Annual Report 2014

Contributing to the quality of HIV care

Stichting HIV Monitoring (SHM), the Dutch HIV monitoring foundation, was founded in 2001. Based in Amsterdam, SHM was appointed by the Dutch Minister of Health, Welfare and Sport as the executive organisation for the registration and monitoring of HIV-infected patients in the Netherlands.

Our mission

To further the knowledge and understanding of the epidemiology and the course of treated and untreated HIV infection.

www.HIV-monitoring.nl

Annual report 2014, approved by the Stichting HIV Monitoring Governing Board on 12 May 2015.

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Foreword

Over the past year, Stichting HIV Monitoring (SHM) has successfully continued its mission of monitoring the HIV epidemic in the Netherlands by systematically collecting, analysing and reporting data concerning people with HIV in clinical care. Importantly, this mission can be accomplished only by a fruitful collaboration with health care professionals in the 27 HIV treatment centres throughout the Netherlands. As a result of this collaboration, SHM is uniquely positioned to provide a truly nationwide picture of the outcome of care for those living with HIV and, thereby, to contribute significantly to monitoring the quality of care. Moreover, this allows SHM to provide individual treatment centres with regular updates of their own centre-specific data, which enables the centres to critically review and improve their performance where needed.

Apart from monitoring HIV-specific outcomes, such as degrees of viral load suppression, immune recovery, emergence of HIV drug resistance and overall survival, SHM also invests much time and effort in monitoring non-AIDS co-morbidities, which continue to gain in importance as patients with HIV in care survive into older age. Furthermore, the efforts to expand and improve the data collection for viral hepatitis B and C co-infections in those with HIV that were started some time ago have been successfully continued. This investment in forming a high-quality collection of data on hepatitis C co-infection will now allow efficient monitoring of the efficacy, effectiveness and safety of the novel combinations of direct acting antivirals against hepatitis C that are increasingly becoming available in the Netherlands. In turn, lessons learned through the monitoring of patients with HIV and hepatitis B or C co-infection have paved the way to explore the possibilities for monitoring patients with hepatitis B and C mono-infection.

2014 saw SHM undergo an independent evaluation of its activities and performance by the consultancy bureau, Beerenschot, on behalf of SHM's main funder, the Centre for Infectious Disease Control of the Netherlands' National Institute for Public Health and the Environment (*Centrum voor Infectieziektenbestrijding-Rijksinstituut voor Volksgezondheid en Milieu*; CIb-RIVM). The report's findings, based on consultation of a wide range of national and international stakeholders, underlined the high quality of SHM's activities, products and services, and their important contributions to HIV surveillance and quality of care in the Netherlands. Furthermore, the report stressed the importance of SHM's data in facilitating clinical and public health research, not only nationally, but also through European and even global collaborations. Moreover, in terms of expanding SHM's activities to other disease areas, the report concluded that SHM's data management system was a suitable option for the national collection of data on hepatitis B and C mono-infections. In the wake of the recent innovative additions to the therapeutic arsenal for hepatitis C, such a national hepatitis database is increasingly called for. Currently, further consultations convened by CIb-RIVM and involving all relevant stakeholders in the field of viral hepatitis in the Netherlands are ongoing to reach a consensus on how this can best be achieved.

In 2014, the Academic Medical Center-University of Amsterdam's Clinical Research Unit announced that the system on which SHM's data warehouse is based, Oracle Clinical, is to be phased out over the next three years. In response, SHM swiftly initiated the process of finding a suitable alternative, while at the same time using it as an the opportunity to modernise the data collection process, in part by making it more compatible with the electronic patient record systems now in use throughout the HIV treatment centres. Supported by an IT consultancy firm, the first steps in the process have been undertaken and, at the time of writing, a shortlist of three candidate alternatives to Oracle Clinical has been drawn up. A final selection will be made half way through 2015.

Sadly, 2014 will forever be marked by the tragic shooting down of Malaysian Airlines flight MH17 in July, in which so many people lost their lives, including a number of people actively involved in the fight against HIV and AIDS. Amongst them were the chair of SHM's advisory board, Prof. Joep Lange, and his partner, Jacqueline van Tongeren. They were not only longstanding colleagues from the start of the HIV epidemic, but also good friends of mine. Joep has left behind a formidable legacy in HIV research, and both he and Jacqueline worked tirelessly to improve the lives of people living with HIV globally. SHM will continue to do justice to their legacy, striving for excellence in all our activities, both through our own research and through national and international collaborations.

Over the past year, SHM has continued to make an important contribution to various European and other more global HIV observational cohort collaborations, in terms of both data and science. Such a contribution makes it possible to tackle scientific questions that cannot be answered by any individual cohort alone, and outcomes of this research regularly result in modifications to HIV treatment guidelines. One multidisciplinary collaboration, in which SHM is a partner, bears witness to Joep Lange's vision for combatting HIV. This project, named the H-TEAM (*HIV Transmission Elimination Amsterdam*) project, was launched at the end of 2014, and aims to reduce the number of new HIV infections in Amsterdam through close multi- and interdisciplinary collaboration by all stakeholders involved in HIV prevention and care in Amsterdam. For certain components of the project, collaborations have been set up with centres outside Amsterdam, such as the Erasmus Medical Center in Rotterdam. This newly-formed consortium involves collaboration between public health, academia, civil society, key-affected communities, and industry.

Finally, I would like to express our gratitude to all the people living with HIV who are in clinical care for allowing us to capture their data, store blood samples and to learn how we may continue to improve their care.

Prof. Peter Reiss, MD, PhD

Director

Amsterdam, 12 May 2015

Message from the governing board chair

Stichting HIV Monitoring (SHM) continues to make an important contribution to the quality of care of HIV-infected people throughout the Netherlands. The latest figures published by SHM have revealed that there are approximately 17,750 HIV-infected people in care in the Netherlands and around 1,100 persons with new diagnoses enter into care annually. Moreover, SHM's research has highlighted a worrying number of people who apparently remain unaware of their HIV status. In addition, SHM has shown that, in 2013, 43% of newly-diagnosed patients presented with a late diagnosis. These findings illustrate that the battle against HIV and AIDS has not yet been won in the Netherlands, and underline the need for a continued concerted effort to identify and treat HIV-infected individuals at an early stage of infection, and to ensure these individuals remain linked to medical care. Not only is this in the interest of the HIV-infected individual, but it will also benefit the wider population by slowing down the epidemic. The continuous monitoring of HIV and its treatment, as carried out by SHM, is essential in achieving these goals.

In the Netherlands, HIV patient care is well-structured and is provided through 8 academic and 19 non-academic treatment centres. To safeguard optimal care for persons living with HIV, these treatment centres are now required to undergo a certification process. SHM plays a key role in this process by providing the centre-specific data required for the formal certification as an HIV treatment centre. In doing so, SHM is helping to form a national benchmark against which treatment centres can compare their own outcomes.

In terms of research output, SHM continues to be involved in both national and international projects and collaborations, resulting in important findings that can subsequently be used as the basis for treatment and healthcare management guidelines.

I join my colleague and director of SHM, Peter Reiss, in mourning the loss of lives in the MH17 aircraft disaster. In particular, we will continue to miss Prof. Joep Lange's invaluable contributions to SHM and the field of HIV.

Finally, it remains for me to express my gratitude to the healthcare professionals and patients for their ongoing contributions to the work carried out by SHM, and to thank all the SHM employees for their dedication and hard work over the past year.

Dr Frank Kroon

Chairman of the Governing Board

Amsterdam, 12 May 2015

Progress report

Introduction

Stichting HIV Monitoring (SHM) contributes to the knowledge of HIV by studying the course of the infection and the effect of its treatment. In the Netherlands, SHM follows the treatment of every registered HIV-infected man, woman and child. In this way we are able to comprehensively map the HIV epidemic and HIV treatment outcomes in the Netherlands.

Since its founding in 2001, SHM has worked with HIV treatment centres throughout the Netherlands to develop a framework for systematically collecting HIV data for the long-term follow-up of all registered patients. The Netherlands is the only country in the world to have such a framework, which enables healthcare professionals to aspire to the highest standard of HIV care.

Continuous collection of data is essential for the work of SHM and is carried out at 27 HIV treatment centres and subcentres, and at 4 paediatric HIV centres in the Netherlands. This is performed either by staff of the treatment centre or by SHM data collectors in cooperation with the responsible HIV physician. Patient data are collected anonymously and then entered into the registration database for storage and analysis.

The progress report includes an overview of the 27 treatment centres, as well as overviews of SHM's organisation, data collection, database and data quality management. It also includes reports on registration and monitoring and on the Amsterdam Cohort Studies, which receives its funding through SHM. An overview of SHM's national and international collaborations and ways in which SHM disseminated information during 2014 are also reported.

HIV treatment centres

The monitoring of HIV-infected adults is a collaborative effort involving Stichting HIV Monitoring (SHM) and a total of 27 health institutes that are acknowledged by the Dutch Minister of Health, Welfare and Sport as HIV treatment centres or subcentres. In addition, HIV-infected children and adolescents are monitored in four institutes that are recognised as paediatric HIV treatment centres.

In 2014, the following health institutes were involved as centres or subcentres for adult HIV care (in alphabetical order by town):

1	Medisch Centrum Alkmaar (MCA)	Alkmaar
2	Flevoziekenhuis	Almere
3	Academic Medical Center of the University of Amsterdam (AMC-UvA)	Amsterdam
4	HIV Focus Centrum (DC Klinieken)	Amsterdam
5	Onze Lieve Vrouwe Gasthuis (OLVG)	Amsterdam
6	Sint Lucas Andreas Ziekenhuis	Amsterdam
7	Slotervaartziekenhuis	Amsterdam
8	Medisch Centrum Jan van Goyen (MC Jan van Goyen)	Amsterdam
9	VU Medisch Centrum (VUmc)	Amsterdam
10	Rijnstate	Arnhem
11	HagaZiekenhuis (Leyweg site)	Den Haag
12	Medisch Centrum Haaglanden (MCH, Westeinde site)	Den Haag
13	Catharina Ziekenhuis	Eindhoven
14	Medisch Spectrum Twente (MST)	Enschede
15	Admiraal De Ruyter Ziekenhuis	Goes
16	Universitair Medisch Centrum Groningen (UMCG)	Groningen
17	Kennemer Gasthuis	Haarlem
18	Medisch Centrum Leeuwarden (MCL)	Leeuwarden
19	Leids Universitair Medisch Centrum (LUMC)	Leiden
20	MC Zuiderzee	Lelystad
21	Maastricht UMC+ (MUMC+)	Maastricht
22	Radboudumc	Nijmegen
23	Erasmus MC	Rotterdam
24	Maasstad Ziekenhuis	Rotterdam
25	St Elisabeth Ziekenhuis	Tilburg
26	Universitair Medisch Centrum Utrecht (UMC Utrecht)	Utrecht
27	Isala (Sophia site)	Zwolle

Centres for the treatment and monitoring of paediatric HIV were:

A	Emma Kinderziekenhuis (EKZ), AMC-UvA	Amsterdam
B	Beatrix Kinderziekenhuis (BKZ), UMCG	Groningen
C	Erasmus MC-Sophia	Rotterdam
D	Wilhelmina Kinderziekenhuis (WKZ), UMC Utrecht	Utrecht

SHM has contracts with each centre or subcentre for the collection of demographic, epidemiological, clinical, virological, immunological, and pharmacological data for HIV-infected patients who are followed in one of these hospitals. These contracts are automatically renewed every three years.

In addition to its work in the Netherlands, in collaboration with, and upon the request of, the Red Cross Blood Bank in Willemstad, Curaçao, SHM provides assistance in collecting data from HIV-infected persons seen by HIV-treating physicians at the St. Elisabeth Hospital in Curaçao (SEHOS).

Stichting HIV Monitoring organisation

Stichting HIV Monitoring (SHM) is overseen by a governing board that includes members who represent academic and general hospitals, health insurers, the Netherlands HIV Association (*Hiv Vereniging Nederland*, HVN), the Dutch Association of HIV-Treating Physicians (*Nederlandse Vereniging van HIV Behandelaren*, NVHB) and the Academic Medical Center of the University of Amsterdam (AMC-UvA). The board members approve SHM's budget and the content of the annual report.

In addition, SHM has an advisory board that reviews SHM's activities from a strategic perspective and advises the director and the governing board.

The SHM working group, consisting of members and reviewers, advises the director on executive matters regarding use of data stored in the national HIV database for scientific purposes. Consequently, the working group is also responsible for reviewing research proposals submitted to SHM.

SHM's director has the final responsibility for the organisation's day-to-day activities. SHM's primary activities are carried out by two units, one for the collection of patient data and quality control and the other for data processing and analysis. In addition to these units, SHM has a support unit.

The data collectors employed by SHM form part of the patient data and quality control unit, which had an average of 15.83 FTEs in 2014. This unit is also responsible for administering patient registrations (new registrations and discontinued registrations) and for assigning an anonymous identification code to each registered patient.

The data monitors, assistant data monitors, and data managers are also part of the patient data and quality control unit. In 2014, the average number of FTEs for these data quality staff was 8.66. Data management activities, another responsibility of this unit, are partly outsourced to the Clinical Research Unit (CRU) of the department of Clinical Epidemiology and Biostatistics at the AMC-UvA. At least twice a year, in February/March and in June/July, a data freeze takes place to produce a dataset for data processing and analysis. The patient data and quality control unit is managed by Sima Zaheri (0.8 FTEs). During 2014, the average number of FTEs for staff in the patient data and quality control unit was 24.49.

The data processing and analysis unit is staffed by researchers in the field of epidemiology, statistics, mathematical modelling of HIV and modelling of transmission networks. Together, these researchers implement the HIV registration programme, the results of which are presented in the annual SHM Monitoring Report published near the time of World Aids Day. The researchers also contribute to publications involving analyses of the collected data in peer-reviewed international scientific journals. This unit supports and

collaborates nationally with researchers in the HIV treatment centres, and internationally with research groups working with comparable observational cohorts in the field of epidemiology and treatment of HIV. This group also organises support for research applications by national and international researchers, both during the preparatory phase and after approval.

In 2014, the data processing and analysis unit had one assistant researcher participating in a PhD programme. This programme involves mathematical modelling of the impact of various interventions to control the HIV epidemic in the Netherlands. This unit also supported two other PhD programmes in 2014: one that compared the effect of combination antiretroviral therapy (cART) on HIV-infected individuals treated in Curaçao with that of cART on HIV-infected patients from the Netherlands Antilles treated in the Netherlands (successfully completed at the time of writing), and a second that focuses on the optimisation of quality of care for HIV-infected patients receiving care at HIV treatment centres in the Netherlands. In 2014, an average of 5.24 FTEs were assigned to the data processing and analysis unit, led by SHM director Peter Reiss (0.95 FTE).

The primary activities of SHM are supported by the office staff, which includes the secretariat, financial and personnel administration and financial management. The office staff are supervised by SHM's human resources, office and finance manager, Daniëlle de Boer (0.66 FTE). In 2014, the average number of FTEs for the office staff was 2.4.

Up to 1 February 2014, management of the communications department was carried out by the human resources, office, finance, and communications manager. Since 1 February 2014, the communications department has become a separate support unit, with an average FTE of 0.68 in 2014. This unit is led by Catriona Ester (0.69 FTE in 2014). The average FTEs for the support units, including the communications department, was 3.77 in 2014. This number has remained constant over the recent years.

As of 31 December 2014, SHM had an average total of 35.91 FTEs. In addition, SHM covers the costs for a total of 9.2 FTEs for data collectors and data entry staff who are employed by the HIV treatment centres and who are not on the SHM staff. The average sick leave during 2014 was 2.77%, which represents a 0.18% increase compared to 2013.

A list of members of SHM's governing board, advisory board, working group and personnel can be found in *Appendix 1: Composition of SHM*.

Data collection, database & data quality management

The patient data and quality control unit has four main activities:

- Data collection and data entry;
- Source data verification;
- Helpdesk and protocol management;
- Data management.

In addition to these four activities, the patient data and quality control unit runs various projects to ensure ongoing improvements in data collection quality and efficiency. This efficiency in data collection and quality of data in SHM's database is achieved using SHM's quality management system (QMS). The QMS is based on the principles of the PDCA (plan-do-check-adjust) cycle, ISO 9000 QMS standards, and scientific knowledge of data quality.

In 2014, SHM continued to improve its data production processes in line with its QMS. The key priorities for 2014 were:

- To standardise and improve data collection, data quality management and data processing;
- To improve the infrastructure for information and communications technology (ICT) and data management processes;
- Where possible, to centralise the collection of data by specially-trained SHM staff;
- To centralise the collection of complex, specialised data by specially-trained SHM staff;
- To establish an automated link that allows laboratory data from hospital computer systems to be entered directly and anonymously into the SHM database;
- To continue the innovation programme launched in 2013 to maximise digitalised data collection and minimise manual input;
- To intensify the quality control of collected data by concentrating on information that is essential for the output and on consistency within patient data;
- To coach and train data collectors and data quality staff.

