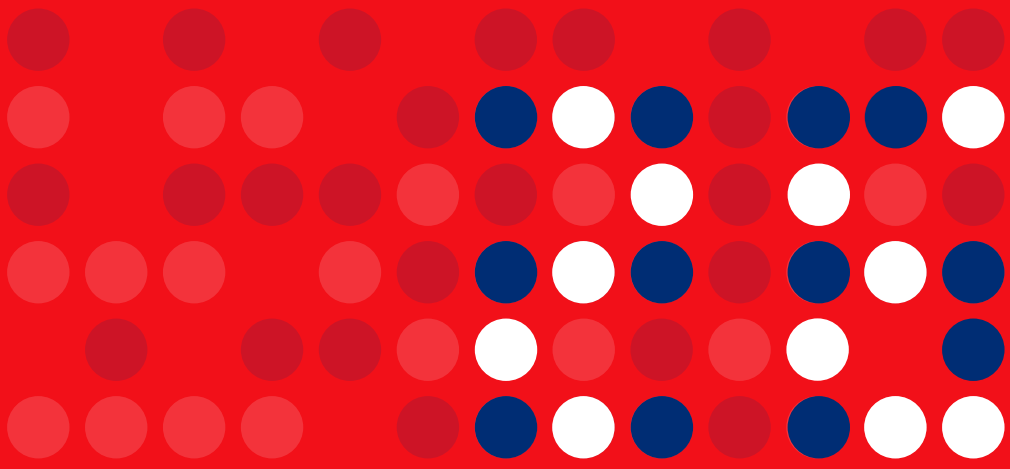
Human Immunodeficiency Virus (HIV)
Infection in the Netherlands

hiv Monitoring

HIV Monitoring Report 2026

Chapter 12: The Amsterdam Cohort Studies (ACS) on HIV infection: annual report 2025



12. The Amsterdam Cohort Studies (ACS) on HIV infection: annual report 2025

Carien Blomaard, Neeltje Kootstra, Lia van der Hoek, Vita Jongen and Janneke Heijne

Introduction

The Amsterdam Cohort Studies (ACS) on HIV infection and AIDS 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/inject drugs (PWUD/PWID) was initiated in 1985 and discontinued in 2016[1-5].

In 2024, the cohort celebrated the milestone of 40 years of follow-up. From the outset, research in the ACS has taken a multidisciplinary approach, integrating epidemiology, social science, virology, immunology, and clinical medicine in one study team. This unique collaboration has been highly productive, significantly contributing to the knowledge and understanding of many different aspects of HIV-1 infection, as well as other infections [e.g., viral hepatitis B and C (HBV and HCV) and human papillomavirus (HPV)]. This expertise, in turn, has contributed directly to advances in prevention, diagnosis, and management of these infections.

Collaborating institutes and funding

Within the ACS, the following institutes collaborated in 2025 to bring together data and biological sample collections, and to conduct research:

- **Public Health Service of Amsterdam** (*Gemeentelijke Gezondheidsdienst Amsterdam, GGD Amsterdam*): Department of Infectious Diseases
- **Amsterdam University Medical Centers, location Academic Medical Center (AMC)** (Amsterdam UMC): Department of Medical Microbiology and Infection prevention, Laboratory of Experimental Virology (LEV), Experimental Immunology, Laboratory for Viral Immune Pathogenesis, and Internal Medicine (Department of Infectious Disease)
- **Stichting hiv monitoring** (SHM)

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 Netherlands of the National Institute for Public Health and the Environment *(Rijksinstituut voor Volksgezondheid en Milieu - Centrum voor Infectieziektenbestrijding, RIVM-CIb)*.

Ethics statement

The ACS has been conducted in accordance with the ethical principles set out in the Helsinki declaration. Participation in the ACS is voluntary and written informed consent is obtained from each participant. The most recent version for the study protocol for the MSM cohort was approved by the Amsterdam UMC medical ethics committee in 2022.

