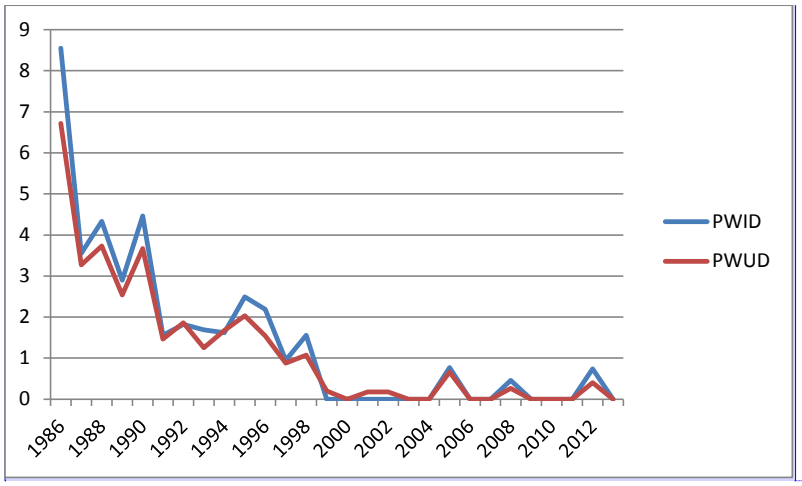
2016. The HIV incidence in PWUD has been stable since 2008, with between zero to less than one case per 100 person years. As follow up was restricted to a selection of PWUD and inclusion stopped in 2014, followed by closure of the cohort in 2016, the yearly observed incidence of PWUD can only be presented until 2013. *Figure 8.1* and *8.2* show the yearly observed HIV incidence rates for MSM and PWUD from the start of the ACS through 2016 and 2013, respectively.

***Figure 8.1:*** *HIV incidence per calendar year in the Amsterdam Cohort Studies (ACS) among men who have sex with men (MSM), 1985-2016.*




**Opmerking [CE1]:** Zest:
X-as: toevoegen: *Calendar year*

***Figure 8.2:*** *HIV incidence per calendar year in the Amsterdam Cohort Studies (ACS) among people who use drugs, 1986-2013.*




**Opmerking [CE2]:** Amy: in het bestand 'getallen voor drukker' lijkt dit grafiek te zijn omgedraaid. Er is een piek in 2012. Welke moeten we aanhouden?

**Opmerking [G3]:** Het figuur in dit bestand klopt. Ik snap niet helemaal waarom de figuur in het bestand van de drukker wat anders weergeeft, want met de getallen die daar in de table staan kun je wel het goede figuur maken. De getallen in de tabel voor de drukker kloppen

**Opmerking [CE4]:** Zest:
1)X-as: toevoegen: *Calendar year*
2) Y-*as: HIV incidence per 100 person years*

***Legend:*** *PWID=people who inject drugs; PWUD=people who use drugs (including injecting).*

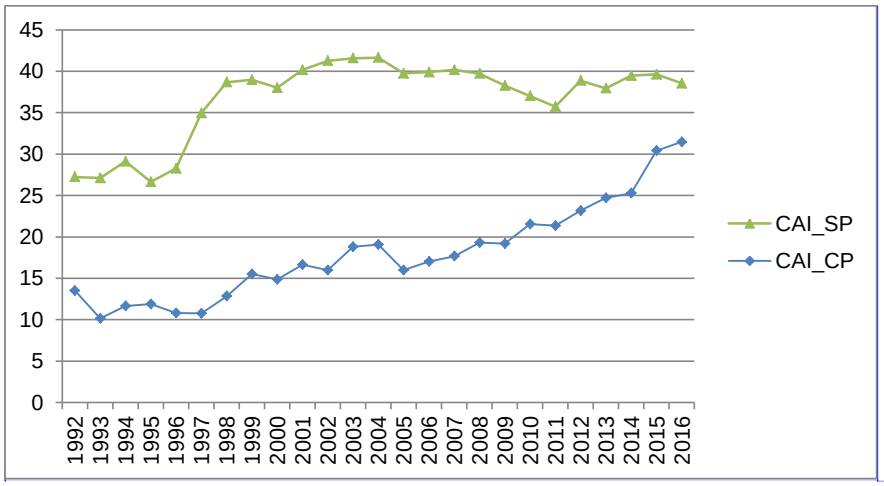
**Combination antiretroviral therapy (cART) uptake**

Of all 320 HIV-positive MSM from the ACS visiting the HIV Focus Centre, the Jan van Goyen Medical Centre or one of the other HIV treatment centres in the Netherlands in 2016, treatment data were available for 317 men. Of these, 314 (99%) received some form of antiretroviral therapy. Of the 308 MSM for whom viral load results were available in 2016, 286 (93%) had a viral load of <50 copies/ml (M2000rt assays).