The results achieved in 2014 are described in the paragraph below.

Standardisation, automation and steps for improvements

Improvement and standardisation of manual data collection

In 2014, 20 sections of the data collection protocols were evaluated and improved. This review resulted in changes in the collection of data on HIV transmission and recent HIV infections, diabetes mellitus, cardiovascular disease, viral hepatitis, and liver work-ups. In addition, questionnaires have been drawn up to support the treatment teams in history-taking, and to subsequently help the treatment teams obtain structured and standardised information from patients at their annual visits. This information covers subjects that are

not standardly recorded in medical records, such as smoking, alcohol and drug use, and family history. These questionnaires will be finalised for implementation after a feasibility study and consultation with the treatment teams.

In 2013, a help-desk system was implemented to support the data collectors in extracting data from the information sources in the HIV treatment centres, and in coding and entering data into the national SHM database in accordance with SHM protocols. This system was further optimised in 2014. During 2014, the help-desk received 751 queries from data collectors, which is twice as many as in 2013. The reason for this increase is two-fold. First, data collectors are more aware of the help-desk service and are therefore making more use of it, and, secondly, changes to data collection protocols have generated a greater need for explanations regarding these changes. Of the 751 queries received in 2014, 233 could be answered directly by the responsible data quality staff. In total, 172 queries were resolved by a protocol or code change. The remaining queries that required long-term solutions have been scheduled for 2015.

Centralised data collection

The efficiency and quality of data collection and data entry in the treatment centres appears to be linked to the availability of data collectors in these centres. This can be improved through centralisation of data collection, which requires the mobile deployment of specially-trained staff from SHM's head office (central data collectors). In 2014, data collection in the Slotervaartziekenhuis in Amsterdam was centralised in this manner, in consultation with the hospital's principle HIV-treating physician.

In 2014, specially-trained central data collectors carried out both prospective and retrospective data collection and entry into the national SHM database of hepatitis-related data from the following three patient groups:

- HIV-infected patients with viral hepatitis C infection (HCV) in all HIV treatment centres (n=512);
- HIV-infected patients with viral hepatitis B (HBV) infection in all HIV treatment centres (n=1,954);
- Patients with chronic HBV mono-infection who are being followed as part of an SHM collaboration with UMC Utrecht and Rijnstate Arhem (*Harmonic: Comparison of the natural course, morbidity and mortality, and effects of treatment in patients with HBV mono-infection and HIV/HBV co-infection*).

Improvements in data entry software

In 2014, we completed the digitalisation of new and discontinued registrations. Following an intensive acceptance test phase, the new registration system, developed by the Academic Medical Center-University of Amsterdam's Clinical Research Unit (CRU), was implemented in all HIV treatment centres at the end of 2014.

Since the Windows 7 operating system is now in use in almost all HIV treatment centres, the SHM database, Oracle Clinical, required upgrading. In February 2014, the CRU carried out the move from Oracle Clinical RDC classic version 4.5.3 to version 4.6.6.

In May 2014, the CRU announced that Oracle Clinical would be phased out over the next three years. SHM therefore put together a project brief ('Oracle Clinical replacement') to identify a suitable alternative to Oracle Clinical. The plan also includes new opportunities for modernising and future-proofing SHM's data collection process in line with ICT developments taking place within the electronic patient record systems in HIV treatment centres. The first steps involved drawing up a statement of requirements, identifying potential candidates and selecting the best applications. The IT consultancy firm, Furore, has been requested to provide support in this process.

The statement of requirements was drawn up in September 2014. This was subsequently followed by a market survey to identify candidate replacement systems that also have the capacity to encompass future innovations and to allow possible coupling with electronic patient records in the future. This led to a long-list of seven options. The suppliers of these systems were all sent the statement of requirements; after studying the statement of requirements, four of the approached parties withdrew from process. The three remaining candidates on the short-list were given additional information about the data processes and anonymised patient scenarios. In 2015, these candidates will present their system to SHM, after which the products will be compared and, hopefully, one system will be selected. The new data entry database will subsequently undergo a proof of concept and an acceptance test phase.

Patient reports, graphs and standard data queries

In 2014, the patient and custom reports, graphs and standard data queries in Microsoft Report Builder were maintained, further developed where needed, and improved. Additional data overviews were drawn up to enable the data collectors and data quality staff to work more effectively and efficiently, such as:

- Overviews from the new registration database to provide information on items such as new registrations, discontinued registrations and patients lost to follow-up;
- Overviews to monitor the back-log in data collection and entry;
- Overviews to monitor both the Lab-Link process (Lab-Link is the automated link by which laboratory results are transferred directly from the hospital computer system in an anonymised form to the SHM database) and the Lab-Link data;
- Overviews to support the quality control planning.

In addition, the management reports have also been expanded to support the team leaders of the various departments within the patient data and quality control unit.

Standardisation of Lab-Link

The move to standardise Lab-Link was continued in 2014. Based on the standard Lab-Link protocol that was developed in collaboration with the AMC's CRU and General ICT Service (ADICT) for sending laboratory results as HL7 messages (an international standard for electronic data exchange between healthcare information systems), in 2014 Lab-Link was tested and implemented in the Kennemer Gasthuis Haarlem, Slotervaart-ziekenhuis Amsterdam, and Maastricht UMC+. In total, 12 treatment centres now use Lab-Link, representing laboratory data from 55% of the patients included in the SHM database; this is a 7% increase from 2013. The standard protocol for Lab-Link has also been discussed in the OLVG Amsterdam, Rijnstate Arnhem and UMC Groningen. In 2014, the AMC continued to transfer results directly from the laboratory computer system using an internal connection.

Harmonisation of Lab-Link data

A Lab-Link 'mapping tool' has been developed by the CRU in Microsoft Access. This tool receives and standardises laboratory results from different treatment centres with different terminology. In 2014, 1,574 combinations of laboratory terms and accompanying samples were harmonised using this tool.

'Digitalisation' innovation programme

In 2014, Furore completed the feasibility study initiated in 2013 to investigate the accelerated implementation of Lab-Link, the possibility of broadening the use of Lab-Link, and the simplification of data extraction from electronic patient records by data collectors. The final report detailed the processes involved in both manual data collection and digital data collection, and identified bottlenecks in these processes. Areas that offered potential solutions for innovation and improvement, based on the current ICT situation, were subsequently translated into concrete recommendations. In terms of Lab-Link, these recommendations resulted in the following outcomes:

- Application landscape diagram: an overview of the application landscape in which Lab-Link is used, offering an overview of the associated systems and the possibility of identifying comparable situations in the different HIV treatment centres. Of relevance in this context are the laboratory applications (e.g., GLIMS and TDS), the electronic patient records (e.g., ChipSoft, XCare), and the integration applications (in most cases, Cloverleaf). In addition, this application landscape offers insight into which areas require tailor-made solutions, and thus provides guidance on how to efficiently set up the link between Lab-Link and the systems used in the remaining 15 HIV treatment centres.
- Awareness of which clinical data warehouses are in development within HIV treatment centres to monitor standardisation of unstructured data, thereby enabling possible data extraction in the future: broadening of Lab-Link.
- More widespread use of the HL7 protocol for sending messages.

- Implementation of a tool (HL7 message parser) to increase the speed at which the HL7 messages are read and checked for errors.
- Further automation of a number of steps in internal processes to reduce the process time.

The recommendations for manual data collection have been included in the statement of requirements for the new data entry database that will replace Oracle Clinical.

Centre-specific reports

Standard reports for each centre are presented twice a year on a password-protected area of the SHM website to provide treatment teams in the treatment centres with an overview of developments, trends and issues within their own patient populations. In 2014, these centre-specific reports were updated and presented to the HIV treatment centres on two occasions.

Improvements to data warehouse and data processing

SHM's data warehouse is located on an SQL (structured query language) server in the AMC, and extracts data from all SHM source systems. The data warehouse is updated daily with data that were manually entered into the national SHM database on the previous day, and with data sent by treatment centres via Lab-Link. The clear distinction between the production environment and the acceptance test environment allows efficient generation of data views for data analyses and reports, while maintaining quality. In 2014, the data warehouse contained 344 data views that provided daily overviews of SHM data and made these data available for analysis and presentation to treatment centres in table and report form. A data freeze takes place twice a year, after which the raw data tables from the data warehouse are processed to yield tables suitable for data analysis. The data are cleaned, clustered, and coded according to the standard protocols of various national and international collaborations and the Anatomical Therapeutic Chemical (ATC) classification. In 2014, these data processing steps resulted in data sets for centre-specific reports, the *Co-morbidity and Aging with HIV* (*AGE$_h$IV*) study and ZiZo (*Zichtbare Zorg*, Visible Care). In addition, data processing and data set generation was carried out for four international collaborations, D:A:D, COHERE, EPPIC and BEEHIVE.

Volume of data collection

Table 1 summarises the results of the data collection. The total volume of manual data collection decreased by 2% in 2014 compared with 2013. This decrease in manual data collection is the result of a 12% increase in the volume of automated data collection via Lab-Link, with automated data transfer from the hospital computer systems replacing manual entry of laboratory data. This shift is in line with SHM's automation strategy, which aims to improve efficiency by reducing manual data collection. The volume of manual collection of data on viral hepatitis infections in HIV-infected patients rose by 3% in 2014 compared to 2013. This rise reflects an effort undertaken in 2014 to retrospectively collect data on chronic HBV infection. The total volume of data collected rose by 4% in 2014, reflecting the increase in 2014 in the number of patients for whom data had to be collected.

Table 2 presents the percentage of patients with delays in data collection (backlog) at each HIV treatment centre. A distinction is made between an estimated backlog of more than 365 days (long-term backlog) and one of less than 365 days (short-term backlog). The estimation is based on the difference between the predicted time and the actual time between the most recent patient visit and the next visit. The predicted time is calculated on the basis of the frequency of visits in the year prior to the most recent visit. A difference of 180 days or less is not considered a delay.

In 2014, the average long-term backlog in data collection remained at 0%, while the average short-term backlog decreased by 3%. This is an excellent result, given that, in 2014, the data collectors not only focused on collecting and entering follow-up data, but also focused strongly on resolving discrepancies and improving the quality of existing data. Furthermore, new items were introduced, such as data on HBV and HCV in HIV-infected patients, and HBV mono-infection data were also collected in the context of a study. This decrease in the backlog of data collection was also partly due to ongoing efforts to train data collectors in efficiently organising the data collection process, where individual patient reports and standard data queries are used to monitor backlogs and establish priorities.

Quality control

The automated quality checks to support the manual quality checks by data quality staff and the efficiency improvements introduced in 2012 were expanded in 2014. *Table 3* presents the results of the automated quality checks in 2014. In total, 170 validation rules were defined and 17,520 records with discrepancies were selected and checked by the data collectors. These records were made available to the data collectors through user-friendly online reports. The number of records with discrepancies dropped by 19% in 2014, despite an increase in the number of validation rules. This highlights the effectiveness of automated quality checks and the resulting improvements in data quality compared to the previous year.

Automated checks, developed in 2013, were also carried out on the Lab-Link data in 2014. One-off checks for acceptance of new Lab-Links were carried out on data in an acceptance test environment, while structural checks on Lab-Link data were performed three times on Lab-Link data in the production environment. The Lab-Link data were specifically checked for following points:

- Anonymisation of HL7 messages from within the HIV treatment centre;
- Completeness of the HIV treatment centre's patient population from which HL-7 messages are expected;
- Completeness of the selected components and time-span of laboratory results, in line with expectations and agreements made with the HIV treatment centre;
- Accuracy of messages transmission frequency, based on agreements with HIV treatment centre;

- Correct format of HL-7 messages;
- Accuracy and completeness of transmitted laboratory results, based on a random selection and comparison with laboratory results in the electronic patient records (carried out by the data collectors).

Table 4 shows the results of the manual quality checks performed by the SHM data quality staff in 2014. These manual checks focus on collected data that are essential for SHM's output, on a random selection of new items for which data were collected in 2014, on complex data that can be used as training material for personal coaching of data collectors, and on consistency within the data.

In 2014, data from 502 patients were randomly selected and checked. Data related to cause of death and co-morbidity, defined as 'endpoints', continued to be checked in 100% of cases in 2014. Additional data were also collected and classified for data analysis. SHM's data quality staff did not carry out any manual quality checks in 2014 to detect potential missed comorbidities; instead, these quality checks, which, in 2014, targeted missing cases of diabetes mellitus, were automated in the form of reports that were presented directly to the data collectors for verification. This move to improve efficiency is reflected in *Table 3* in the increase in the number of validation rules and records (n=791), under the heading 'Missing and/or inconsistent laboratory data'. These automated checks resulted in the detection of 13 missed cases of diabetes mellitus.

As part of the personal coaching programme for the 42 data collectors, an average of four patient files from each data collector were selected. The results of the quality controls were discussed with the responsible data collector and item-specific training was provided.

In the course of 2014, data from 1,800 patients were checked manually by SHM data quality staff. In addition, for all patients (n=798) for whom data collectors reported cardiovascular disease or other endpoints in the national SHM database in 2014, the data collected from their files were validated and classified. Data on additional diagnostics were also collected, and cause of death was verified and classified for 211 deceased patients. On average, each HIV treatment centre was visited 20 times by the SHM data quality staff member responsible for that centre.

The number of patients whose files were quality-controlled decreased by 30% in 2014 compared with 2013. This decrease reflects the completion of a one-off undertaking in 2013 to complete retrospective collection of data on co-morbidities and cause of death. As a result of this increased effort, data on co-morbidities and cause of death for all HIV-infected patients registered with SHM have been validated and are now complete, thus creating more data analysis opportunities for research into these subjects.

Training

In 2014, nine new SHM data collectors were trained for the role of data collector and were also give training on relevant medical information relating to HIV, data collection protocols and the data entry system.

In addition to the personal coaching of data collectors, two review days were organised in April and October 2014 for all data collectors. The review day in April focused on liver work-ups, and liver cases were discussed in small groups. During the October review day, the new protocol for the collection of diabetes mellitus data was introduced through presentations and case studies. In addition, Dr Maren Blonk, hospital pharmacist and researcher at Radboudumc, gave a talk on the clinical pharmacology of antiretroviral medication. This was followed by a discussion of cases based on practical examples drawn from the data collection process. During this day, SHM's data quality staff also explained the new registration database, digital registration and termination of registration, and online reporting. Finally, the results of SHM's helpdesk system were presented.

In 2014, three new quality control staff were given training on all medical aspects of HIV infection and on how to recognise related data in the electronic patient records. In addition, two new members of the data management team were given a tailored training in SAS® software during two internal training days in September. Finally, in December 2014, some of the data quality staff took part in a training on recognising various infectious diseases.

Table 1: Data collection results 2004–2014.