The Amsterdam Cohort Studies (ACS)

The cohort of men who have sex with men (MSM)

In 1984 and 1985, men who had had sexual contact with at least one other man in the preceding six months were enrolled, independent of their HIV status. In the first 6 months of the recruitment period, 750 MSM, of which one-third with HIV, were enrolled. Over a 40-year follow-up, minor changes in the inclusion criteria for ACS were introduced, mainly concerning HIV status and age. From 1985 to 1988, men without HIV 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 preceding six months. Between 1988 and 1998, MSM with HIV were also enrolled because of the cohort involvement in HIV treatment trials. From 1995 to 2004, only men aged 30 years or younger, with at least one male sexual partner in the previous six months, could be included in the study. Since 2005, men without HIV of all age groups have been eligible to participate in the ACS if they live in, or are closely connected to the city of Amsterdam and had at least one male sexual partner in the preceding six months. In line with the advice issued by the International Scientific Advisory Committee in 2013, the cohort continues to strive to recruit young MSM (aged 30 years or younger). From 2022 onwards, we aimed to actively follow 825 MSM (750 without HIV and 75 with HIV). Currently, eligible for enrolment are individuals of at least 16 years old, who were assigned male sex at birth and who have not undergone gender reassignment surgery, live in the Amsterdam area or are involved in MSM-related activities in Amsterdam, and who have had sex with at least one man in the preceding six months.

Men who seroconverted for HIV within the ACS remained in the cohort until 1999, when follow-up of a selection of MSM with HIV was transferred to the MC Jan van Goyen. In 2003, the 'HIV Research in Positive Individuals' (Hiv Onderzoek onder Positieven, HOP) protocol was initiated. Individuals with a recent HIV infection when entering the study 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 (sexual) behavioural data are collected by questionnaires, coordinated by the GGD Amsterdam, and clinical data (for PWH) are provided by SHM. Every six months, participants complete a standardised questionnaire designed to obtain data regarding: medical history, (sexual) behaviour and substance use, uptake of prevention measures (including PrEP, doxyPEP, and condom use), underlying psychosocial determinants, health care use, signs of depression and other psychological disorders, and demographics.

As of 31 December 2025, 3,048 MSM have been included in the ACS since its initiation in 1984. These MSM contributed a total of 71,635 cohort visits at the GGD Amsterdam. Of these 3,048 MSM, 609 were living with HIV at entry into the study and 269 seroconverted for HIV during follow-up.

On 31 December 2025, 670 HIV-negative participants and 39 participants with HIV were in follow-up (meaning that they had at least one study visit in 2024 or 2025). Of these, 643 HIV-negative participants and 37 participants with HIV had at least one visit in 2025. 24 were newly enrolled in the cohort in 2025, all MSM without HIV with a median age of 34 years at enrolment. Two MSM seroconverted in 2025.

In this chapter, we report on the MSM actively participating in the ACS in 2025:
- The median age was 48 years at their last cohort visit in 2025;
- The majority were born in the Netherlands (84%) and a resident of Amsterdam (80%);
- 81% of the MSM had a college/university degree.

ACS biobank

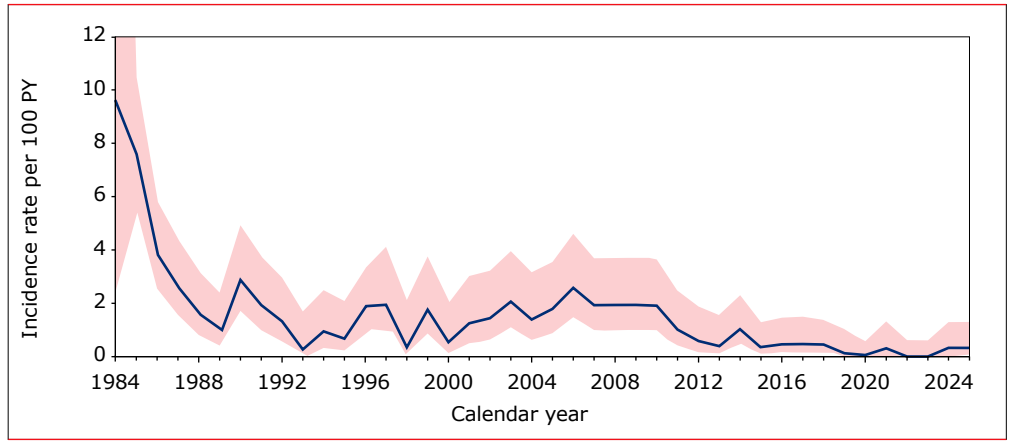
The ACS biobank, at the Amsterdam UMC, location AMC, stores all samples (plasma/serum, peripheral blood mononuclear cells) taken in the context of the ACS study. In addition to samples taken at routine ACS study visits, the biobank also contains samples collected for sub-studies and affiliated studies embedded in the ACS. Over the past 40 years, more than 350,000 samples have been stored for ongoing and future research.