**Risk behaviour of MSM in ACS**

Information from the questionnaires completed by 610 HIV-negative MSM during cohort visits in 2016 showed higher proportions of condomless anal intercourse (CAI) with steady partners (39.6%) compared to casual partners (30.4%). Trends in CAI among HIV-negative MSM participating in the ACS, especially CAI with casual partners, continue to show a gradual increase from 1996 onwards. (*Figure 8.3*).

***Figure 8.3:*** *Trends shown by the Amsterdam Cohort Studies (ACS) in condomless anal intercourse (CAI) with casual and steady partners in the past six months among HIV-negative men who have sex with men (MSM) with a casual and/or steady partner, 1992-2016.*




**Opmerking [CE5]:** Zest
1) x-as: *Calendar year*
2) y-as: Proportion of CAI
3) streepje tussen CAI en SP of CP vervangen met een spatie

***Legend:*** *CAI=condomless anal intercourse; SP=steady partner; CP=casual partner.*

**STI screening among MSM in ACS**

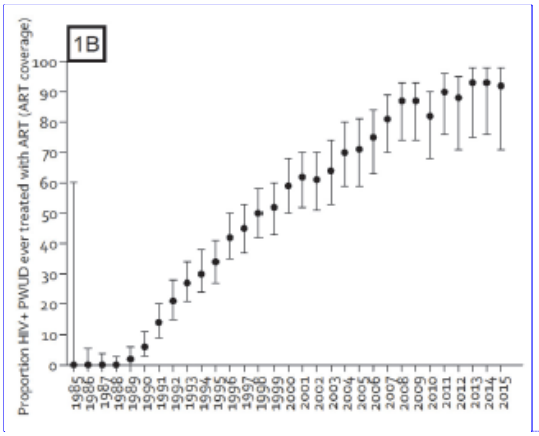
Since October 2008, all MSM in the ACS have been routinely screened for chlamydia and gonorrhoea by polymerase chain reaction (PCR) techniques using urine samples and pharyngeal and rectal swabs. Cases of syphilis are detected by *Treponema pallidum* haemagglutination assay (TPHA). In 2016, a total of 665 MSM from the ACS were screened for STI. The overall prevalence of any STI (i.e., chlamydia, gonorrhoea, syphilis, and HCV) was 15.9% (99/621) among HIV-negative MSM and 29.5% (13/44) among HIV-positive MSM.

**HIV and HCV treatment uptake among PWUD in ACS**

ART coverage increased over time, from 5.7% in 1990 and 42.2% in 1996 to 91.7% in 2015 (see *Figure 8.4*). The proportion of PWUD initiating ART ranged from 4.8% in 1990 to 33.3% in 2011. At eight years after HIV seroconversion, the cumulative probability of ART uptake was 42.5% in the pre-cART era and 61.5% in the cART era. HCV treatment initiation peaked in 2006 (9.7%). HCV treatment coverage was 43.9% in 2015 (see *Figure 9.5*), but lower among HIV co-infected (23.5%) than HCV mono-infected PWUD (52.5%). In 2015, 3.0% initiated HCV treatment with direct-acting antivirals. [Van Santen D, et al. Intern J Drug Pol. 2017;47:95-101]

**Opmerking [CE6]:** Catriona: add reference

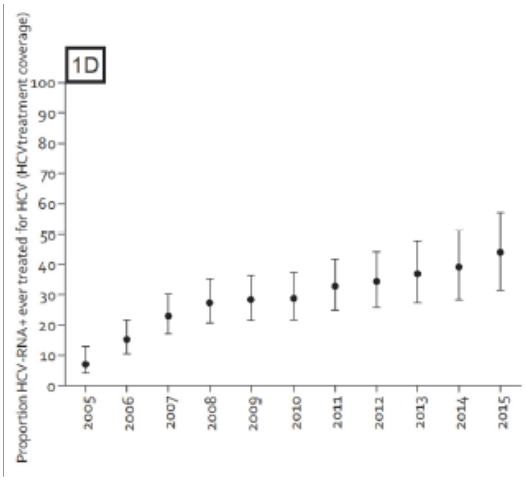
***Figure 8.4:*** *The proportion of HIV-positive people who use drugs (PWUD) participating in the Amsterdam Cohort Studies (ACS) ever treated with ART, 1989-2015.* ***[***Van Santen D, et al. Intern J Drug Pol. 2017;47:95-101]