	2014	2013	2012	2011
Manual data collection				
HIV-infected adults				
Baseline	51,147	65,447	74,184	155,783
Follow-up	2,137,424	2,565,426	3,776,800	2,198,375
End of follow-up	5,331	4,457	4,161	4,872
Laboratory results	6,133,151	7,325,242	7,001,369	5,891,432
Subtotal (data points)	8,327,053	9,960,572	10,856,514	8,250,462
HIV-infected children				
Baseline	1,499	1,521	994	2,090
Follow-up	44,588	44,768	48,776	67,897
End of follow-up	436	215	268	623
Laboratory results	182,590	199,208	184,863	385,037
Subtotal (data points)	229,113	245,712	234,901	455,647
HIV-exposed children				
Baseline			104	1,105
Follow-up			521	4,860
End of follow-up			170	1,148
Laboratory results			1,484	15,037
Subtotal (data points)			2,279	22,150
Pregnancies				
Baseline	202	528	430	407
Follow-up and end of pregnancies	17,490	12,142	9,967	9,180
Laboratory results	19,396	21,065	5,590	9,528
Subtotal (data points)	37,088	33,735	15,987	19,115
HIV and viral hepatitis co-infected adults				
Baseline	25,669	15,765	4,376	
Follow-up	46	49	21	
Laboratory results	2,728,610	2,066,095	619,330	18,656
Liver diagnostics	20,262	19,652	3,398	
Subtotal (data points)	2,774,587	2,101,561	627,125	18,656

2010	2009	2008	2007	2006	2005	2004
87,005	121,962	95,818	18,199	23,010	27,177	46,488
2,051,617	1,822,878	1,715,076	1,672,864	1,650,518	1,427,391	1,068,278
4,617	4,213	4,404	5,117	5,120	4,251	3,443
5,601,697	5,356,569	5,135,508	5,090,289	5,272,109	4,139,877	3,798,835
7,744,936	7,305,622	6,950,806	6,786,469	6,950,757	5,598,696	4,917,044
449	1,608	441	527	1,243	2,983	756
26,570	47,785	40,901	68,464	138,798	137,542	30,589
162	360	168	248	654	1,299	229
86,869	218,464	166,969	366,370	412,443	606,533	187,900
114,050	268,217	208,479	435,609	553,138	748,357	219,474
808	128	755	674			
3,774	1,331	5,095	4,214			
791	205	641	532			
8,429	2384	11,271	1,591			
13,802	4,048	17,762	7,011			
188	116	206	164	428	673	
4,331	3,007	7,018	5,409	11,738	16,947	
5,764	4,888	11,689	9,073	27,759	35,820	
10,283	8,011	18,913	14,646	39,925	53,440	
16,440	19,492	21,559				
16,440	19,492	21,559				

Table 1 continued

	2014	2013	2012	2011
Viral hepatitis mono-infected adults				
Baseline	11,474			
Follow-up	32,867			
Laboratory results	636,926			
Liver diagnostics	3,169			
End of follow-up	269			
Subtotal (data points)	684,705			
Total manual data collection (data points)	**12,052,546**	**12,341,580**	**11,736,806**	**8,766,030**
% change in manually collected data	*-2%*	*5%*	*33%*	*11%*
Difference compared with previous year	**-289,034**	**604,774**	**2,970,776**	**866,519**
Automated data collection				
Number of laboratory results per year	2,427,062	2,170,555	3,758,558	3,612,404
Estimated data points	12,135,310	10,852,775	18,792,790	14,449,616
Lab-Link as % of total laboratory results	56	53	70	61
% change Lab-Link data	*12%*	*-5%*	*4%*	*734%*
Total manual and automated data collection	**24,187,856**	**23,194,355**	**30,529,596**	**29,920,355**
% change in total data	*4%*	*0%*	*1%*	*1%*
Patients with data in follow-up				
Cummulative number HIV-infected patients with data	17,916	17,243	17,118	16,223
Number of hepatitis mono-infected patients with data	224			
% increase in patients in follow-up with data	*4%*	*1%*	*6%*	*9%*

2010	2009	2008	2007	2006	2005	2004
7,899,511	**7,605,390**	**7,217,519**	**7,243,735**	**7,543,820**	**6,400,493**	**5,136,518**
4%	*5%*	*0%*	*-4%*	*18%*	*25%*	
294,121	**387,871**	**-26,216**	**-300,085**	**1,143,327**	**1,263,975**	
433,254	389,015	222,668	119,668	95,685		
1,733,016	1,556,060	890,672	478,672	382,740		
9	9	11	6	5		
11%	*75%*	*86%*	*25%*			
16,373,068	**14,635,345**	**13,026,353**	**12,619,227**	**12,116,271**	**10,554,877**	**8,808,198**
12%	*16%*	*3%*	*4%*	*15%*	*20%*	
14,877	14,138	13,296	11,666	10,275	9,399	8,537
5%	*6%*	*14%*	*14%*	*9%*	*10%*	

Table 2: Percentage of patients followed in each treatment centre with average data collection backlog of more than, and less than, 365 days.

		> 365 days		< 365 days	
HIV treatment centres	**Location**	**2014**	**2013**	**2014**	**2013**
MCA	Alkmaar	0%	0%	0%	2%
Flevoziekenhuis	Almere	0%	0%	11%	21%
AMC-UvA	Amsterdam	0%	0%	5%	5%
HIV Focus Centrum	Amsterdam	0%	-	1%	-
MC Jan van Goyen	Amsterdam	0%	0%	6%	11%
OLVG	Amsterdam	0%	0%	2%	6%
Slotervaartziekenhuis	Amsterdam	0%	2%	4%	7%
Sint Lucas Andreas Ziekenhuis	Amsterdam	0%	1%	0%	11%
VUmc	Amsterdam	0%	1%	1%	15%
Rijnstate	Arnhem	0%	0%	1%	1%
HagaZiekenhuis - Leyweg	Den Haag	0%	1%	0%	2%
MCH - Westeinde	Den Haag	0%	1%	4%	22%
Catharina Ziekenhuis	Eindhoven	0%	0%	14%	17%
MST	Enschede	0%	0%	0%	2%
UMCG	Groningen	0%	0%	11%	31%
Kennemer Gasthuis	Haarlem	0%	1%	11%	10%
MCL	Leeuwarden	0%	0%	14%	10%
LUMC	Leiden	0%	0%	4%	2%
MC Zuiderzee	Lelystad	0%	0%	8%	12%
MUMC+	Maastricht	0%	0%	21%	13%
Radboudumc	Nijmegen	0%	0%	1%	2%
Erasmus MC	Rotterdam	0%	1%	9%	13%
Maasstad Ziekenhuis	Rotterdam	0%	0%	1%	8%
St. Elisabeth Ziekenhuis	Tilburg	0%	2%	9%	2%
UMC Utrecht	Utrecht	0%	0%	8%	3%
Admiraal De Ruyter Ziekenhuis	Goes	0%	0%	7%	3%
Isala - Sophia	Zwolle	0%	0%	1%	10%
Mean		**0%**	**0%**	**6%**	**9%**

Table 3: Number of automated validation rules per criterion and number of records sent to data collectors for verification.

	2014		2013		2012	
Selection criteria for quality checks	Validation rules (n)	Records (n)	Validation rules (n)	Records (n)	Validation rules (n)	Records (n)
Consistency checks						
Missing and/or inconsistent baseline data	24	881	26	1,698	25	2,759
Missing and/or inconsistent demographic data	11	245	12	247	7	431
Missing and/or inconsistent adverse events data	8	93	8	178	6	522
Missing and/or inconsistent antiretroviral medication data	18	2,549	16	3,626	15	20,697
Missing and/or inconsistent CDC event data	5	64	5	126	6	161
Missing and/or inconsistent data on viral hepatitis infection	6	137	7	291		
Missing and/or inconsistent co-medication data	4	144	4	202	4	337
Missing and/or inconsistent laboratory data	32	5,522	26	2,986		
Missing and/or inconsistent end of follow-up data	10	359	10	610	10	1,297
Cross comparisons based on HICDEP[a]	52	7,526	48	11,565		
Total number of quality checks	**170**	**17,520**	**162**	**21,529**	**41**	**23,014**

[a] *HICDEP: HIV Cohorts Data Exchange Protocol*

Table 4: Number of patient files checked by data monitors, according to data selection criterion.

Selection criteria for quality checks	2014	2013	2012
Random selection			
Random selection of adverse event data	0	0	0
Random selection of antiretroviral medication data	0	3	0
Random selection of baseline data	0	0	56
Random selection of CDC event data	0	0	0
Random selection of co-medication data	0	0	0
Random selection of data on pregnancies	229	88	
Random selection of data on viral hepatitis B infection	135	169	
Random selection of data on viral hepatitis C infection	138	0	
Random selection of all patient data	0	0	0
Random selection of data from last year of follow-up	0	0	0
Subtotal random selection	**502**	**260**	**56**
Consistency checks			
Inconsistencies in adverse event data	0	0	32
Inconsistencies in antiretroviral medication data	0	0	0
Inconsistencies in baseline data	0	0	0
Priority analysis of baseline data	160	0	0
Inconsistencies in CDC event data	0	0	0
Inconsistencies in co-medication data	0	0	0
Inconsistencies in laboratory data	156	0	0
Subtotal consistency checks	**316**	**0**	**32**
Detection of missed co-morbidities, defined as endpoints			
Cardiovascular disease		184	
Diabetes mellitus		280	
Chronic liver disease		219	
Renal disease		84	
Non-AIDS-defining malignancies		36	
Subtotal of detected missed co-morbidities		**803**	
Co-morbidity and cause of death checks			
Total cardiovascular disease	357	652	186
Myocardial infarction	*(77)*	*(106)*	*(51)*
Invasive cardiovascular procedures	*(98)*	*(131)*	*(49)*
Diabetes mellitus	*(168)*	*(312)*	*(54)*
Stroke	*(14)*	*(103)*	*(32)*
Chronic liver disease	32	41	12
Terminal kidney disease	25	85	16
Non-AIDS-defining malignancies	173	332	294
Cause of death in 100% of cases	211	247	227
Subtotal of co-morbidity and cause of death checks	**798**	**1,357**	**735**
Subtotal personal coaching of data collectors	**184**	**309**	**168**
Total number of quality checks	**1,800**	**2,729**	**991**
Change (%) per year	**-30%**	**175%**	**-9%**

	Number of patient files							
	2011	2010	2009	2008	2007	2006	2005	2004
	0	0	0	0	2	1	0	0
	1	0	2	8	3	13	6	0
	81	0	0	0	52	17	7	1
	0	0	0	1	2	11	0	0
	0	0	0	0	0	2	0	0
				1		129		
	0	1	0	2	1	17	87	118
	0	0	0	0	0	38	126	203
	82	**1**	**2**	**12**	**60**	**228**	**226**	**322**
	237	1,147	74	1,056	30	69	1	0
	2	2	23	209	1	18	3	0
	11	0	0	116	362	97	161	0
	0	0	10	0	207	0	0	0
	1	2	3	257	122	289	0	0
	0	0	4	2	7	17	0	0
	1	4	16	93	18	5	0	0
	252	**1,155**	**130**	**1,733**	**747**	**495**	**165**	**0**
	223	219	167	55	92	151	108	45
	(38)	*(46)*	*(36)*	*(16)*	*(17)*	*(31)*	*(33)*	*(14)*
	(49)	*(49)*	*(43)*	*(14)*	*(10)*	*(40)*	*(16)*	*(10)*
	(76)	*(101)*	*(62)*	*(19)*	*(40)*	*(55)*	*(37)*	*(16)*
	(60)	*(23)*	*(26)*	*(6)*	*(25)*	*(25)*	*(22)*	*(5)*
	23	10	22					
	34	12	13					
	137	177	381					
	185	152	113	108	128	151	27	1
	602	**570**	**696**	**163**	**220**	**444**	**145**	**46**
	154	**124**	**114**	**241**	**268**	**216**	**0**	**0**
	1,090	**1,850**	**942**	**2,149**	**1,295**	**1,254**	**536**	**368**
	-41%	**96%**	**-56%**	**66%**	**3%**	**179%**	**19%**	

Facts and figures: registration & monitoring of HIV-infected individuals

This chapter provides a summary of the patient population registered in Stichting HIV Monitoring's database as of 31 December 2014.

General

As of 31 December 2014, a cumulative total of 23,345 persons with HIV infection were registered through the Dutch HIV treatment centres by Stichting HIV Monitoring (SHM) (*Table 5*), of whom 1,111 were newly-registered in 2014 (*Table 6*). Of the 23,345 persons, 18,645 (80%) were men, and 4,700 (20%) were women. A total of 249 persons were registered with an HIV treatment centre specialising in children and adolescents.

Further clinical data were collected for 22,947 registered patients. The remaining 398 (1.7%) persons indicated that they opposed the collection of such data.

In 2014, data were collected from 18,134 (78%) persons. Of the 5,211 (22%) persons with no data collected in 2014, 2,247 had died before 2014, 1,135 had moved abroad and 1,829 had disappeared from care for an unknown reason or had objected to the collection of such data. Taking into account those persons who had objections to data collection and those who died in 2014, as of 31 December, there remained 17,965 HIV-infected persons in care for whom data were collected in 2014.

Adults

Of the 22,947 persons registered in 2014, 22,538 were adults at the time of registration, comprising 18,173 (81%) men and 4,365 (19%) women. The most common route of HIV transmission was sexual contact with other men (73%) in men and heterosexual contact (88%) in women. The median age at diagnosis was 37.2 (interquartile range [IQR] 30.3-45.0) years for men and 31.3 (IQR 26.0-38.8) years for women. At the end of 2014, 3% of the group had been aware of their positive HIV status for less than a year, 19% had known for 1 to 5 years, 25% had known for 5 to 10 years, and 42% had known for more than 10 years, while for 0.5% the HIV diagnosis date had not, or not yet, been registered. The remaining 10% of the 22,535 adults had died. The median follow-up duration was 8.2 (IQR 3.9-13.9) years: 7.9 years for men and 9.2 years for women. The total follow-up in the adult group was 213,024 person years.

Of the 1,050 HIV-positive adults newly registered in 2014 for whom further clinical data were collected, the main transmission route remained sexual contact with other men (77%) in men and heterosexual contact (93%) in women. The median age at diagnosis was 38.4 (IQR 29.9-48.3) years in men and 35.5 (IQR 28.1-46.0) years in women.

Children

Of the 22,947 persons registered as of 31 December 2014, 409 (2%) were children or adolescents. This group consisted of 194 (47%) boys and 215 (53%) girls. The median age at diagnosis was 2.9 (IQR 0.6-9.9) years for boys and 3.6 (IQR 0.6-15.4) years for girls. In the majority of cases, the route of infection was vertical mother-to-child transmission (70%); in 20% of cases, the route of infection was recorded as sexual transmission. In total, 32% of the infected children were born in the Netherlands, and 56% were born in sub-Saharan Africa. The median duration of follow-up was 8.2 (IQR 3.9-13.9) years: 7.9 years for boys and 9.2 years for girls. The total follow-up for the group of children and adolescents was 3,884 person years.

In 2014, 26 children and adolescents (10 boys and 16 girls; 23 children aged between 0 and 12 years and 3 adolescents aged 13-17 years) were newly registered. Nineteen of the 26 children and adolescents came from sub-Saharan Africa.

Pregnant women

The total number of registered pregnancies increased from 2,659 in 2013 to 2,825 in 2014. These pregnancies occurred in 1,628 women. In 55% of the cases, HIV was diagnosed before the start of the pregnancy, and, in 45% of cases HIV was diagnosed during the pregnancy. The transmission route of HIV in the pregnant women was mainly through heterosexual contact (94%); in 1% of the pregnant women, transmission occurred through injecting drug use. The median age during the first pregnancy was 29 (IQR 25-33) years. In 36% of the women, combination antiretroviral therapy (cART) was started before the first pregnancy was diagnosed, and in 50% of the women, cART was started during the pregnancy. In 26% of cases, gestation lasted less than 16 weeks; in those women who were still pregnant after the initial 16 weeks, the median gestation period was 39 (IQR 37-40) weeks. Of the pregnancies, 74% resulted in the birth of a child, 30% of which involved C-section. Despite the introduction of a national HIV screening programme for pregnant women in 2004, nine children have since been infected with HIV through vertical transmission in the Netherlands. In the case of four of these children, the mothers were not diagnosed as HIV-positive until after the birth of the child. In two cases, the mothers had tested HIV-negative during the pregnancy screening and must have become infected with HIV later on in the pregnancy. Another child's mother was known to be HIV-positive during pregnancy, but for unknown reasons was not treated for HIV. In the two remaining cases, whether the mothers had undergone pregnancy screening was unknown.

Table 5: Cumulative numbers and percentages of HIV-infected patients registered and monitored by SHM in one of the HIV treatment centres in the Netherlands and in Curaçao on 31 December 2014.