ACS in 2025: HIV and STI among MSM

HIV incidence

The observed HIV incidence rate among MSM participating in the ACS has declined over time (*Figure 12.1*). Between 1985 and 1993 HIV incidence declined significantly, then stabilized between 1993 and 1996, before rising again in the period 1996 to 2009. Since 2009, the HIV incidence decreased again. Two participants seroconverted in 2025.

Figure 12.1: *HIV incidence per calendar year in the Amsterdam Cohort Studies (ACS) among men who have sex with men (MSM), 1984–2025.*



PrEP use

373/643 (58%) participants without HIV reported PrEP use in 2025. Of these, 177 (47.5%) obtained PrEP through the national PrEP program at the Centre of Sexual Health, 163 (43.7%) through their GP, 16 (4.3%) through an Internal Medicine specialist or another physician and 17 (4.6%) obtained their pills through informal routes (e.g. cross-border clinics, sexual or social networks, self-prescribed or online offered pills).

STI screening

Since October 2008, all MSM participating in the ACS are routinely screened for bacterial STIs during their cohort visits (in addition to HIV testing). This is in accordance with the standard care offered by the Centre of Sexual Health Amsterdam. Chlamydia testing was part of standard care until December 2024; since January 2025, chlamydia is tested only in the presence of symptoms. Chlamydia and gonorrhea were tested with nucleic acid amplification techniques using urine samples and pharyngeal and rectal swabs. Syphilis was screened for by *Treponema pallidum haemagglutination* assay.

In 2025, STI data were available from the Centre of Sexual Health Amsterdam for 668 MSM (with 1,561 visits including extra STI visits) participating in the ACS. Of these, 119 (17.8%) were diagnosed with at least one positive bacterial STI test (93 (13.9%) gonorrhea, 29 (4.3%) chlamydia and 19 (2.8%) syphilis). For MSM with and without HIV, 11 out of 36 (30.6%) and 108 out of 632 (17.1%) MSM were diagnosed with at least one positive bacterial STI test, respectively.

Until August 2024, participants using PrEP were screened for STIs 3-monthly, whereas other participants were screened 6-monthly, according to national PrEP guidelines. Following the revised national PrEP guidelines, STI screening is now offered 6-monthly to both PrEP users and those not using PrEP. Trends of any bacterial STI incidence among MSM without HIV, and stratified by PrEP use and no PrEP use, between 2009 and 2025 are shown in *Figure 12.2* and *12.3*. The annual incidence rate of any bacterial STI for MSM without HIV increased over time (*Figure 12.2*). MSM who used PrEP in the preceding 6 months were diagnosed with STIs more often than MSM who did not (*Figure 12.3*).

Figure 12.2: *Any bacterial STI incidence per calendar year in the Amsterdam Cohort Studies (ACS) among men who have sex with men (MSM) without HIV with at least two study visits, 2009–2025.*