**Opmerking [CE7]:** Zest:
1) linksboven 1B verwijdern

***Legend:*** *PWUD=people who use drugs; ART=antiretroviral therapy.*

***Figure 8.5:*** *The proportion HVC RNA-positive people who use drugs (PWUD) participating in the Amsterdam Cohort Studies (ACS) ever treated for HCV, 2005-2015.* ***[***Van Santen D, et al. Intern J Drug Pol. 2017;47:95-101]



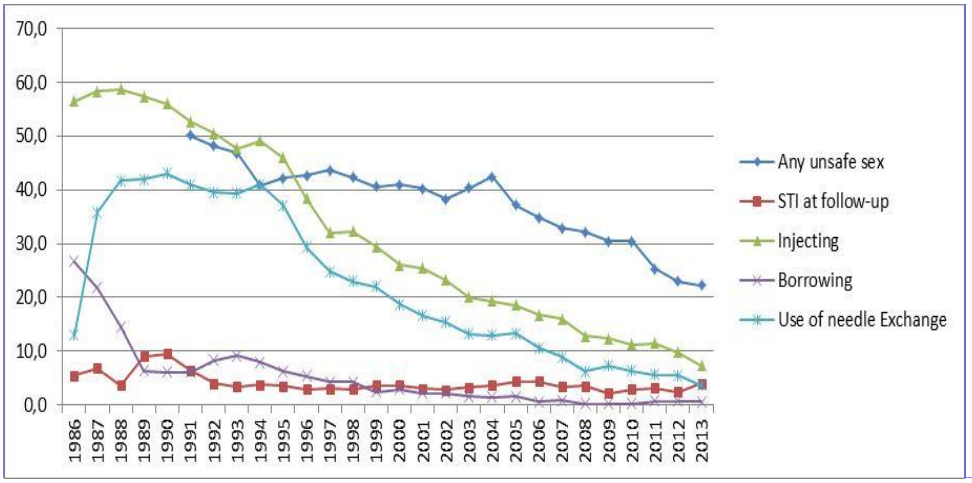

**Opmerking [CE8]:** Zest:
1) linksboven: 1D verwijderen
2) y-as: verbindingstreepje tussen HCV en RNA verwijderen

***Legend:*** *HCV=hepatitis C virus.*

**Risk behaviour of PWUD in ACS**

As follow up was restricted to a selection of PWUD and inclusion stopped in 2014, and the cohort was closed in 2016, trends in risk behaviour of PWUD can only be presented until 2013. In HIV-negative PWUD, reports of both injection and borrowing needles significantly declined over the period 1985-2013. Reports of high-risk sexual behaviour at follow-up visits decreased before 1996, then remained relatively stable until 2005, and further decreased to approximately 22% in 2013. Reports of STI have remained relatively stable at approximately 1% in recent years (see *Figure 8.6*).

***Figure 8.6:*** *Proportion of visits per calendar year at which injecting and high-risk sexual behaviour was reported amongst people who use drugs (PWUD) who were HIV-negative on entry to the Amsterdam Cohort Studies (ACS), 1986-2013.*




**Opmerking [CE9]:** Zest:
1) X-as: *Calendar year*
2)Y-as: *Proportion of visits*
3) Y-as: ‘,’0’ verwijderen. Dus 0, 10, 20, 30 etc….
4) Legende: streepje tussen *follow* en *up* vervangen met spatie
5)Legende: geen hoofdletter bij *Exchange*

***Legend:*** *STI=sexually transmitted infection.*

**ACS 2016 research highlights**

**IP-10, a marker of HIV-1 disease progression**

Elevated blood CXCL10/IP-10 levels during primary HIV-1 infection have been described as an independent marker of rapid disease onset and one that is more robust than peak viraemia or CD4 cell nadir. IP-10 enhances the recruitment of CXCR3+ cells, which include major HIV target cells, raising the question whether it promotes the establishment of viral reservoirs. Data from four cohorts of HIV+ patients were analysed, allowing us to study IP-10 levels before infection (data from ACS), as well as during controlled and uncontrolled viraemia (data from ANRS cohorts). Pre-existing elevated IP-10 levels, but not sCD163, were associated with rapid CD4 T-cell loss upon HIV-1 infection. During primary HIV infection, IP-10 levels, and to a lesser extent IL-18 levels, correlated with cell-associated HIV DNA, while 26 other inflammatory soluble markers did not. IP-10 levels tended to differ between HIV controllers with detectable and undetectable viraemia. [Ploquin MJ, et al. PloS Pathog. 2016; 12:e1005774]