		Total		Alive		Deceased		Objection[a]		Data in 2014[b]		No data in 2014			
												Deceased before 2014[c]		Other[d]	
HIV treatment centre	**Location**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Adults															
MCA	Alkmaar	317	1.4	289	91.2	28	8.8	2	0.6	263	83.0	26	8.2	28	8.8
Flevoziekenhuis	Almere	170	0.7	164	96.5	6	3.5	2	1.2	152	89.4	5	2.9	13	7.6
AMC-UvA	Amsterdam	2,796	12.1	2,485	88.9	311	11.1	8	0.3	2,159	77.2	300	10.7	337	12.1
HIV Focus Centrum	Amsterdam	493	2.1	490	99.4	3	0.6	0	0.0	493	100.0	0	0.0	0	0.0
MC Jan van Goyen	Amsterdam	293	1.3	254	86.7	39	13.3	5	1.7	203	69.3	38	13.0	52	17.7
OLVG	Amsterdam	3,284	14.2	2,930	89.2	354	10.8	132	4.0	2,488	75.8	335	10.2	461	14.0
Slotervaartziekenhuis	Amsterdam	834	3.6	693	83.1	141	16.9	9	1.1	596	71.5	138	16.5	100	12.0
St Lucas Andreas Ziekenhuis	Amsterdam	399	1.7	353	88.5	46	11.5	0	0.0	322	80.7	45	11.3	32	8.0
VUmc	Amsterdam	612	2.6	530	86.6	82	13.4	8	1.3	447	73.0	77	12.6	88	14.4
Rijnstate	Arnhem	739	3.2	670	90.7	69	9.3	2	0.3	601	81.3	67	9.1	71	9.6
HagaZiekenhuis – Leyweg	Den Haag	704	3.0	623	88.5	81	11.5	28	4.0	481	68.3	78	11.1	145	20.6
MCH – Westeinde	Den Haag	1,015	4.4	935	92.1	80	7.9	38	3.7	766	75.5	77	7.6	172	16.9
Catharina Ziekenhuis	Eindhoven	604	2.6	568	94.0	36	6.0	3	0.5	499	82.6	32	5.3	73	12.1
MST	Enschede	561	2.4	458	81.6	103	18.4	2	0.4	349	62.2	98	17.5	114	20.3
UMCG	Groningen	870	3.8	793	91.1	77	8.9	16	1.8	694	79.8	72	8.3	104	12.0
Kennemer Gasthuis	Haarlem	452	2.0	400	88.5	52	11.5	2	0.4	355	78.5	48	10.6	49	10.8
MCL	Leeuwarden	282	1.2	258	91.5	24	8.5	0	0.0	232	82.3	22	7.8	28	9.9
LUMC	Leiden	684	3.0	626	91.5	58	8.5	29	4.2	532	77.8	55	8.0	97	14.2
MC Zuiderzee	Lelystad	63	0.3	63	100.0	0	0.0	1	1.6	57	90.5	0	0.0	6	9.5
MUMC+	Maastricht	842	3.6	716	85.0	126	15.0	3	0.4	610	72.4	121	14.4	111	13.2
Radboudumc	Nijmegen	706	3.1	634	89.8	72	10.2	15	2.1	572	81.0	67	9.5	67	9.5
Erasmus MC	Rotterdam	2,400	10.4	2,140	89.2	260	10.8	8	0.3	1,829	76.2	249	10.4	322	13.4
Maasstad Ziekenhuis	Rotterdam	677	2.9	627	92.6	50	7.4	4	0.6	578	85.4	45	6.6	54	8.0
St. Elisabeth Ziekenhuis	Tilburg	1,063	4.6	998	93.9	65	6.1	13	1.2	878	82.6	58	5.5	127	11.9
UMC Utrecht	Utrecht	1,612	7.0	1,445	89.6	167	10.4	48	3.0	1,268	78.7	154	9.6	190	11.8
Admiraal De Ruyter Ziekenhuis	Goes	178	0.8	166	93.3	12	6.7	3	1.7	136	76.4	12	6.7	30	16.9
Isala – Sophia	Zwolle	446	1.9	420	94.2	26	5.8	17	3.8	356	79.8	25	5.6	65	14.6
Total adults		**23,096**		**20,728**	**89.7**	**2,368**	**10.3**	**398**	**1.7**	**17,916**	**77.6**	**2,244**	**9.7**	**2,936**	**12.7**

Table 5 continued

HIV treatment centre	Location	Total n	Total %	Alive n	Alive %	Deceased n	Deceased %	Objection[a] n	Objection[a] %	Data in 2014[b] n	Data in 2014[b] %	No data in 2014: Deceased before 2014[c] n	No data in 2014: Deceased before 2014[c] %	No data in 2014: Other[d] n	No data in 2014: Other[d] %
Children/adolescents															
EKZ, AMC-UvA	Amsterdam	79	31.7	79	100.0	0	0.0	0	0.0	76	96.2	0	0.0	3	3.8
BKZ, UMCG	Groningen	24	9.6	24	100.0	0	0.0	0	0.0	23	95.8	0	0.0	1	4.2
Erasmus MC – Sophia	Rotterdam	75	30.1	73	97.3	2	2.7	0	0.0	60	80.0	2	2.7	13	17.3
WKZ, UMC Utrecht	Utrecht	71	28.5	70	98.6	1	1.4	0	0.0	59	83.1	1	1.4	11	15.5
Total children/adolescents		**249**		**246**	**98.8**	**3**	**1.2**	**0**	**0.0**	**218**	**87.6**	**3**	**1.2**	**28**	**11.2**
Curaçao															
SEHOS	Willemstad	930	98.4	770	82.8	160	17.2	1	0.1	522	56.1	156	16.8	252	27.1
SEHOS kinderkliniek	Willemstad	15	1.6	5	33.3	10	66.7	0	0.0	0	0.0	10	66.7	5	33.3
Total Curaçao		**945**		**775**	**82.0**	**170**	**18.0**	**1**	**0.1**	**522**	**55.2**	**166**	**17.6**	**257**	**27.2**

[a] *Objection: consent not given for collection of clinical data*

[b] *Data in 2014: registered by SHM in 2014, or deceased during or after 2014, or last contact with an HIV treatment centre during or after 2014.*

[c] *No data in 2014 – deceased before 2014: patients who are not included in 'data in 2014' and who had died before 2014.*

[d] *No data in 2014 – other: patients who are not included in 'data in 2014' because they moved abroad before 2014 or because they had no contact with their HIV treatment centre in 2014 for an unknown reason.*

Table 6: HIV-infected patients registered in 2014 and monitored by SHM in HIV treatment centres in the Netherlands and in Curaçao.

		Total		Alive		Deceased		Objection[a]	
HIV treatment centre	**Location**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Adults									
MCA	Alkmaar	16	1.5	16	100.0	0	0.0	1	6.3
Flevoziekenhuis	Almere	9	0.8	9	100.0	0	0.0	0	0.0
AMC-UvA	Amsterdam	93	8.6	93	100.0	0	0.0	1	1.1
HIV Focus Centrum	Amsterdam	28	2.6	28	100.0	0	0.0	0	0.0
MC Jan van Goyen	Amsterdam	14	1.3	14	100.0	0	0.0	1	7.1
OLVG	Amsterdam	130	12.0	127	97.7	3	2.3	6	4.6
Slotervaartziekenhuis	Amsterdam	7	0.6	7	100.0	0	0.0	0	0.0
St Lucas Andreas Ziekenhuis	Amsterdam	21	1.9	21	100.0	0	0.0	0	0.0
VUmc	Amsterdam	33	3.0	33	100.0	0	0.0	0	0.0
Rijnstate	Arnhem	38	3.5	38	100.0	0	0.0	0	0.0
HagaZiekenhuis - Leyweg	Den Haag	26	2.4	26	100.0	0	0.0	0	0.0
MCH - Westeinde	Den Haag	78	7.2	78	100.0	0	0.0	9	11.5
Catharina Ziekenhuis	Eindhoven	42	3.9	42	100.0	0	0.0	1	2.4
MST	Enschede	27	2.5	25	100.0	2	7.4	1	3.7
UMCG	Groningen	54	5.0	53	98.1	1	1.9	4	7.4
Kennemer Gasthuis	Haarlem	19	1.7	18	94.7	1	5.3	0	0.0
MCL	Leeuwarden	25	2.3	24	96.0	1	4.0	0	0.0
LUMC	Leiden	26	2.4	26	100.0	0	0.0	0	0.0
MC Zuiderzee	Lelystad	4	0.4	4	100.0	0	0.0	0	0.0
MUMC+	Maastricht	45	4.1	44	97.8	1	2.2	0	0.0
Radboudumc	Nijmegen	37	3.4	36	97.3	1	2.7	0	0.0
Erasmus MC	Rotterdam	109	10.0	109	100.0	0	0.0	0	0.0
Maasstad Ziekenhuis	Rotterdam	47	4.3	47	100.0	0	0.0	0	0.0
St. Elisabeth Ziekenhuis	Tilburg	54	5.0	53	98.1	1	1.9	5	9.3
UMC Utrecht	Utrecht	64	5.9	63	98.4	1	1.6	2	3.1
Admiraal De Ruyter Ziekenhuis	Goes	15	1.4	15	100.0	0	0.0	0	0.0
Isala - Sophia	Zwolle	26	2.4	26	100.0	0	0.0	4	15.4
Total adults		**1,087**		**1,075**	**98.9**	**12**	**1.1**	**35**	**3.2**
Children/adolescents									
EKZ, AMC-UvA	Amsterdam	9	37.5	9	100.0	0	0.0	0	0.0
BKZ, UMCG	Groningen	1	4.2	1	100.0	0	0.0	0	0.0
Erasmus MC - Sophia	Rotterdam	9	37.5	9	100.0	0	0.0	0	0.0
WKZ, UMC Utrecht	Utrecht	5	20.8	5	100.0	0	0.0	0	0.0
Total children/adolescents		**24**		**24**	**100.0**	**0**	**0.0**	**0**	**0.0**
Curaçao									
SEHOS	Willemstad	59	100.0	59	100.0	0	0.0	1	1.7

[a] *Objection: consent not given for collection of clinical data*

Monitoring of treatment

In 2014, 90% of the 22,947 patients were treated with cART, whereas 8% of the patients had not yet started treatment. No data had been registered for 0.9% of patients, and 0.7% were being treated with non-cART regimens.

In total, 94% of the first-line cART regimens used in 2014 consisted of tenofovir in combination with emtricitabine as the nucleotide/nucleoside reverse transcriptase inhibitor (NRTI) backbone. Efavirenz was the most widely-used supplement to this backbone in 2012 and 2013, but was superseded by cobicistat-boosted elvitegravir in 2014 (*Table 7*).

Table 7: *Most frequently-used first-line cART combinations in 2012-2014.*

	2012		2013		2014		Total	
	n	%	n	%	n	%	n	%
TDF+FTC+EFV	435	34.3	412	28.9	154	17.0	1,001	27.8
TDF+FTC+DRV/r	188	14.8	263	18.4	117	12.9	568	15.8
TDF+FTC+RPV	140	11.0	291	20.4	119	13.2	550	15.3
TDF+FTC+EVG/c	0	0.0	36	2.5	342	37.8	378	10.5
TDF+FTC+NVP	171	13.5	130	9.1	23	2.5	324	9.0
TDF+FTC+ATV/r	117	9.2	99	6.9	30	3.3	246	6.8
TDF+FTC+RAL	28	2.2	42	2.9	23	2.5	93	2.6
AZT+3TC+LOP/r	36	2.8	27	1.9	10	1.1	73	2.0
TDF+FTC+LOP/r	16	1.3	17	1.2	3	0.3	36	1.0
AZT+3TC+NVP	20	1.6	9	0.6	4	0.4	33	0.9
ABC+3TC+NVP	11	0.9	13	0.9	5	0.6	29	0.8
ABC+3TC+DRV/r	7	0.6	11	0.8	7	0.8	25	0.7
TDF+FTC+EFV+DRV/r	13	1.0	7	0.5	4	0.4	24	0.7
TDF+FTC+RAL+DRV/r	8	0.6	7	0.5	7	0.8	22	0.6
Overig	79	6.2	62	4.3	56	6.2	198	5.5
Totaal	**1,269**	**100.0**	**1,427**	**100.0**	**904**	**100.0**	**3,600**	**100.0**

Legend: *cART=combination antiretroviral therapy, TDF=tenofovir, FTC=emtricitabine, EFV=efavirenz, DRV/r=darunavir/ritonavir, RPV=rilpivirine, EVG/c=elvitegravir/cobicistat, NVP=nevirapine, ATV/r=atazanavir/ritonavir, RAL=raltegravir, LOP/r=lopinavir/ritonavir, AZT=zidovudine, 3TC=lamivudine, ABC=abacavir.*

To date, in 2014, 56 new cases of AIDS were recorded in patients treated with cART, corresponding to an incidence of 4.3 (95% confidence interval [CI] 3.2-5.6) per 1,000 person years. This number is likely to increase slightly once short-term data backlogs have been processed.

In 2014 there were 117 deaths in patients treated with cART. The incidence was 8.3 (95% CI 6.9-10.0) per 1,000 person years, which is comparable to previous years.

Antiretroviral resistance

In 2014, data on the results of genotyping of the HIV reverse transcriptase and protease genes were obtained from four virology laboratories involved in monitoring resistance. At this time, a cumulative total of 12,303 sequences have been collected, 227 of which were collected in 2014 (*Table 8*).

Table 8: Number of HIV-1 reverse transcriptase and protease gene sequences generated by each virology laboratory and registered with SHM as of 31 December 2014.

		Number of sequences obtained	
Laboratory	**Before 2014**	**In 2014**	**Total**
AMC-UvA, Amsterdam	4,901	131	5,032
UMCU, Utrecht	3,623	0	3,623
LUMC, Leiden	[a]1,649	[a]74	1,723
Erasmus MC, Rotterdam	823	22	845
VUmc, Amsterdam	[a]510	[a]0	510
Slotervaartziekenhuis, Amsterdam	179	0	179
CLB[b], Amsterdam	391	0	391
Totaal	**12,076**	**227**	**12,303**

[a] *Exact numbers not available at time of printing.*

[b] *Central Laboratory for the Blood Transfusion Service.*

Since 2003, complete resistance to at least one antiretroviral agent has been detected in 156 (3%) of the 5,142 newly-diagnosed patients for whom sequences were available within a year of diagnosis. These included 24 patients with resistance to protease inhibitors, 31 patients with resistance to lamivudine and emtricitabine, 39 patients with resistance to other NRTIs and 116 patients with resistance to non-nucleoside reverse transcriptase inhibitors. In 2014, sequences were available for 113 patients within one year of diagnosis, and two of these patients were completely resistant to at least one agent.

Hepatitis B and hepatitis C co-infections

Infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) can cause liver cirrhosis, liver fibrosis and hepatocellular carcinoma (HCC). In combination with HIV, the course of such diseases is likely to be accelerated. Therefore, HBV and HCV are also monitored regularly in the HIV-infected population over time. Chronic HCV co-infection is defined as the presence of HCV RNA for at least 6 months after infection. Based on this definition, in 2014, chronic co-infection with HCV was found in 6.5% of the monitored HIV-infected patients. Chronic HBV co-infection was detected in 7% of the monitored HIV-infected patients, and chronic co-infection with both HBV and HCV was found in 0.5% of the monitored HIV-infected patients. Of the patients with chronic HBV co-infection, 9.3% had hepatic fibrosis, 9.0% had hepatic cirrhosis, and 0.9% had HCC. In patients with chronic HCV co-infection, these figures were 21%, 13% and 0.8%, respectively.

Sample collection and storage

Since the start of the AIDS Therapy Evaluation in the Netherlands (ATHENA) project in 1996, an estimated total of 461,740 plasma samples from patients in follow-up have been stored in microbiology laboratories at the HIV treatment centres or in laboratories associated with the centres. This sample collection is exceptionally valuable for clinical epidemiologic research into resistance development over time and into the response of HIV-1 subtypes, other than the most common subtype B, to antiviral therapy. The outcome of such research carries implications both for the quality of care of individual patients and for public health.

Registration of HIV-infected individuals in Curaçao

The registration and monitoring of HIV-infected persons being followed in the St. Elisabeth Hospital in Willemstad, Curaçao, has continued during the past years. Results from the monitoring in Curaçao were presented in the Monitoring Report 2014. In total, 945 patients were registered, of whom 59 were newly registered in 2014.

Key outcomes and recommendations

On 1 December 2014, Stichting HIV Monitoring published its scientific report, 'Monitoring Report 2014 – Human Immunodeficiency Virus (HIV) Infection in the Netherlands'. A summary of the main findings reported in this publication, based on data collected up to 1 June 2014, is presented below.

The HIV epidemic in the Netherlands

As of June 2014, a total of 17,750 persons living with HIV in the Netherlands (17,558 adults, and 192 children and adolescents) were in care in one of the 27 designated HIV treatment centres. Of these 17,750, 91% (16,081) had started combination antiretroviral therapy (cART), and of these 16,081, 91% (14,602) had suppressed viraemia to below the level of quantification at the time of their last available HIV-RNA measurement. These results are impressive when compared to figures from other parts of the world. However, it is also important to realise that of the total 25,000 individuals that the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates were living with HIV in the Netherlands in 2012, 24% are likely to be unaware of their infection; this means that about 7,250 infected persons have not yet been diagnosed or linked to care and, importantly, still contribute to fuelling the epidemic.

In 2013, an estimated 1,100 patients newly entered care, which is comparable to the annual number reported in the last 3 years. In 2013, the majority (71%) of newly-diagnosed infections were in men who have sex with men (MSM), 23% were acquired through heterosexual contact, 0.3% through injecting drug use (IDU), and 6% through other or unknown modes of transmission. Although the rate of newly-diagnosed cases stabilised in the key affected population of MSM, and even steadily declined amongst MSM 35 to 44 years of age, it continued to increase in MSM both 25 years and younger and 55 years and older, as well as in heterosexuals 45 years and older. Of note, almost one quarter of all newly diagnosed patients entering into care in 2013 were 50 years or older. Overall, over 90 percent of persons newly diagnosed with HIV entered into specialised care within 6 weeks after diagnosis. There is little variation in these figures, regardless of whether individuals were diagnosed at a community health service or sexually-transmitted infections (STI) clinic, a hospital or a general practice.