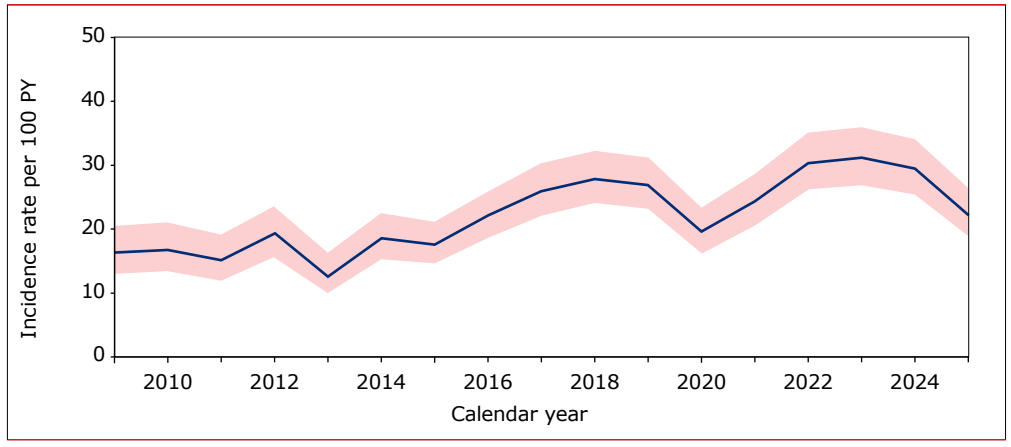
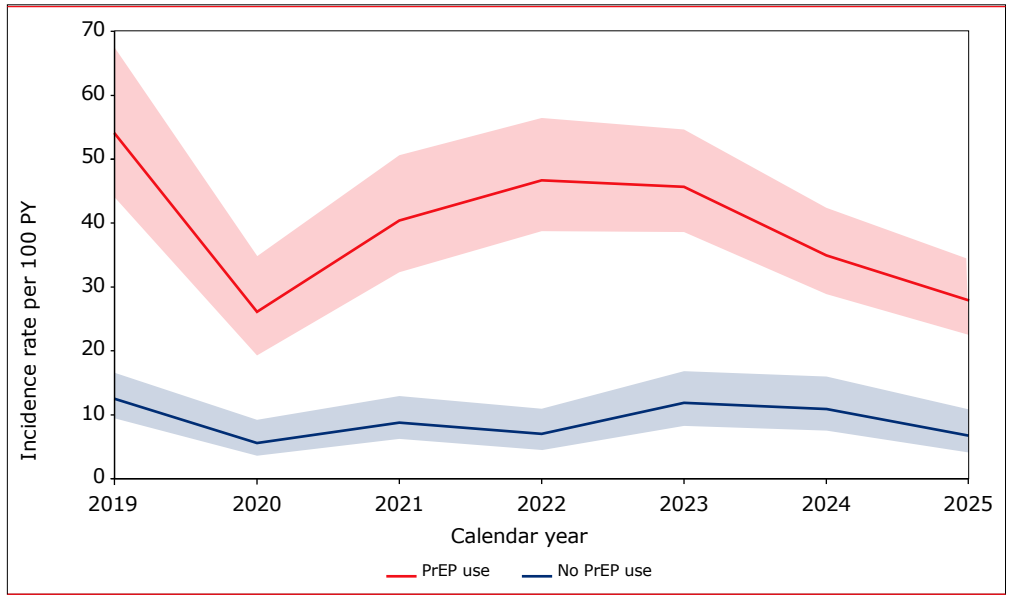


Figure 12.3: *Any bacterial STI incidence per calendar year in the Amsterdam Cohort Studies (ACS) stratified by PrEP use in the preceding 6 months, among men who have sex with men (MSM) without HIV with at least two study visits, 2019–2025.*



ACS 2025 research highlights

Barriers and missed opportunities in PrEP uptake, use and care among men who have sex with men with recent HIV infection

Some men who have sex with men entering HIV care indicated having PrEP experience prior to diagnosis. Semi-structured in-depth interviews on PrEP among MSM diagnosed with HIV from 2019 onwards with previous PrEP experience were conducted to identify barriers and missed opportunities in PrEP uptake, care and use[6]. Of the 11 included MSM, most reported significant PrEP-uptake delay because of the limited NPP capacity and high threshold of accessing PrEP from GPs (e.g. stigma, lack of sexual health expertise). Additional uptake or use barriers included anticipated/experienced side-effects, burden of daily pill-taking or event-driven regimen complexity, the latter leading to PrEP discontinuation. Missed opportunities in counseling on adherence and safer sex alternatives after discontinuation were reported. Most interviewees considered informal PrEP unsuitable. We conclude that HIV diagnoses at or shortly after PrEP initiation emphasize the importance of ensuring rapid and timely PrEP access. Uptake barriers at GPs, stigma related to sexuality, lack of expertise, and missed care opportunities need to be addressed. Early detection of PrEP protocol/user-mismatch and counseling on safer sex alternatives after discontinuation are pivotal for sustainable HIV prevention.

Incidence of hepatitis C virus infection and associated determinants among men who have sex with men without HIV in Amsterdam, the Netherlands, between 2012 and 2021

This study was conducted to assess the prevalence, incidence, and determinants of hepatitis C virus (HCV) infection among men who have sex with men without HIV in Amsterdam[7]. Data of 926 participants from the Amsterdam Cohort Studies (2012–2021) were used, including repeated serological testing and behavioral questionnaires. The results showed a very low prevalence of past/current HCV infection at baseline (0.2%) and an incidence rate of 0.05 per 100 person-years, with only three incident infections observed between 2014 and 2018. Incident infections were associated with receptive condomless anal sex, a higher number of sexual partners, recent or ever injecting drug use, and engaging in fisting. Phylogenetic analysis revealed that one HCV-RNA sequence was closely related to HCV sequences from MSM with HIV. Thus, while HCV infection is uncommon among MSM without HIV, the risk of infection seems to increase among those with specific behaviors.