**New target to tackle HIV**

Monoclonal antibodies were isolated from an elite neutraliser from the ACS. We found an antibody with very potent neutralising properties. Using negative stain electron microscopy and other techniques, we found that this antibody bound to a novel target epitope, showing the fusion peptide on the envelope glycoprotein needed to infect target cells as a site of vulnerability. In addition, we also constructed soluble native-like envelope glycoproteins from early virus variants of the same elite neutraliaer. The availability of a native-like Env trimer and a broadly neutralising antibody (bNAb) from the same elite neutraliaer opens new avenues for HIV vaccine design aimed at generating similar bNAbs against a key functional site on HIV. [van Gils MJ, et al. Nat Microbiol. 2016; 2:16199]

**The power of the ACS: tracing the origin of the hepatitis B virus (HBV) G variant in Amsterdam**

HBV genotype G (HBV-G) is an aberrant genotype with little sequence divergence, suggesting that it has a recent origin. HBV-G is also strongly associated with people who inject drugs (PWID) and MSM. To estimate the prevalence and possible time of introduction of HBV-G into the MSM community in Amsterdam, we retrospectively analysed 226 blood plasma samples from HBsAg positive MSM enrolled in the ACS dating from 1984-1999 using HBV genotype-specific PCR assays. Of the 226 ACS samples, 149 were HBV DNA positive. Of those, 104 were HBV-A+, 5 were HBV-G+ and 40 showed a dual infection with HBV-A and HBV-G. Infection with HIV-1 was significantly associated with a lower HBV DNA plasma viral load (pVL), but not with the prevalence of HBV-G. Early virus isolates from 1985 already contained the typical HBV-G characteristics: stopcodons in the preCore region and a 36-nt insert in the core gene. In addition, a G1776A mutation was observed in half of the strains. Thus, HBV-G was introduced into the Amsterdam MSM community before 1985. These early isolates show extremely limited sequence variation with modern isolates, suggesting a low evolutionary rate. HBV-G acquisition was independent of HIV-1 infection, but HIV-1 infection was associated with a significantly reduced HBV pVL, indicating a beneficial effect of initial HIV-1 infection on HBV replication. [Cornelissen M, et al. BMC Infectious Diseases 2016; 16:268]

**Group sex**

The association between group sex and lower condom use during anal sex and higher proportions of STI were assessed and compared to dyadic sex among HIV-negative MSM between 2009 and 2012. The sample consisted of 465 MSM who either reported *both* group and dyadic sex (at n=706 visits) or dyadic sex *only* (at n=1339 visits) in the preceding six months. Logistic regression with generalised estimating equations was used to investigate the association between sexual setting (group versus dyadic sex), CAI, and STI. Group sex was reported at 35% (706/2045) of visits. Condomless sex was more often reported during dyadic than group sex (odds ratio [OR] 3.64; 95% CI 2.57–5.16). Men who had group sex were more likely to be diagnosed with gonorrhoea compared to men with dyadic sex (OR 1.71; 95% CI 1.08–2.97), but this effect was not retained in the multivariable model. Results demonstrate that MSM are more likely to use condoms during group sex than dyadic sex. Thus, for some, group sex may not necessarily be risky for HIV infection compared to dyadic sex. However, group sex may be a higher-risk setting for acquiring STIs other than HIV, such as gonorrhoea. [Van den Boom, et al. Sex Transm Infect 2016; 43(2):99-104]

**Cost-effectiveness of HCV treatment among PWID**

The cost-effectiveness of four HCV treatment strategies among PWID and treatment scale-up were assessed. An individual-based mathematical model was used describing HIV and HCV transmission and disease progression among PWID in a declining HCV epidemic, as observed in Amsterdam, and a stable HCV epidemic. We assessed the incremental cost-effectiveness ratio (ICER, costs in €/quality-adjusted life year (QALY)) of four treatment strategies: 1) PegIFN/RBV; 2) sofosbuvir/RBV for genotype 2±3 and dual DAA for genotype 1±4; 3) Dual DAA for all genotypes; 4) Dual DAA with 3x treatment uptake. In both types of epidemic, dual DAA therapy was the most cost-effective strategy. In the declining epidemic, dual DAA yielded an ICER of 344 €/QALY while in the stable epidemic dual DAA led to cost-savings. Scaling-up treatment was also highly cost-effective. We conclude that HCV treatment with DAA-containing regimens is a highly cost-effective intervention among PWID. [van Santen DK, et al. PLoS One. 2016; 11(10):e0163488]