The rates of testing for HIV appear to be increasing in certain settings. Moreover, fortunately, the proportion of patients who are identified and start cART earlier in their infection (including during primary HIV infection) continues to increase, particularly amongst MSM, although this increase is less pronounced in women and heterosexual men. This is reflected in the CD4 count, both at diagnosis and at start of cART, gradually having risen over time to a median of 417 and 360 cells/mm^3, respectively, in 2013. Of note, the likelihood of patients starting cART at higher CD4 counts has also clearly increased. Whilst in 2012, 29% of patients with a CD4 count of 500 cells/mm^3 had begun cART within 6 months of diagnosis, this proportion rose to 41% in 2013. Nonetheless, far too many patients continue to present late

for care. In 2013, 43% of newly-diagnosed patients presented late for care, i.e., with AIDS or a CD4 count less than 350 cells/mm^3, and 12% presented with advanced HIV disease, i.e., with a CD4 count less than 200 cells/mm^3 or AIDS. Generally, the likelihood of presenting late for care or with advanced HIV disease was greater for men with heterosexually acquired infection, individuals originating from South and South-East Asia and Sub-Saharan Africa, and individuals aged 45 years or older.

Improved transdisciplinary strategies that target all factors sustaining the epidemic are clearly needed to achieve a significant decline in the rate of new infections. The aim of these strategies should be to simultaneously reduce the likelihood of HIV infection in key populations at risk, identify infected individuals early, rapidly link all infected persons to care, and start combination antiretroviral therapy in a timely manner.

Combination antiretroviral therapy in adults and quality of treatment and care

Guidelines for the choice of first-line cART are closely adhered to in the Netherlands. Most patients who first initiated cART in 2013 and 2014 did so with a once-daily regimen, including tenofovir/emtricitabine as the backbone. The availability of novel single-tablet fixed-dose regimens, which combine tenofovir/emtricitabine with either the non-nucleoside reverse transcriptase inhibitor (NNRTI) rilpivirine or the cobicistat-boosted integrase inhibitor elvitegravir, has clearly resulted in an increased use of these novel regimens.

Virological response to first-line cART has gradually improved during the era of cART: between 2011 and 2013, 87% of patients who first initiated cART achieved viral suppression to below the level of HIV-RNA quantification within 9 months. Importantly, earlier observations that patients younger than 30 years, those born outside the Netherlands, and those starting cART at a CD4 count >500 cells/mm^3 were less likely to achieve early viral suppression were no longer seen in those who had first begun treatment in the last three years. Of the patients who first initiated cART from 1999 onwards and were continuously on treatment and still in follow-up at 13.5 years, 94% had suppressed viraemia to less than 50 copies/ml.

Overall, 7.5% of the treatment-naive patients who first initiated cART from 1999 onwards have experienced virological failure (defined as time to the first of two consecutive plasma HIV-RNA levels >200 copies/ml after 24 weeks on therapy) to first-line cART. Importantly, the annual proportion of patients experiencing virological failure according to this definition has declined over time to as little as 3%. Nonetheless, as expected, when virological failure does occur, it remains associated with a substantial risk of drug resistance.

International collaborative cohort analyses of the prevalence and incidence of patients experiencing triple-class virological failure (defined as failure of at least two nucleoside reverse transcriptase inhibitors (NRTI), one NNRTI and one ritonavir-boosted protease

inhibitor), to which Stichting HIV Monitoring contributes data, have demonstrated an important improvement in the prognosis of such patients over time, both in terms of their likelihood of achieving resuppression of viraemia and a reduced progression to AIDS and death. These trends are likely mainly driven by the availability of newer drugs with better tolerability, ease of use and limited cross-resistance, indicating the continued public health benefit of the introduction of new drugs.

The proportion of patients achieving greater immunological recovery on cART continues to improve year after year. Nonetheless, a substantial number of patients fail to achieve restoration of CD4 cells to levels above which the risk of both traditionally HIV-associated and non-AIDS-related morbidity may no longer be accentuated as a result of the infection. This particularly holds true for those who commence treatment at a more advanced level of immunodeficiency. In 2013, 13% of patients in care had a last available CD4 measurement less than 350 cells/mm^3. Patients who start cART at a CD4 count of more than 350 cells/mm^3 and have sustained fully suppressed viraemia after 8 years, including patients aged over 50 at the time of treatment initiation, are likely to achieve long-term CD4 counts similar to those in the general population. Similar trends were observed in the patients' ability to achieve a CD4/CD8 ratio greater than 1, which may be a marker of reduced residual immune activation whilst on suppressive cART. A median CD4/CD8 ratio above 1 was achieved after 3.5 and 8 years of suppressive cART, if CD4 cell counts at the start of cART were ≥500 cells/mm^3, and between 350 and 500 cells/mm^3, respectively. Further analyses, including in collaboration with other cohorts, are ongoing to address whether CD4/CD8 ratios independent of CD4 counts are associated with an increased risk of morbidity, including from non-AIDS events.

Although tolerability of cART has continued to improve with time and larger numbers of patients remain on their initial regimen for a longer time, drug intolerance or toxicity is still the most common reason for a change of initial treatment. MSM, women and older patients were more likely to change their initial regimen because of toxicity. This likelihood was higher in MSM, especially when treatment was started at CD4 counts above 500 cells/mm^3.

As larger numbers of clinically asymptomatic, newly-identified patients with HIV are expected to start treatment earlier, continued development of drugs that are better tolerated and improvements in individualised patient management remain necessary to further improve the durability of initial treatment.

Morbidity and mortality

Mortality rates remain low in HIV-infected patients in care in the Netherlands. There has been a sustained decline in death from AIDS, with a shift towards death from other causes. Non-AIDS co-morbidities, including non-AIDS-defining malignancies (NADM), cardiovascular disease (CVD) and chronic liver disease, comprise a sizable fraction of those other causes. Of note, however, the proportion of patients dying of AIDS (nearly 25%) remained substantial

between 2007 and 2013. Once more, this seems to be largely driven by late presentation and late entry into care, and stresses the importance of identifying and linking individuals to care earlier in the course of the infection. It is interesting to note that a recent analysis by the Collaboration of Observational HIV Epidemiological Research Europe (COHERE), to which SHM is an important contributor, showed that the incidence of AIDS-defining illnesses was higher in individuals with a current CD4 count of 500 to 749 cells/mm^3 compared to those with a CD4 count of 750 to 999 cells/mm^3; in addition, the incidence did not decrease further at higher CD4 counts, even in patients suppressed on cART. These findings suggest that immune reconstitution may not be complete until the CD4 count increases to more than 750 cells/mm^3.

Similarly high CD4 counts achieved on cART, for example by commencing treatment at higher levels than the current average in the Netherlands, will contribute to preventing the most frequently-observed non-AIDS co-morbidities. However, the extent of this contribution remains to be determined. In particular, analyses of the most recent SHM dataset tend to show that prior AIDS and/or low nadir or current CD4 count are independently associated with an increased risk of cardiovascular disease, diabetes mellitus, chronic kidney disease and non-AIDS malignancies.

As expected, older age was also found to be an important risk factor for these co-morbidities that are traditionally associated with ageing. In this context, it is important to note that the proportion of older individuals with newly-diagnosed HIV entering care in the Netherlands continues to increase over time; in 2013, 24% were 50 years or older compared to 20% in 2012. At the same time, the age distribution of the overall patient population with HIV in care in the Netherlands has also changed, with 39% currently older than 50 years (37% in 2012). Of particular concern is the increasing proportion of patients with multiple co-morbidities, the risk of which appears to be increased in those with HIV. Data from the AGE$_h$iV Cohort Study, in which SHM collaborates with the Academic Medical Center, the Amsterdam Institute for Global Health and Development and the Public Health Service (*Gemeentelijke Gezondheidsdient*, GGD) in Amsterdam, show that both the presence of multiple co-morbidities and individual cases of hypertension, cardiovascular disease, peripheral arterial disease and chronic kidney disease are significantly more prevalent amongst those with HIV than in an uninfected control population of a similar age distribution. Besides older age, smoking and a positive family history (for hypertension, myocardial infarction, diabetes mellitus, or hypercholesterolaemia), duration of time spent with a CD4 count less than 200 cells/mm^3, increasing levels of markers of inflammation and innate immune activation, central obesity and longer prior exposure to ritonavir at total doses of ≥400 mg daily were independently associated with the prevalence of co-morbidity.

Ageing of the population in care may also explain why cardiovascular risk assessment using the algorithm developed by the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study group indicates a gradual increase from 12.8% in 2007 to 14.9% in 2013 in the

proportion of patients at either high (5-10%) or very high (≥10%) risk of developing coronary heart disease in the next 5 years. Although cardiovascular risk management seems to have improved over time, the observation that over half of patients at high or very high risk were not known to be using a statin clearly indicates further room for improvement.

Whilst the overall incidence of non-AIDS-defining malignancies in the population with HIV in care has remained stable over time since the introduction of cART, the absolute number and proportion of deaths due to these malignancies has increased. Given the known markedly increased risk of anal cancer in HIV-infected MSM, the observation that the overall incidence of anal cancer slowly decreased over time from 1.2 cases per 1,000 person years in 2002-2003 to 0.6 cases per 1,000 person years in 2012-2013 is relatively reassuring. The gradual increase in CD4 count at time of HIV diagnosis and start of cART, which has been most notable amongst MSM, may have contributed to this trend. Collaborative analyses conducted on much larger datasets as part of the D:A:D study are needed to provide the statistical power to address the possible contribution of prolonged exposure to particular antiretrovirals on the risk of developing (individual) non-AIDS malignancies, including anal cancer.

Awareness of the role of modifiable, often lifestyle-related risk factors, like smoking, and their management by both physicians and HIV-infected individuals, particularly those who are older or otherwise at high a priori risk of certain co-morbidities, offers important hope of ensuring a lower co-morbidity burden and healthy ageing. This applies not only to conditions such as cardiovascular disease and diabetes mellitus, but also to measures to prevent cancer, chronic kidney disease and bone loss. At the same time there is clear room for improvement in the use of known effective biomedical interventions for primary and secondary prevention according to general guidelines.

Hepatitis B and C co-infections

Screening for viral hepatitis B (HBV) and C (HCV) co-infection has, with time, increasingly become part of the standard of care in the Netherlands. As a result, the presence or absence of HBV or HCV infection is now documented for virtually all HIV-infected patients in care in the Netherlands. Approximately 12% of patients had evidence of ever having been exposed to HCV, 6% were documented as having chronic infection and 1.5% had acute infection. Seven percent of patients were shown to have chronic HBV infection.

HCV genotype 1 infection was the most common genotype in patients with either chronic or acute HCV infection, and most patients with HCV infection were male and from the Netherlands or other European countries. Importantly, the incidence of acute HCV infection observed in recent years amongst MSM remains high, having risen from 0.54 cases per 1,000 person years in 2003 to 5.5 per 1,000 person years in 2011, and 4.2 per 1,000 person years in 2013. This clearly indicates the need for continued preventive efforts in these men, including the use of the use of novel highly effective combination therapies for HCV.

An estimated 32% of HIV-infected patients overall and 24% of MSM either had not been exposed to HBV or had not been successfully vaccinated and may remain at risk of acquiring HBV. Thus, it is important that efforts are undertaken to increase successful vaccination rates amongst this subgroup of patients.

Co-infected patients with a longer duration of infection were at increasing risk of progressing to chronic liver disease, including hepatocellular carcinoma (HCC). Ten years after a known diagnosis of viral hepatitis, HCC had developed in 3% of patients with chronic HCV and 1% of patients with chronic HBV. Of note, the likelihood of dying from chronic liver disease from 2000 onwards had declined in patients with chronic HBV, probably due to increasing use of tenofovir as part of combination therapy for HIV.

The uptake of HCV treatment has markedly increased in recent years. Among the HIV/HCV co-infected patients currently known to be in care, 59% have ever been exposed to treatment for their HCV infection. Among patients treated with a combination of pegylated interferon alpha (peg-IFN alpha) and ribavirin (RBV), only 39% overall could be considered cured. The direct-acting antivirals boceprevir or telaprevir became available in the Netherlands early in 2012. Combining either of these agents with peg-IFN alpha and RBV has improved response rates for HCV genotype 1 infection, yet the results remain suboptimal. Moreover, these regimens are associated with clinically significant toxicities and drug-drug interactions with cART. Of the 1,187 HCV/HIV co-infected patients who receive ongoing care in one of the Dutch HIV treatment centres, a total of 907 (76%) remain in need of effective HCV therapy, 485 of whom have never yet received HCV treatment and 422 in whom prior treatment was unsuccessful.

The availability of combinations of direct-acting pan-genotypic antivirals against HCV that are much better tolerated and more efficacious is eagerly awaited. It is hoped that these combinations, which will potentially allow the use of interferon-free regimens, will contribute to further reducing the burden of severe chronic liver disease, hepatocellular carcinoma and liver-related mortality amongst persons living with HIV. In addition, joined with additional preventive measures, they may contribute to reducing the rate of incident HCV infection among the key affected population of MSM.

HIV in pregnant women and in children

Universal first trimester screening for HIV in pregnant women and the increasingly effective use of cART during pregnancy has made perinatal transmission of HIV extremely rare in the Netherlands, although cases of incident HIV infection following a negative first trimester screen have been documented later during pregnancy.

Together with the observation that approximately 10% of HIV-infected pregnant women do not have fully suppressed viraemia around the time of delivery this indicates the need for continued vigilance, to ensure zero vertical transmissions of HIV.

Treatment outcomes for children living with HIV in the Netherlands and receiving care in one of the four designated paediatric treatment centres are generally favourable. These outcomes include long-term immunologic responses to cART, particularly in vertically-infected children who have started treatment below two years of age. More and more of these children, however, are transitioning into adult care. Around 30% of the children who have transitioned into adult care and are retained in care currently do not have fully suppressed viraemia. This illustrates that optimisation of long-term care for this particularly vulnerable and difficult-to-manage group of young individuals is sorely needed.

Amsterdam Cohort Studies

The Amsterdam Cohort Studies (ACS) on HIV and AIDS started in 1984 with men who have sex with men (MSM) and was expanded in 1985 to include injecting and non-injecting drug users (DU). The original aims were to investigate the epidemiology, psychosocial determinants, natural history, and pathogenesis of HIV-1 infection and AIDS, as well as to evaluate the effect of interventions in HIV-negative and HIV-positive men and women. In the past decade, the focus has broadened to include the epidemiology and natural history of blood-borne and sexually transmitted infections (STI), other than HIV. In recent years, this research has been extended with prospective testing for STI and human papillomavirus infection.

From the outset, research in the ACS has taken a multidisciplinary approach. The collaborating institutes within the ACS framework are Sanquin Blood Supply Foundation, the Public Health Service of Amsterdam (*Gemeentelijke Gezondheidsdient*; GGD Amsterdam), the Academic Medical Center of the University of Amsterdam, the University Medical Centre Utrecht, the Jan van Goyen Medical Centre, HIV Focus Centrum, and Stichting HIV Monitoring (SHM). The ACS infrastructure is financed primarily through a contribution from the National Institute for Public Health and the Environment (*Rijksinstituut voor Volksgezondheid en Milieu*, RIVM), and each participating institute also makes a financial contribution. The scientific studies are funded separately by external sources.

The ACS is unique in its follow-up of two populations at risk of HIV infection, namely HIV-negative MSM and HIV-negative DU. These populations are followed through the GGD. Following the Scientific Advisory Committee's positive evaluation in 2013, the decision was made to slim down the follow-up of DU. This process was set in motion in January 2014. Four groups are still being actively followed: all HIV-positive DU, all HCV seroconverters, all HIV-negative and HCV-negative DU who have injected for more than 2 years and who are therefore more likely to have been exposed to HIV and/or HCV (multiple-exposure group), and a control group of 15 HIV-negative DU (non-multiple-exposure group). At the same time, the group of HIV-negative MSM was expanded by almost 100 new participants in 2014, with the aim of having approximately 750 HIV-negative participants in active follow-up by the end of 2016. The recruitment also included special efforts to include younger MSM in the ACS.

The HIV-infected MSM included in the ACS remain in active follow-up. This follow-up takes place primarily through the regular HIV medical care and through monitoring by SHM. In addition to the standard medical care, study samples are collected and stored for specific immunological and virological studies. These samples are collected from HIV-negative individuals, HIV seroconverters who became infected during the ACS follow-up, and individuals who were already HIV-infected at inclusion in the ACS.