Uncovering Metabolic Control of HIV Latency

A major challenge in curing HIV is understanding how the virus remains dormant within long-lived cellular reservoirs. We developed an innovative flow cytometry–fluorescent in situ hybridization (flow-FISH) assay that directly detects HIV-infected cells ex vivo without requiring viral reactivation[8]. Using this approach, we distinguished cells expressing abortive versus elongated HIV-1 transcripts and isolated these rare populations for transcriptomic analysis. Our findings revealed distinct mitochondrial gene expression signatures associated with latent HIV infection. Importantly, enhancing mitochondrial function stimulated HIV transcription in cells from people living with HIV, providing direct evidence that cellular metabolism contributes to the maintenance of viral latency. These results identify mitochondrial function and immunometabolic pathways as promising targets for HIV cure strategies aimed at disrupting viral persistence.

Timing of HIV Treatment Shapes Long-Term Monocyte Immune Function

Despite effective antiretroviral therapy (ART), people living with HIV often experience persistent immune dysregulation. We investigated how the timing of ART initiation influences communication between key innate immune sensing pathways in monocytes, focusing on interactions between Toll-like receptor 8 (TLR8) and RIG-I-like receptors (RLRs)[9]. Our study showed that monocytes from individuals who started ART during acute HIV infection initially displayed cytokine responses similar to those of HIV-negative individuals. However, these responses gradually declined over time and became comparable to those observed in individuals who initiated treatment during chronic infection. In contrast, chronically treated individuals exhibited reduced production of immune-regulatory cytokines and increased inflammatory responses. These findings suggest that early ART initiation temporarily preserves monocyte immune function but may not fully prevent long-term alterations in innate immune responses. The results highlight a potential early therapeutic window for interventions aimed at maintaining immune health and reducing chronic inflammation in people living with HIV.

Long-term effect of temporary ART initiated during acute HIV and the effect of long treatment interruption

In a randomized controlled trial with people treated with temporary ART versus untreated during acute HIV infection, the effect of long treatment interruption was investigated[10]. In a total of n=64 participants, either treated with 24- or 60-week ART from acute HIV infection onwards or no treatment during HIV acute infection, the participants (re)initiated ART after a median period of 116 weeks. The study revealed a long-term suppressive effect of early ART on the viral reservoir as the reservoir size and activity during chronic infection ART were lower in those who had been pre-treated during early infection several years before, compared with those who had not. Importantly, the long treatment interruption did not have a disadvantageous effect on the virological or immunological response during reinitiation of ART, as upon restart of therapy, the reservoir returned to its early-ART level. This finding provides confidence that treatment interruption, e.g. for HIV-1 curative intervention purposes, does not lead to a risk for a larger virus reservoir.

Vaccination studies: At the Laboratory of Experimental Virology of the Amsterdam UMC, HIV-1 Envelope proteins are designed to be used in vaccination strategies. Among the sequence sources used for protein structure design, there were several HIV-1 Envelope sequences from participants of the Amsterdam Cohort Studies. Because of this historical link with the ACS we include here two scientific highlights on Phase 1 vaccine clinical trials.

Phase 1 clinical trial with HIV-1 protein vaccine; Safe and capable of eliciting cross-reactive binding antibody responses in humans

A protective vaccine will be the most powerful instrument to reduce HIV-1 infections worldwide and help bring about a lasting end to the AIDS epidemic. A single-centre, randomised, open-label, uncontrolled, phase 1 clinical trial was performed to assess the safety and immunogenicity of an HIV-1 group M native-like trimer Envelope glycoprotein vaccine (ConM SOSIP.v7)[11]. The trial was done in HIV-negative adults at the Amsterdam UMC. Twenty-four individuals were enrolled to receive three doses of the protein vaccine in a liposome formulation containing a high dose of the TLR4-agonist MPLA as adjuvant. Overall, the vaccine was safe and well-tolerated. Furthermore, the vaccine elicits robust HIV-1 strain-specific binding and cross-reactive neutralising antibody responses in nearly all vaccinees. Post-hoc exploratory analyses demonstrate that female-born participants have 22- and 6-fold higher neutralisation titres after the second and third vaccination, respectively. Whether the differences found in immunological outcomes between females and males are caused by genetic, hormonal or environmental factors remains to be determined. Nevertheless, sex-based differences in response to vaccines and adjuvants need to be considered moving forward, since new HIV infections in women are on the rise, with young women and girls accounting for 45% of new HIV-1 infections globally and 63% of new infections in Sub-Saharan Africa.