**Steering committee**

In 2016, the steering committee met three times. Twelve proposals for use of data and/or samples (serum/PBMC) were submitted to the committee: six from the AMC Medical Microbiology department, four from the AMC Experimental Immunology, and 2 from GGD Amsterdam. Eight of the proposals were collaborations with groups outside the ACS. Nine requests were approved, and three were declined even after revision.

**Publications in 2016 that include ACS data**

**Motives of Dutch men who have sex with men for daily and intermittent HIV pre-exposure prophylaxis usage and preferences for implementation: A qualitative study**

Bil JP, van der Veldt WM, Prins M, Stolte IG, Davidovich U.

*Medicine (Baltimore). 2016;95(39):e4910*

**Changing incidence and risk factors for Kaposi sarcoma by time since starting antiretroviral therapy: Collaborative analysis of 21 European cohort studies**

Cancer Project Working Group for the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) study in EuroCoord.

*Clin Infect Dis. 2016; 63(10):1373-1379*

**The neutralizing antibody response in an individual with triple HIV-1 infection remains directed at the first infecting subtype**

Cornelissen M, Euler Z, Van den Kerkhof TLGM, Van Gils MJ, Boeser-Nunnink BDM, *et al. AIDS Res Hum Retroviruses. 2016;32(10-11):1135-1142*

**Widespread hepatitis B virus genotype G (HBV-G) infection during the early years of the HIV-1 epidemic in Dutch men having sex with men**

Cornelissen M, Zorgdrager F, Bruisten SM, Bakker M, Berkhout B, van der Kuyl AC.

*BMC Infect Dis. 2016; 16:268*

**HCV monoinfection and HIV/HCV coinfection enhance T-cell immune senescence in injecting drug users early during infection**

Grady BP, Nanlohy NM, van Baarle D.

*Immun Ageing. 2016;13:10*

**Higher rates of triple-class virological failure in perinatally HIV-infected teenagers compared with heterosexually infected young adults in Europe**

Judd A, Lodwick R, Noguera-Julian A, Gibb DM, Butler K, et al. Pursuing Later Treatment Options II (PLATO II) Project Team for the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) in EuroCoord.

*HIV Med. Sept. 2016 [Epub ahead of print]*

**Hepatitis C virus broadly neutralizing monoclonal antibodies isolated 25 years after spontaneous clearance**

Merat SJ, Molenkamp R, Wagner K, Koekkoek SM, van de Berg D, *et al.*

*PLoS One. 2016;11(10):e0165047*

**The effect of HIV infection on anal and penile human papillomavirus incidence and clearance: a cohort study among MSM**

Mooij SH, van Santen DK, Geskus RB, van der Sande MA, Coutinho RA, et al.

*AIDS. 2016;30(1):121-32.*

**Limiting cumulative HIV viremia copy-years by early treatment reduces risk of AIDS and death**

Olsen AD, Walker AS, Suthar AB, Sabin C, Bucher HC, et al. CASCADE Collaboration in EuroCoord.

*J Acquir Immune Defic Syndr. 2016;73:100-108*

**A novel astrovirus-like RNA virus detected in human stool**

Oude Munnink BB, Cotten M, Canuti M, Deijs M, Jebbink MF, *et al.*

*Virus Evol. 2016;2(1):vew005*

**A novel genus in the order Picornavirales detected in human stool**

Oude Munnink BB, Cotten M, Deijs M, Jebbink MF, Bakker M, *et al.*

*J Gen Virol. 2015;96(11):3440-3*

**Interferon lambda 4 genotype is associated with jaundice and elevated aminotransferase levels during acute hepatitis C virus infection: findings from the InC3 Collaborative**

Page K, Mirzazadeh A, Rice TM, Grebely J, Kim AY, *et al.*

*Open Forum Infect Dis. 2016;3:ofw024.*

**The impact of transient combination antiretroviral treatment in early HIV infection on viral suppression and immunologic response in later treatment** Pantazis N, Touloumi G, Meyer L, Olson A, Costagliola D, et al. CASCADE Collaboration in EuroCoord.