As of 31 December 2014*, 2,650 MSM and 1,661 DU were included in the ACS. Since the start of the ACS, MSM have visited the GGD 54,810 times and DU have visited the GGD 27,657 times. In 2014, 738 MSM, 124 of whom were HIV-positive, were actively followed by the GGD. Of these participants, 97 were newly recruited and none died. A total of 218 DU (29 HIV-positive) were in active follow-up at the GGD in 2014; there were no new inclusions in this group in 2014, and 13 participants died. The preliminary HIV incidence in 2014 was 1.12 per 100 person years among MSM, and there were no new HIV infections among DU. These figures may still change as collection of data for 2014 is not yet complete.

** Total numbers for 2014 were still being collected and were not yet complete at time of printing.*

Collaborations

National collaborations

AMC-UvA

SHM collaborates with the Academic Medical Centre (AMC) of the University of Amsterdam (UvA) on various projects. Led by Prof. Peter Reiss (Department of Global Health (a subdivision of the department of infectious disease), AMC, Amsterdam; and director of SHM), the *Co-morbidity and Aging with HIV* (AGE_hiV) cohort study aims to assess the incidence and prevalence of a broad range of co-morbidities and known risk factors for these co-morbidities in HIV-infected patients compared with non-HIV-infected individuals. Another collaboration closely associated with the AGE_hiV cohort study, is the COBRA (*Co-morbidity in relation to AIDS*) programme, which aims to further investigate these issues in collaboration with a number of European partners, for example by identifying reliable biomarkers of co-morbidity and ageing in the context of HIV (refer to *http://fp7-cobra.eu* for further information). As a COBRA partner, SHM collaborates with the AMC and provides the data collection infrastructure for monitoring the incidence and prevalence of a number of these co-morbidities. The results obtained from this research may be used to inform and adapt national and international guidelines for prevention and management of co-morbidities in ageing HIV-infected individuals.

SHM also makes a contribution in terms of expertise in methodology and data management to the *HIV Transmission Elimination Amsterdam* (H-Team) project, led by the Amsterdam Institute for Global Health and Development and the department of Global Health at the AMC. The project is a multidisciplinary and interdisciplinary collaboration involving various stakeholders from preventative and curative HIV care and from other target groups (including Public Health Service Amsterdam (*Gemeentelijke Gezondheidsdient*; GGD Amsterdam), SOA Aids Nederland, Dutch HIV Association (*HIV vereniging Nederland*), Amsterdam hospitals, Maastadziekenhuis in Rotterdam, Leids Universitair Medisch Centrum (LUMC), Erasmus MC, and the National Institute for Public Health and the Environment) that aims to reduce the number of new HIV infections in Amsterdam.

In addition to these activities, SHM collaborates with the AMC, together with Onze Lieve Vrouw Gasthuis and LUMC on the Quality of Care programme. This programme, for which SHM was awarded an Aids Fonds grant in 2012, aims to investigate the determinants (patient, medical professional and hospital-related) that lead to a higher quality of care. Under the direction of Suzanne Geerlings (AMC), the Quality of Care programme continued in 2013.

CIb-RIVM

The Centre of Disease Control of the Netherlands National Institute for Public Health and the Environment (*Centrum voor Infectieziektenbestrijding-Rijksinstituut voor Volksgezondheid en Milieu*; CIb-RIVM), headed by Prof. Jaap van Dissel, uses data collected

by SHM to coordinate data on the registration of new HIV infections within the framework of the national HIV registration and surveillance programme.

SHM's registration activities are closely associated with the CIb with regard to HIV and other sexually transmitted diseases such as hepatitis B (HBV) and hepatitis C (HCV), as well as infectious diseases such as tuberculosis. The CIb-RIVM and SHM renewed an agreement at the beginning of 2009 to exchange data collected through the SHM framework for purposes of surveillance carried out by the CIb-RIVM.

Since 1 January 2012, SHM's funding from the Ministry of Health, Welfare and Sport has been routed via the CIb-RIVM.

GGD Amsterdam

SHM contributes to the *MSM Observational Study of Acute Infection with Hepatitis C* (MOSAIC) study coordinated by the GGD Amsterdam. The MOSAIC study involves a cohort of men who have sex with men (MSM) with chronic HIV infection who have contracted an acute hepatitis C (HCV) infection. The aims of the study are to look at the contribution of this group to the transmission of HIV; to explore the driving factors of the HCV epidemic and HIV's role in it; and to examine the impact of acute HCV infection, reinfection and treatment on disease progression. SHM and GGD Amsterdam also work together on the Amsterdam Cohort Studies (ACS, reviewed earlier in this report), in collaboration with the AMC-UvA. The ACS is primarily funded through the CIb-RIVM and, as of 1 January 2015, the funding is included in the structural institute grant awarded to SHM by the CIb-RIVM.

Harmonic

Harmonic is a collaboration launched in 2014 between two HIV/hepatitis treatment centres in the Netherlands, UMC Utrecht and Rijnstate in Arnhem, and SHM, to compare patients with a hepatitis B (HBV) mono-infection with those with HIV/HBV co-infection. This retrospective study aims to compare the natural course of HBV, the morbidity and mortality associated with the infection, and the effect of treatment between mono-infected and HIV co-infected patients. SHM contributes to *Harmonic* by making data available on HIV/HBV co-infected individuals registered in SHM's database, and by implementing the data collection of HBV mono-infection at both study sites. Furthermore, SHM provides database management, data sets for analysis, and contributes analytic and scientific support and supervision.

International collaborations

EuroCoord

The *European Coordinating Committee for the Integration of Ongoing Coordination Actions Related to Clinical and Epidemiological HIV Research* (EuroCoord) was established by several of the largest HIV cohorts and collaborations within Europe - CASCADE, COHERE,

EuroSIDA, and the *Paediatric European Network for the Treatment of AIDS* (PENTA). The overall aim of EuroCoord is to use the scientific strengths of each collaboration to ensure that the best, most competitive research is performed. It is a large, integrated network with a common virtual database, which currently contains data from more than 250,000 HIV-infected individuals from many different settings within and outside Europe. EuroCoord's multidisciplinary approach allows HIV research into a number of key areas aimed at improving the management and quality of life of HIV-infected individuals, whilst also exploring differences within subgroups.

SHM also participates in the EuroCoord *Collaborative HIV and Anti-HIV Drug Resistance Network* (CHAIN) project. CHAIN is a large-scale, integrated project designed to effectively and durably combat new and existing anti-HIV drug resistance in clinical settings, with a special emphasis on eastern Europe, and in heavily-affected resource-poor regions in Africa. The objective is to compare virological, immunological and clinical outcome up to 12 to 16 months after initiation of combination antiretroviral therapy (cART), according to markers of virus variability (specific mutations, subtypes), with relevance to the drugs in the regimen.

ACHI$_E$V$_{2E}$

A Collaboration on HIV-2 Infection (ACHI$_E$V$_{2E}$) was established in 2005 as a collaboration of 13 observational cohort studies or centres in 10 European countries, Gambia, and North America that record demographic and clinical data on HIV-2-infected patients. Since HIV-2 is found mainly in western Africa and only occasionally in Western countries, a limited number of studies have specifically focused on HIV-2. In particular, the effect of antiretroviral treatment on outcome has not been studied in detail. ACHI$_E$V$_{2E}$ aims to fill this gap by studying different aspects of treated HIV-2 infection.

ART-CC

The *Antiretroviral Therapy Cohort Collaboration* (ART-CC), coordinated by Prof. Jonathan Sterne, University of Bristol, is a long-standing international collaboration that includes 19 cohort studies in Europe and North America. ART-CC was initiated to carry out prognostic studies to assess the effect of combination antiretroviral therapy (cART) in therapy-naive patients. In 2014, Prof. Peter Reiss and Dr Ard van Sighem represented SHM in the ART-CC steering group. ART-CC has financial support from the Medical Research Council of the United Kingdom.

An overview of papers published by ART-CC in 2014 can be found under 'Scientific output in 2014'.

CASCADE

Concerted Action on SeroConversion to AIDS and Death in Europe (CASCADE) was established in 1997 as a collaboration between 25 cohorts of documented HIV seroconverters from 15 European countries, Australia, Canada and Africa. CASCADE's main aim is to monitor the course of HIV infection from the time of infection onwards. Through pooling data, issues can

be addressed that cannot be reliably addressed from single studies alone. The Amsterdam Cohort Studies (ACS) participates in this study through their HIV seroconverted participants. CASCADE is part of EuroCoord, the collaboration that encompasses all EU-funded cohort studies in the field of HIV (*http://www.eurocoord.net*).

An overview of papers published by CASCADE in 2014 can be found under 'Scientific output in 2014'.

COHERE

The *Collaboration of Observational HIV Epidemiological Research in Europe* (COHERE) is a unique collaboration of 33 cohorts in Europe that helps to answer scientific questions requiring a large sample size of patients that the contributing cohorts cannot answer individually and that do not overlap with existing collaborations between participating COHERE cohorts. COHERE'S mission is to conduct epidemiological research on the prognosis and outcome of HIV-infected populations from across Europe, including pregnant mothers, children and adults. Two regional coordinating centres have been established, one in Bordeaux and one in Copenhagen. COHERE is part of EuroCoord, the collaboration that encompasses all EU-funded cohort studies in the field of HIV (*http://www.eurocoord.net*).

An overview of papers published by COHERE in 2014 can be found under 'Scientific output in 2014'.

D:A:D study

The *Data Collection on Adverse Events of Anti-HIV Drugs* (D:A:D) is a prospective multi-cohort study that focuses on the potential association between antiretroviral drugs and cardiovascular disease, liver and renal disease, and non-AIDS-defining malignancies. Prof. Jens Lundgren (Rigshospitalet & University of Copenhagen) coordinates the study, and Prof. Peter Reiss is the principal investigator on behalf of SHM/ATHENA.

An overview of papers published by the D:A:D study in 2014 can be found under 'Scientific output in 2014'.

DIDE

The *Department of Infectious Disease Epidemiology* (DIDE) is part of the Faculty of Medicine, Imperial College in London. Prof. Christophe Fraser, Prof. Tim Hallett and Prof. Sir Roy Anderson coordinate the collaboration with SHM. The DIDE and SHM have collaborated since 2002, focusing on DIDE's statistical and mathematical support of SHM for analysis of observational cohort data and execution of the HIV registration programme. An important goal of the DIDE research programme is to gain more insight into the interplay of variables that determine the typical progress of infection in a host or in a particular population. Techniques that can provide answers to such questions include the study of the qualities of nonlinear differential equations, organisation and management

of large-scale field studies into the transmission and control of an infection in populations, and analysis of large data sets.

The long-standing collaboration with DIDE has resulted in a model analysing the impact of large-scale administration of combination antiretroviral therapy (cART) on the epidemic in the Netherlands and in another model comparing quality of care in the Netherlands. Yet another study focuses on the variation in HIV-1 plasma RNA setpoints, the clustering around those setpoints that maximise the transmission potential and the changes in viral setpoint over time.

In a separate project, *Bridging the Epidemiology and Evolution of HIV in Europe* (BEEHIVE), the DIDE and SHM collaborate with the AMC-UvA and the Sanger Institute, UK, on a viral whole genome association study. The aim of this study is to identify viral virulence factors, which could ultimately shed new light on the pathogenesis of HIV.

ECDC

The *European Centre for Disease Prevention and Control* (ECDC) is an EU agency that aims to strengthen Europe's defences against infectious diseases. ECDC works in partnership with national health protection bodies across Europe to improve and develop continent-wide disease surveillance and early warning systems. By working with experts throughout Europe, ECDC pools Europe's health knowledge to develop authoritative scientific opinions about the risks posed by current and emerging infectious diseases.

In 2014, SHM continued its leading role in a collaborative project to better estimate the prevalence of HIV in Europe and within individual European countries. This project was commissioned by the ECDC in Stockholm. SHM collaborates in this project together with Prof. Christophe Fraser from the DIDE at Imperial College in London, Prof. Andrew Phillips from the Department of Population Health at University College London, Dr Daniela De Angelis from the Medical Research Council Biostatistics Unit at Cambridge University and Prof. Matthias Egger from the Institute of Social and Preventive Medicine at the University of Bern.

EPPICC

The *European Pregnancy and Paediatric HIV Cohort Collaboration* (EPPICC) conducts epidemiological research on the prognosis and outcome of HIV infections in pregnant women and children, as well as in children exposed to HIV *in utero*, across Europe. EPPICC currently consists of 13 studies, including the *European Collaborative Study* (ECS). As the number of children infected with HIV in Europe is relatively small, a single network running paediatric trials and cohorts is essential to efficiently answer research questions in this population. EPPIC is part of EuroCoord, the collaboration that encompasses all EU-funded cohort studies in the field of HIV (*http://www.eurocoord.net*). Within EuroCoord, EPPICC is part of the HIV in children collaboration, *Paediatric European Network for Treatment of AIDS* (PENTA).

An overview of papers published by EPPICC in 2014 can be found under 'Scientific output in 2014'.

EuroSIDA

The EuroSIDA study is a prospective, observational cohort study of more than 16,500 patients followed in 103 hospitals in 32 European countries, plus Israel and Argentina. The main objective of the study is to assess the impact of antiretroviral drugs on the outcomes in the general population of HIV-infected patients in Europe. The Netherlands is represented through the participation of the AMC in Amsterdam. At the request of the principal investigator of EuroSIDA in the AMC, Prof. Peter Reiss, SHM collects data from the AMC in Amsterdam for EuroSIDA. EuroSIDA is part of EuroCoord, the collaboration that encompasses all EU-funded cohort studies in the field of HIV (*http://www.eurocoord.net*).

An overview of papers published by EuroSIDA in 2014 can be found under 'Scientific output in 2014'.

HIV-CAUSAL

The *HIV Cohorts Analyzed Using Structural Approaches to Longitudinal Data* (HIV-CAUSAL) collaboration is a multinational collaboration of prospective studies of HIV-infected individuals from six European countries and the United States. It aims to answer three main questions: when to start antiretroviral therapy, what antiretroviral regimen to use initially, and when to switch to another regimen. Because these questions are unlikely to be answered by a single study, there is a need for this type of collaborative project. The HIV-CAUSAL collaboration pools data collected for clinical purposes within healthcare systems that have few barriers to access in the populations they serve. The collaboration is designed to inform evidence-based guidelines and planning of clinical trials. In addition, it facilitates the understanding of, and training in, causal modelling across leading HIV observational research groups in the United States and Europe.

An overview of papers published by HIV-CAUSAL in 2014 can be found under 'Scientific output in 2014'.

RDI

The HIV *Resistance Response Database Initiative* (RDI) is made up of a small research team based in the United Kingdom, an international scientific advisory group, and a network of collaborators and supporters. The main activities of the RDI are exploring the relationship between changes in the genetic code of HIV (genotype), as well as other clinical and laboratory factors and response to HIV drug therapy, on the basis of which computational models are developed to help physicians and their patients select the best individualised combination of drugs in situations where resistant measurements are not possible (*http://www.hivrdi.org*).

An overview of papers published by RDI in 2014 can be found under 'Scientific output in 2014'.

Dissemination

Stichting HIV Monitoring (SHM) actively disseminates data and information about its activities through a wide variety of communication channels. In doing so, we aim to provide information to health care providers, researchers, other health care professionals, people living with HIV, the media and other interested parties.

Monitoring Report 2014, HIV Infection in the Netherlands

Each year, SHM publishes a Monitoring Report just before December 1, World AIDS Day. The Monitoring Report presents major developments in the HIV epidemic in the Netherlands and describes the effects of treatment on the course of HIV infection and on the HIV epidemic, with data extending back to 1996.

The 2014 Monitoring Report confirmed that certain positive trends in the Netherlands continued in 2014. In particular, the data confirmed more frequent HIV testing, earlier diagnosis and earlier start of treatment, particularly in men who have sex with men, but unfortunately not in other key-affected populations. However, despite these encouraging findings, late diagnosis remains a problem, as does HIV infection in the group of people who are infected but probably unaware of their HIV status. This group is thought to contribute markedly to fuelling the epidemic in the Netherlands.

Mortality rates remain low in HIV-infected individuals in care in the Netherlands, with a shift from AIDS-related death to death from other causes, in particular non-AIDS co-morbidities. Moreover, non-AIDS co-morbidities related to age, such as cardiovascular disease and non-AIDS-related malignancies, are increasing as the number of older HIV-infected patients continues to increase; these age-related diseases are also more common in HIV-infected patients than in the general population. Taken together with the observation that there remained a substantial number of AIDS-related deaths between 2007-2013 due to late presentation and entry into care, these findings further underline the importance of earlier HIV diagnosis, start of treatment and continuity of HIV care in specialised treatment centres.