Phase 1 clinical trial with HIV-1 protein vaccine; Targeting HIV broadly neutralizing antibody precursors in humans with atomic precision

It is now believed that the essential first step in a successful HIV vaccination is the activation of rare low-affinity broadly-neutralizing antibody-producing precursor B cells, also known as germline B cells, followed by vaccination-based guidance of these B cells to produce effective neutralizing antibodies. Specific engineered HIV-1 Envelop glycoproteins are needed for such a strategy, a first immunogen (prime Env) for priming precursor B cells and a second (Shape Env) and third (Polish Env) immunogen to respectively shape and polish the primed precursor B cells towards production of highly effective broadly neutralizing antibodies. In a phase 1 clinical trial with 47 participants (recruited at the Rockefeller University (USA), George Washington University (USA) and at the Amsterdam UMC) vaccination was done three times with an especially designed HIV-1 Env immunogen to establish the required maturation of B cells[12]. There were memory B cells in the vaccinees, with substantial affinity maturation indicating proper priming and maturation. Cryo-electron microscopy subsequently revealed that the antibodies from the vaccinees often resembled the VRC01-class broadly neutralizing antibodies in terms of atomic contacts with Env. Monoclonals of this class that target the receptor binding site of the virus (CD4), have the most powerful HIV-neutralising capacity known to date.

Current and upcoming ACS research projects

Data collected within the ACS are currently used for multiple research projects. As 2024 marked the 40th anniversary of the study, we are studying trends in HIV and STI incidence and sexual behavior over 40 years of follow-up. Trends and current norms and negotiation experiences regarding condom use are studied in greater detail. Quantitative and qualitative studies on individual and contextual motives underlying choices of HIV prevention strategies (including condoms, PrEP, and viral load sorting) are ongoing, and conducted in collaboration with Maastricht University. A recent collaboration with the University of Groningen focuses on chemsex patterns over time and the contextual factors influencing the use of chems, such as chemsex within steady relationships and the influence of social media and dating app norms and features.

Data Preparedness of the Amsterdam Cohort Studies

The ACS team supports the Open Science movement, and aims to improve the findability, accessibility, interoperability, and reusability (FAIR) of the ACS (meta) data. In 2025, a grant was awarded by the NWO (Open Science Infrastructure | Open Science NL) to further implement the identified improvements regarding findability, accessibility, interoperability, and reusability of the ACS (meta) data. This project is a continuation of a prior project funded by ZonMw.

This project aims to facilitate Open Science practice of the Amsterdam Cohort Studies (ACS) through investment in the data infrastructure, following the FAIR principles (findability, accessibility, interoperability and reusability). Since 1984 ACS captures longitudinal data of men who have sex with men, through a unique interdisciplinary collaboration between academic (Amsterdam UMC) and public health institutes (GGD Amsterdam).

This project facilitates and accelerates (new) research by optimizing findability, making metadata and a data-request protocol accessible through a data catalogue and website. Interoperability and reusability will be improved by making the metadata machine-readable, and by publishing the provenance of the data.

Steering committee

In 2025 the steering committee met four times. Eight proposals for use of ACS data or samples (serum/PBMC) were submitted to the committee: seven from Medical Microbiology and Infection Prevention (MMI, Amsterdam UMC, location AMC) and one international collaborative project involving Imperial College London, WHO Copenhagen and the GGD Amsterdam. The ACS reviewed the proposals, after which all requests were approved.

Research Meetings

An internal ACS research meeting with Amsterdam UMC and GGD researchers was held on 23 February 2025, during which ACS researchers presented research findings.

Publications in 2025 that included ACS data

- Hage K, Koole J, Boyd A, Matser A, Davidovich U, Bakker M, van der Hoek L, Koopsen J, Rebers S, Schinkel J, Prins M. Incidence of hepatitis C virus infection and associated determinants among men who have sex with men without HIV in Amsterdam, the Netherlands, between 2012 and 2021. Eur J Gastroenterol Hepatol. 2025 Oct 1;37(10):1173-1179. doi: 10.1097/MEG.0000000000003008
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Amsterdam Cohort Studies (ACS) participants

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