*AIDS. 2016;30(6):879-888*

**Kaposi sarcoma risk in HIV-infected children and adolescents on combination antiretroviral therapy from sub-Saharan Africa, Europe, and Asia**

Pediatric AIDS-Defining Cancer Project Working Group for IeDEA Southern Africa, TApHOD, and COHERE in EuroCoord.

*Clin Infect Dis. 2016;63(9):1245-1253*

**Elevated basal pre-infection CXCL10 in plasma and in the small intestine after infection are associated with more rapid HIV/SIV disease onset**

Ploquin MJ, Madec Y, Casrouge A, Huot N, Passaes C, *et al.*

*PLoS Pathog. 2016;12(8):e1005774*

**Historical trends in the hepatitis C virus epidemics in North America and Australia** Rodrigo C, Eltahla AA, Bull RA, Grebely J, Dore GJ, *et al.* InC3 Study Group.
*J Infect Dis. 2016;214(9):138301389*

**The effects of alcohol on spontaneous clearance of acute hepatitis C virus infection in females versus males**
Tsui JI, Mirzazadeh A, Hahn JA, Maher L, Bruneau J, *et al.*
*Drug Alcohol Depend. 2016;169:156-162*

**Is group sex a higher-risk setting for HIV and other sexually transmitted infections compared with dyadic sex among men Who have sex with men?**
Van den Boom W, Davidovich U, Heuker J, Lambers F, Prins M, *et al.*
*Sex Transm Dis. 2016;43(2):99-104*

**HIV-1 escapes from N332-directed antibody neutralization in an elite neutralizer by envelope glycoprotein elongation and introduction of unusual disulfide bonds**
Van den Kerkhof TL, de Taeye SW, Boeser-Nunnink BD, Burton DR, Kootstra NA, *et al.*
*Retrovirology. 2016;13(1):48*

**Probability of N332 glycan occupancy on HIV-1 gp120 modulates sensitivity to broadly neutralizing antibodies**
Van den Kerkhof TLGM, Van Gils MJ, Boeser-Nunnink BD, Burger, JA, Schuitemaker H, Sanders RW.
*AIDS.* 2016;*30(14):2179-84*

**An HIV-1 antibody from an elite neutralizer implicates the fusion peptide as a site of vulnerability**
Van Gils MJ, Van den Kerkhof TLGM, Ozorowski G, Cottrell CA, Sok D, *et al.*
*Nature Microbiology 2016;2:16199.*

**Cost-effectiveness of hepatitis C treatment for people who inject drugs and the impact of the type of epidemic; extrapolating from Amsterdam, the Netherlands**

Van Santen DK, de Vos AS, Matser A, Willemse SB, Lindenburg K, *et al.*

*PLoS One. 2016;11(10):e0163488*

**Children and young people with perinatal HIV in Europe: epidemiological situation in 2014 and implications for the future**

Writing group for the Kids to Adults Working Group and Data Management and Harmonisation Group in EuroCoord.

*Euro Surveill. 2016;21(10):1-7.*

**Theses in 2016 that include ACS data**

Laurentia Setiawan – 19 April 2016: **HIV-1 adaptation to the host.**

Supervisor: Prof. T.B.H. Geijtenbeek (AMC); co-supervisor: Dr. N.A. Kootstra (AMC).

Bas Oude Munnink – 22 June 2016: **The challenges of virus discovery in human fecal samples.**

Supervisor: Prof. M.D. de Jong (AMC); co-supervisor: Dr. L van der Hoek (AMC).

Tom van den Kerkhof – 21 April 2016: **HIV-1 vaccine design: Learning from natural infection.**

Supervisor: Prof. J. Schuitemaker (AMC); co-supervisor: Dr R.W Sanders (AMC).

Joost Vanhommerig – 23 September 2016: **Epidemiology and diagnosis of acute hepatitis C virus infection.**

Supervisor: Prof. M. Prins (AMC/GGD Amsterdam); co-supervisors: Dr. C.J. Schinkel (AMC) and Dr. S.M. Bruisten (GGD).

Titia Heijman – 22 december 2016: **From insights into STI testing strategies to sexual risk dynamics in MSM.**

Supervisor: Prof. M. Prins (AMC/GGD Amsterdam); co-supervisors: Dr. E. Davidovich (GGD Amsterdam) and Dr. I.G. Stolte (GGD Amsterdam).