SHM also documents the presence or absence of hepatitis B virus or hepatitis C virus (HCV) co-infection in all HIV-infected patients in care in the Netherlands. Data on HIV and HCV co-infection presented in the 2014 Monitoring Report revealed that just over 1 in 20 HIV patients had a chronic HCV infection. These patients carry a significant risk of developing chronic liver disease and liver cancer. Moreover, more than three quarters of HIV/HCV co-infected patients in care remain in need of effective HCV therapy. The recent introduction of novel direct-acting antiviral agents is expected to bring about marked changes in these numbers and their impact on the HIV/HCV co-infected population will continue to be closely monitored.

SHM website and eNewsletters

During the course of 2014, regular updates have been made to the SHM website. News items about SHM or relevant to the field of HIV treatment and research are placed on the homepage at regular intervals and eNewsletters continue to be sent on a quarterly basis in both Dutch and English. The eNewsletters in 2014 featured interviews with a number of national and international experts in the field of HIV, news about research collaborations and other developments within SHM, along with reviews of SHM data presented at international conferences. Themed newsletters have also been developed for distribution at conferences and other events. For example, one newsletter focused primarily on hepatitis and was distributed at the Dutch National Hepatitis Day. The newsletters are all archived on the website and can be accessed via a direct link.

Internal newsletter: 'SHM positief: al het interne nieuws verzameld'

In November 2014, the first internal eNewsletter was sent out. This Dutch-language newsletter (entitled 'SHM Positive: a collection of all the internal news') is intended to further build internal cohesion amongst staff and provides news about personnel changes, upcoming events and other relevant information for employees. The first issues have been well-received and the newsletter will continue to be sent to all employees on a bi-monthly basis.

SHM animation: data quality

Further to the animation produced in 2013 that gives a general visual presentation of SHM and our activities, a second short animated film was developed in 2014. This second animation explains the data collection process in more detail, with an emphasis on the quality control steps carried out along the way. The animation is presented on the homepage of the SHM website and on the data quality page of the website.

Patient leaflet and fact sheet

A simple explanation of SHM's activities and data collection process is also provided in a patient leaflet that was developed in 2014. Building on the images developed for the animations, this leaflet illustrates how anonymous data provided by people living with HIV in the Netherlands help to drive further improvements to HIV care in the Netherlands through national and international research. The leaflet is accompanied by an insert that uses infographics to summarise the latest key figures from the 2014 Monitoring Report. This insert will be updated each year. Both the leaflet and fact sheet insert are to be distributed to new patients by HIV treating physicians and HIV nurse consultants, and were also included in conference bags at NCHIV 2014, the national conference on sexually transmitted diseases and HIV (Soa.hiv.seks), and the annual HIV patient event in the Carré theatre (Smile). The patient leaflet and infographics fact sheet are also available as downloads on the SHM website.

NCHIV 2014

In 2014, SHM researchers presented their work at various national and international conferences, including the 8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV). This annual conference is organised by SHM in collaboration with the Centre for Infectious Disease Control of the National Institute for Public Health and the Environment (*Centrum voor Infectieziektenbestrijding-Rijksinstituut voor Volksgezondheid en Milieu*, CIb-RIVM), the Aids Fonds, the Amsterdam Institute for Global Health and Development, the Academic Medical Center of the University of Amsterdam (Department of Global Health), and the Dutch Association of HIV-Treating Physicians (*Nederlandse Vereniging van HIV Behandelaren*). NCHIV 2014 was attended by just under 300 participants. During the course of the day, there were 18 presentations, including 4 by guest speakers, an update on the HIV epidemic in the Netherlands by SHM director Peter Reiss, and 13 oral abstract presentations on pathogenesis, epidemiology, prevention and treatment of HIV and HIV/HCV co-infection. In addition, close to 50 posters were presented.

Scientific output

In addition to its yearly Monitoring Report, SHM also contributes to the knowledge and understanding of the HIV/AIDS epidemic and the effect of antiretroviral treatment on the course of HIV infection through research projects and scientific publications. In 2014, SHM cohort data was included in 47 publications in peer-reviewed international scientific journals and 60 oral and poster presentations at international peer-reviewed conferences, workshops and meetings. A full overview of the scientific output is included in a later section of this report.

Financial report

Income

In 2014, Stichting HIV Monitoring's (SHM) total income was €4,374,427. The largest portion of this income came from the structural institute grant that the SHM receives each year from the National Institute for Public Health and Environment (*Rijksinstituut voor Volksgezondheid en Milieu* (RIVM)) on behalf of the Ministry of Health, Welfare and Sport (*Ministerie van Volksgezondheid Welzijn en Sport* (VWS)). In addition, SHM participates in various national and international collaborations involving observational cohort studies, for which it receives additional funding.

Income for regular HIV monitoring activities in the Netherlands

SHM is a VWS-recognised healthcare institute with a structural institute grant (VWS grants policy framework).

On 28 January 2014, SHM's governing board established that SHM required a structural institute grant of €3,087,856 for HIV monitoring in 2014. On 4 February 2014, the RIVM/VWS awarded an institute grant of €3,076,307.

In addition, on 29 July 2014, indexation for the wage-sensitive part of the budget was set at 1.94% (€46,028); material costs were not indexed. Consequently, the total budget for 2014 allocated by the VWS to SHM for monitoring HIV in the Netherlands was €3,122,335.

As of 1 June 2013, 17,506 of the registered HIV patients (17,299 adults and 207 children) were in active follow-up in HIV treatment centres. This represents an increase of 2.61% compared to the number of patients in 2012. This increase in the number of patients monitored by SHM was included in the structural institute grant application, but not reflected in the grant awarded by the RIVM.

Income from HIV monitoring–related collaborations

SHM's participation in international and national collaborations is highly important for both individual patients and quality of care. Individual registration and monitoring programmes (such as SHM) are often too small to adequately address certain questions regarding individual comorbidities and prognosis associated with large-scale HIV treatment. Collaborations that combine data from various cohorts make it possible to answer questions that cannot be addressed by individual cohorts, and are also an efficient way of providing reliable insight into the long-term effects of HIV treatment. As such, participation in national and international studies is in line with the SHM's mission and objectives. In 2014, the SHM received €1,192,520 as income from the HIV monitoring-related collaborations listed below. This income is 1.08% higher than that earned through collaborations in 2013.

1. Amsterdam Cohort Studies (ACS)

SHM has been responsible for governing and administering the Amsterdam Cohort Studies (ACS) since 2005. Since 1984, the ACS have been carrying out multidisciplinary research into the epidemiology, psychosocial determinants, the natural course and pathogenesis of HIV-1 infection and, more recently, other blood-borne and sexually-transmitted diseases. The institutes involved in this collaboration make use of data and body samples provided by HIV-1 infected persons and persons at high risk of contracting HIV. Following approval of research proposals that involve collaboration with one or several ACS partners, external parties can also gain access to the data and stored body samples. The RIVM provides the ACS with an annual grant of €500,000. In addition, the collaborating institutes, including the Academic Medical Centre (AMC)-University of Amsterdam (UvA), the Public Health Service of Amsterdam (*Gemeentelijke Gezondheidsdienst*, GGD), SHM, and the University Medical Centre Utrecht (UMCUtrecht), make a financial contribution to the coordination, management and financial management costs. The GGD Amsterdam and the AMC each contribute individually to the storage of patient data and samples.

2. Data collection on Adverse Events of Anti-HIV Drugs (D:A:D study)

The D:A:D study is a large international collaboration between observational cohorts, with the aim of identifying early severe side effects of HIV treatment with antiretrovirals. SHM is a major partner in D:A:D and collects data on adverse effects of treatment and non-AIDS comorbidities in registered patients for the benefit of the D:A:D study. Source data verification ensures that the validity of key endpoints is subject to 100% quality control (in contrast to the 10% applied to HIV monitoring in the Netherlands). As such, SHM's participation in this study contributes significantly to further improving the quality of data on HIV complications and comorbidity in the Netherlands.

In 2014, SHM contributed for the fifteenth time to the data merge and received €453,338 in compensation for this activity from the organisation that coordinates the D:A:D study, the Rigshospitalet, University of Copenhagen in Denmark. D:A:D has been made financially possible by the Oversight Committee for the Evaluation of Metabolic Complications of HAART and various pharmaceutical manufacturers of antiretroviral compounds. The D:A:D funding decreased in 2013 after three of the nine original participating pharmaceutical manufacturers withdrew from the collaboration. As a result, the budget of each participating cohort had to be reduced. Nevertheless, the number of person years added by SHM in 2014 was higher than that added by other participating European cohorts, which meant that SHM received a higher sum than in 2013 (€102,719 more than in 2013).

For the registration and validation of endpoints collected specifically for the D:A:D study, SHM received an additional fee of €55,328 in 2014.

3. EuroSIDA

SHM participates in the EuroSIDA study within a European context. EuroSIDA is collaboration between clinical cohorts and individual treatment centres distributed throughout Europe (including eastern Europe). The Netherlands is involved in this collaboration through the SHM's role in facilitating the provision of data from a small group of patients from the AMC. EuroSIDA carries out research into a broad range of clinical issues relating to HIV, making it possible to compare specific regional differences between centres throughout Europe. For its participation in the EuroSIDA study in 2014, SHM received a payment of €2,917. The knowledge that SHM gains through its participation in EuroSIDA is also valuable in terms of improving the national data collection by SHM in the Netherlands.

4. European Centre for Disease Prevention and Control (ECDC)

The ECDC awarded SHM a grant of €114,667 for the project entitled 'Improving tools to estimate HIV prevalence in EU/EAA countries'. This two-year project (January 2013 through to January 2015), coordinated by SHM, is a collaboration with the University of Bern, Switzerland, and University College London, Imperial College, and the MRC Biostatistics Unit, UK. The project aims to develop methods to improve the reliability of estimates of HIV prevalence in different European countries. This participation should also improve the ability to make such estimates in the Netherlands.

5. Aids Fonds grant

SHM has received a grant from the Aids Fonds for a project entitled 'Controlling the HIV epidemic'. In 2014, the contribution was €45,500. SHM has appointed a PhD student for this project, with the aim of developing a mathematical individual-based model to describe the HIV epidemic in various at-risk groups in the Netherlands. This model should provide greater insight into the factors that drive new HIV infections. Furthermore, it will be possible to study the effect of intervention strategies on the prevention of new HIV infections. In this way, this study should improve our understanding of the course of the HIV epidemic in the Netherlands and give insights into how to fight the HIV epidemic in the Netherlands.

6. EuroCoord funding

In 2014, SHM received a sum of €14,092 from EuroCoord. SHM's participation in EuroCoord improves harmonisation between European HIV cohort data collections, including SHM's cohort in the Netherlands. This, in turn, improves the quality of international collaborations since certain research questions can only be studied by combining databases from several HIV cohorts (including that of the Netherlands).

7. Comorbidity in relation to HIV/AIDS (COBRA)

In 2014, SHM received a payment of €1,679 from the COBRA study. This project is financed by the European Union's 7th framework programme and SHM is one of the 12 COBRA partners in Europe. SHM's main contribution involves data management and analyses for COBRA. The study focuses primarily on investigating whether the reported comorbidities are more common and possibly occur at a younger age in HIV-infected persons compared to non HIV-infected persons. In addition, in-depth research is being done into the various underlying mechanisms, including those associated with HIV infection as well as those associated with the use of antiretroviral treatment. The knowledge acquired from this project will help SHM in establishing priorities for collecting national comorbidity data. Furthermore, the results of the COBRA study may contribute to improving the prevention and treatment of comorbidities in HIV-positive persons.

8. European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC)

For SHM's contribution to the European Cipher study, EPPIC, SHM received a sum of €5,000. EPPICC carries out epidemiological research throughout Europe into the prognosis and outcomes of HIV-infected pregnant women and children, as well as children exposed to HIV *in utero*. Currently, EPPIC comprises 13 studies, including the European Collaborative Study (ECS). Due to the relatively small number of children living with HIV in Europe, it is essential to combine the data within a single network to efficiently address questions arising within this population.

9. Other income

In 2014, SHM received €59,572 from other sources of income. Most of this income arose from salary expenses charged by SHM to HIV treatment centres to cover the costs of assistance provided by SHM for the collection and entering of anonymised patient data. SHM staff are also involved in organising the Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) and the associated salary expenses are charged to Stichting NCHIV.

Expenditure

In 2014, the total expenses of Stichting HIV Monitoring were €4,142,175. Three different types of expenses are outlined below for 2014:

1. Personnel expenses

Personnel expenses once again represented the largest expenditure for SHM during 2014. As per 31 December 2014, SHM had a total of 46 employees (an average of 35.91 FTE). This number does not include employees of HIV treatment centres that carry out their own data collection and for which the treatment centres receive a payment from SHM.

2. Material expenses

In addition to staff expenses in 2014, structural expenses were incurred for the depreciation of automation equipment, database licenses, maintenance of the national HIV monitoring database, data management and other operational costs.

3. Payments to HIV treatment centres for anonymous patient data collection and data entry

In 2014, HIV treatment centres received a payment of €55.87 per patient, based on the number of patients in active follow-up on 31 December 2013 and on the budget set by the RIVM. In 2014, a number of hospitals requested SHM to provide assistance in data collection. The associated costs were deducted from the payment made by SHM to the hospitals in question for patient data collection and entry. In addition, HIV treatment centres received €12.81 per patient as a contribution towards the costs of collecting and storing patients' plasma. Fifteen treatment centres have transferred the role of data collection to SHM.

In total, SHM paid the HIV treatment centres €654,460 for patient data collection and entry and storage of patients' samples.

D:A:D event payments to HIV treatment centres

As part of the D:A:D study, physicians are required to complete Cause of Death (CoDe) forms. SHM paid HIV treatment centres €14,367 for this work.

Amsterdam Cohort Studies payments

In line with the budget, the funding assigned by the RIVM to the ACS is passed on by SHM to the GGD Amsterdam and the AMC. SHM does not charge the ACS any management costs.

Operating result

The interest income was €28,888 in 2014. SHM conducts a very conservative but accurate treasury policy. The operating result (€261,140) indicates that the total expenditure in 2014 remained well within SHM's income for 2014. The largest addition to the reserves is the result of the D:A:D study.

Financial reserves

The total financial reserves of SHM (including contingency reserve, general reserve and earmarked reserves for investment) amounted to €3,545,046 on 31 December 2014.

1. **Contingency reserve**

   The contingency reserve amounted to a positive balance of €69,247 on 31 December 2014. This amount includes the negative 2014 result for HIV monitoring in the Netherlands. The increase in the number of patients has, since 2012, no longer been covered by the structural institute grant. As a result, a negative project result of €185,505 arose for the first time in 2014. This negative result is covered by the previously-built up contingency reserve intended to guarantee operational continuity over a certain period of time.

2. **General reserve**

   From 2002 through 2007, SHM built a general reserve of €382,205. This sum arose through financing from the Healthcare Tariffs Board (Tarieven Gezondheidszorg) and, later, the Dutch Healthcare Authorities (Nederlandse Zorgautoriteit).

3. **Earmarked reserves for HIV-related projects**

   As per 31 December 2014, a total of €3,093,593 has been reserved for HIV-related projects. SHM has committed to participate in these projects for an average of three years.

Contingency reserve as of 31 December 2014

SHM is required to maintain a sufficiently large contingency reserve to cover their financial obligations and risks. Based on the financial obligations and risks, the board has set a target contingency reserve of €2.2 million.

Balance sheet as of 31 December 2014

Assets	31 Dec 14 (€)	31 Dec 13 (€)
Fixed assets		
Tangible fixed assets	19,175	28,956
Total fixed assets	**19,175**	**28,956**
Current assets		
Receivables and accrued assets	359,924	313,053
Liquid assets	4,324,892	4,957,875
Total current assets	**4,684,816**	**5,270,928**
Total assets	**4,703,991**	**5,299,884**

Liabilities	31 Dec 14 (€)	31 Dec 13 (€)
Capital reserves		
Contingency reserve	69,247	154,378
General reserve	382,206	382,206
Earmarked reserves	3,093,593	2,747,322
Total reserves	**3,545,046**	**3,283,906**
Short-term liabilities		
Short-term liabilities and accrued expenses	1,158,944	2,015,978
Total liabilities	**4,703,991**	**5,299,884**

2014 profit and loss account

Profits	2014 (€)	2013 (€)
Total funding	4,314,855	4,198,163
Other operating revenue	59,572	68,991
Total net revenue	**4,374,427**	**4,267,154**
Operating costs		
Personnel expenses	2,214,179	2,109,344
Depreciation of tangible fixed assets	11,451	11,857
Other operating costs	729,822	527,708
Other project-related operating costs	17,896	0
Payments HIV treatment centres	654,460	634,369
Payments D:A:D events	14,367	23,901
Payments Amsterdam Cohort Studies	500,000	500,000
Payments NCHIV	0	239
Total operating costs	**4,142,175**	**3,807,417**
Operating result	**232,252**	**459,737**
Financial profits	30,009	48,553
Financial losses	1,121	707
Year result	**261,140**	**507,583**

Scientific output 2014

In 2014, Stichting HIV Monitoring (SHM) received 8 requests to make use of SHM's cohort data. During the year, 47 articles were published in international peer-reviewed journals. In addition, 60 abstracts were accepted for presentation at 13 meetings and conferences (34 posters and 26 oral presentations). An overview of research projects, publications and presentations can be found on our website, *www.hiv-monitoring.nl*.

Completed research projects

I10042 The use of nevirapine dose escalation in patients who switch from efavirenz to nevirapine

Burger D, Blonk M, Wit F, Smit C, van Luim M, Gelinck L, Sprenger H, Koopmans P

Date of approval: 11 May 2010

This project was terminated because insufficiently accurate data on nevirapine dosing were available to allow the research question to be answered.

I12001 The rate of mother-to-child-transmission of hepatitis C virus in HIV-1 infected mothers

Van de Ende M, Snijdewind I, Smit C, Schutten M, Hartwig N, de Wolf F

Date of approval: 9 February 2012

Publications in 2014

Low mother-to-child-transmission rate of hepatitis C virus in cART treated HIV-1 infected mothers
Snijdewind IJM, Smit C, Schutten M, Nellen FJB, Kroon FP, Reiss P, van der Ende ME.
J Clin Virol. 2015 [In press]

I12106 Differences between HIV-1-infected children in the Netherlands from different countries of origin

Pajkrt D, van Bilsen W, Cohen S

Date of approval: April 2013

Publications in 2014

Country of birth does not influence long-term clinical, virologic, and immunological outcome of HIV-infected children living in the Netherlands: a cohort study comparing children born in the Netherlands with children born in Sub-Saharan Africa
Cohen S, van Bilsen WP, Smit C, Fraaij PL, Warris A, Kuijpers TW, Geelen SP, Wolfs TF, Scherpbier HJ, van Rossum AM, Pajkrt D.
J Acquir Immune Defic Syndr. 2015 Feb 1;68(2):178-185

I13018 Efficacy of lamivudine compared to emtricitabine in nevirapine and efavirenz based antiretroviral therapy: an observational retrospective cohort study

Rokx C, Rijnders B, Verbon A, van de Vijver D

Date of approval: 3 June 2013

Publications in 2014

Increased virological failure in naive HIV-1-infected patients taking lamivudine compared with emtricitabine in combination with tenofovir and efavirenz or nevirapine in the Dutch nationwide ATHENA cohort
Rokx C, Fibriani A, van de Vijver DA, Verbon A, Schutten M, Gras L, Rijnders BJ; AIDS Therapy Evaluation in the Netherlands National Observational Cohort.
Clin Infect Dis. 2015 Jan 1;60(1):143-53. doi: 10.1093/cid/ciu763. Epub 2014 Oct 1

Ongoing research projects

I04034 The Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D)

Reiss P, All HIV treatment Centres in the Netherlands participating in Stichting HIV Monitoring ATHENA Cohort

The study continues to successfully follow close to 50,000 patients from 11 cohorts in Europe, Australia and the United States. Currently the study has accrued more than 300,000 person years of follow-up. The ATHENA cohort continues to rank amongst the top contributors to D:A:D. The DAD Oversight Committee continues to fund the study for the period 2013 through 2016, however at a reduced budget that has resulted in less funding for all participating organisations, including SHM. Funding post-2016 is uncertain.

The study continues to successfully meet the aim to delineate the relationship between the use of antiretroviral drug classes as well as individual drugs one the one hand, and the risk of myocardial infarction, and the additional comorbidity endpoints of end-stage renal disease, chronic severe liver disease and non-AIDS malignancies, on the other hand. The results from the study are regularly presented at major international conferences, published in high-ranking peer-reviewed journals, and also continue to inform and influence changes in national and international HIV treatment guidelines.

For additional information, including recent presentations and publications, please see www.cphiv.dk (under the tab ongoing studies and then D:A:D).

Publications in 2014

Increased risk of cardiovascular disease (CVD) with age in HIV positive men: a comparison of the D:A:D CVD risk equation and general population CVD risk equations
Petoumenos K, Reiss P, Ryom L, Rickenbach M, Sabin C, El-Sadr W, d'Arminio Monforte A, Phillips A, De Wit S, Kirk O, Dabis F, Pradier C, Lundgren J, Law M; D:A:D Study Group.
HIV Med. 2014 Nov;15(10):595-603

Predictors of advanced chronic kidney disease and end-stage renal disease in HIV-positive persons in the D:A:D study
Ryom L, Mocroft A, Kirk O, Ross M, Reiss P, Fux CA, Morlat P, Moranne O, Smith C, El-Sadr W, Law M, Lundgren JD, et al. for the D:A:D study group.
AIDS. 2014 Jan 14;28(2):187-99

Development of a definition for rapid progression (RP) of renal function in HIV-positive persons: the D:A:D study
Kamara DA, Ryom L, Ross M, Kirk O, Reiss P, Morlat P, Moranne O, Fux CA, Mocroft A, Sabin C, Lundgren JD, Smith CJ.
BMC Nephrol. 2014 Mar 25;15(1):51. [Epub ahead of print]

Trends in underlying causes of death in people with HIV from 1999-2011 (D:A:D): a multicohort collaboration
Smith CJ, Ryom L, Weber R, Morlat P, Pradier C, Reiss P, Kowalska JD, De Wit S, Law M, el Sadr W, Kirk O, Friis-Moller N, Monforte Ad, Phillips AN, Sabin CA, Lundgren JD, D:A:D Study Group.
Lancet. 2014 Jul 19:384(9939):241-8. doi: 10.1016/S0140-6736(14)60604-8

Cancer risk and use of protease inhibitor or non-nucleoside reverse transcriptase inhibitor based combination antiretroviral therapy: the D:A:D study
Bruyand M, Ryom L, Shepherd L, Fätkenheuer G, Grulich A, Reiss P, De Wit S, d'Arminio Monforte A, Furrer H, Pradier C, Lundgren J, Sabin C, for the D:A:D Study Group.
J Acquir Immune Defic Syndr. [In press]

Presentations in 2014

A clinically useful risk-score for chronic kidney disease (CKD) in HIV infection
Mocroft A, Lundgren JD, Ross M, Law M, Reiss P, Kirk O, Smith C, Wentworth D, Neuhaus J, Fux CA, Moranne O, Morlat P, Johnson MA, Ryom L on behalf of the Data on Adverse Events (D:A:D) study group, the Royal Free Hospital Clinic Cohort and the INSIGHT study group.
Oral presentation at HIV Drug Therapy Glasgow 2014, UK, 2-6 November 2014

Lack of association between use of efavirenz and death from suicide: D:A:D Study
Smith C, Ryom L, d'Arminio Monforte A, Reiss P, Mocroft A, el Sadr W, Weber R, Law M, Sabin C, Lundgren J on behalf of the Data on Adverse Events (D:A:D) study group.
Oral presentation at HIV Drug Therapy Glasgow 2014, UK, 2-6 November 2014

Gender differences in the use of cardiovascular disease-related interventions among HIV-positive persons: D:A:D Study
Hatleberg C, Ryom L, El-Sadr W, Mocroft A, Reiss P, de Wit S, Dabis F, Pradier C, d'Arminio Monforte A, Rickenbach M, Law M, Lundgren JD, Sabin C, on behalf of the D:A:D Study group.
Oral presentation at HIV Drug Therapy Glasgow 2014, UK, 2-6 November 2014

Association between dideoxynucleoside analogues (d-drugs) and end-stage liver disease (ESLD)
Ryom L, Sabin C, Reiss P, El-Sadr W, D'Arminio Monforte A, De Wit S, Law M, Kirk O, Mocroft A, Smith C, Pradier C, Dabis F, Weber R, Phillips AN and Lundgren JD for the D:A:D Study group.
Presentation at 21st Conference on Retroviruses and Opportunistic Infections, 3-6 March 2014, Boston, USA

Predictors of progression, stabilisation or improvement of eGFR after chronic renal impairment
Ryom L, Mocroft A, Kirk O, Reiss P, Ross M, Moranne O, Morlat P, Smith C, Fux CA, de Wit S, d'Arminio Monforte A, El Sadr W, Sabin CA, Phillips A, Law M, and Lundgren JD for the D:A:D study group.
Presentation at 21st Conference on Retroviruses and Opportunistic Infections, 3-6 March 2014, Boston, USA

Is there continued evidence for an association between abacavir and myocardial infarction risk?
Sabin CA, Reiss P, Ryom L, de Wit S, Kirk O, Weber R, Pradier C, Dabis F, Phillips AN, Lundgren JD for the D:A:D study group.
Presentation at 21st Conference on Retroviruses and Opportunistic Infections, 3-6 March 2014, Boston, USA

I005513 HIV resistance response database initiative (RDI)

Revell A, Larder B, Wang D, Coe D

Date of approval: October 2005

The main activities of the RDI during 2014 using ATHENA data were as follows:

1. The development of new global computational models to predict virological response to treatment without the use of genotype.

Background: the optimal individualised selection of antiretroviral drugs in resource-limited settings is challenging because of the limited availability of drugs and genotyping. Here we describe the development of the latest computational models to predict response to combination antiretroviral therapy without a genotype, for potential use in such settings.

Methods: random forest models were trained to predict the probability of virological response to therapy (<50 copies HIV RNA/ml) following virological failure using the following data from 29,574 treatment change episodes: baseline viral load and CD4 count, treatment history, drugs in the new regimen, time to follow-up and follow-up viral load. The models were assessed during cross-validation and with an independent global test set of 1,700 cases, including 222 from South Africa. The models' accuracy was evaluated in terms of the area under the ROC curve (AUC), sensitivity, specificity, and overall accuracy, using the optimum operating point developed during cross validation as the cut-off for predictions of response and failure.

Results: the models achieved AUCs of 0.81 – 0.85 (mean of 0.83) during cross validation, 0.82 with the global test set and 0.79 with the South African subset. The sensitivities were 71% during cross validation, 69% with the global test set and 68% with the South African cases. Specificity was 80%, 77% and 76% and overall accuracy was 76%, 74% and 73%.

Conclusions: the models predicted virological response to HIV therapy without a genotype as accurately as previous models that included a genotype. They were comparably accurate for cases from South Africa as for elsewhere. These models have the potential to help optimise antiretroviral therapy in resource-limited settings where genotyping is not generally available.

2. The development of local South African models, and comparison with the above global models.

Background: antiretroviral treatment in resource-limited settings (RLS) tends to be relatively homogeneous and shaped by the limited number of drugs available and public health protocols that define what drugs are used at first and second line. It is possible that models trained with limited data from an RLS might be more accurate in predicting treatment outcomes that models trained with a larger but more heterogeneous dataset from around the world. In this study we trained models using South African data and compared their performance with the global models described above.

Methods: random forest models were trained to predict the probability of virological response to therapy (<50 copies HIV RNA/ml) following virological failure using the following data from 3,179 treatment change episodes from South Africa: baseline viral load and CD4 count, treatment history, drugs in the new regimen, time to follow-up and follow-up viral load. The models were assessed during cross-validation and with an independent global test set of 222 from South Africa. The models' accuracy was

evaluated in terms of the area under the ROC curve (AUC), sensitivity, specificity, and overall accuracy, using the optimum operating point developed during cross validation as the cut-off for predictions of response and failure. The performance of the models was compared to that of global models in terms of these parameters as well as using in silico analysis to compare how well the two sets of models performed in identifying potentially effective alternative simple (3-drug) regimens using only the drugs available in that setting.

Results: the models achieved AUCs of 0.73 – 0.90 (mean of 0.80) during cross validation and 0.79 with the South African test cases. The sensitivities were 70% during cross validation, and 64% with the South African cases. Specificity was 79% and 79%, respectively, and overall accuracy was 76% and 74%, respectively. These figures are similar and not significantly different from those achieved by the global models above.

The South African models were able to identify 3-drug regimens that were predicted to be effective (probability of response above the optimum operating point) for 64% of the 222 South African test cases, compared with 95% for the global models. The difference in probability of response for the regimen used in the clinic and the highest scoring alternative identified by the models was 0.14 for the South African models and 0.36 for the global models ($p<0.0001$).

Conclusions: the South African models predicted virological response to HIV therapy without a genotype with comparable accuracy to models developed form a larger heterogeneous dataset. However, they were less able to identify alternative regimens that were predicted to be effective and have a higher probability of response than the regimens used in the clinic. These results indicate that global models rather than local models trained with data from a particular setting are the best strategy for a treatment support tool.

I08044 Primo SHM Rx4 HAART

Grijsen M, Welkers M

Ongoing

Publications in 2014

Temporary treatment during primary HIV infection does not affect virologic response to subsequent long-term treatment
Grijsen ML, Wit FW, Jurriaans S, Kroon FP, Schippers EF, Koopmans P, Gras L, Lange JM, Prins JM, Primo-SHM Study Group.
PLoS One. 2014 Apr 3;9(4):e89639. doi: 10.1371/journal.pone.0089639. eCollection 2014.

I08115 Proposal for collaboration and data exchange between HMF and RIVM for national HIV/AIDS surveillance and data transfer to ECDC in the context of EU obligations for reporting on HIV/AIDS

Op de Coul E, de Wolf F, Vlug J, van Sighem A, van der Sande M

Publications in 2014

Sexually transmitted infections, including HIV, in the Netherlands in 2013
van Aar F, Koedijk FDH, van den Broek IVF, Op de Coul ELM, Soetens LC, Woestenberg PJ, Heijne JCM, van Sighem AI, Nielen MMJ, van Benthem BHB.
RIVM Rapport 150002005/2014

HIV/AIDS surveillance in Europe 2013
European Centre for Disease Prevention and Control/ WHO Regional Office for Europe. *Stockholm: European Centre for Disease Prevention and Control; 2014*

I10021 Characteristics of HIV-1 transmission among men having sex with men in the Netherlands

Ratmann O, van Sighem A, Bezemer D, Reiss P, de Wolf F, Fraser C

Date of approval: May 2010

Background: the number of new HIV infections amongst men having sex with men (MSM) is increasing despite widespread availability of prevention services and antiretroviral therapy (ART). Little guidance as to how to prioritise components of a combination prevention package is currently available.

Objective: to reconstruct an evidence base of past HIV transmission events amongst MSM, to estimate the proportion of HIV transmissions originating from consecutive stages of HIV infection and care in light of these sources, and to estimate the proportion of HIV infections that could be averted through specific components of a combination prevention approach.

Methods: we conducted a combined analysis on molecular genetic and clinical data from HIV-infected individuals in the Dutch ATHENA cohort between 1996 and 2013. Using viral evolutionary analyses, we determined potential transmitters to 617 recipient MSM that were diagnosed with recent HIV infection up to December 2010. Using clinical data, we associated treatment cascade stages with potential transmission intervals.

Results: 1,646 person years of potential transmission intervals were associated with phylogenetic evidence for direct HIV-1 transmission. Between July 1996-December 2010, the estimated proportion of transmissions from undiagnosed men was 71% (95% confidence interval [CI]: 66-73%), 23% (21%-26%) from diagnosed, untreated men, and 6% (5%-8%) from men who initiated ART. ART is highly effective in preventing HIV transmission amongst men, with a relative transmission risk of 6% (2%-9%) compared to diagnosed untreated men with CD4 > 500 cells/mm^3. An estimated 43% (37%-46%) of the 617 recipient MSM were infected by men that were in their first year of infection. With the probable sources of transmission inferred, we modelled hypothetical HIV prevention scenarios between July 2009 to December 2012. In this period, 17% of probable transmitters had a last negative test in the 12 months preceding diagnosis compared to 27% of diagnosed MSM. Therefore, we evaluated hypothetical scenarios in which 30%-70% of probable transmitters had been annually tested for HIV, which in all cases is much higher than current practice. We estimate that 32% (23%-42%) of transmissions could have been averted with 50% annual testing amongst probable transmitters and immediate provision of antiretroviral therapy. We also considered a hypothetical roll-out of pre-exposure prophylaxis (PrEP) to MSM who present for HIV testing but then test negative. We term this strategy test-and-PrEP. Based on findings from three randomised controlled trials, we considered a range in reduction of HIV incidence due to daily or demand-based,

oral single-pill PrEP from 44%-86%. Based on estimates of a 44% reduction of incidence, test-and-PrEP could have averted a similar proportion of transmissions as test-and-treat strategies. Based on estimates of an 86% reduction in HIV incidence, test-and-PrEP could have averted 57% (37%-69%) of transmissions. If, in addition, ART had been provided immediately, these estimated proportions rise to 50% (36%-64%) and 66% (48%-78%), respectively.

Conclusions: Phylogenetic analysis is key to appropriately target biomedical prevention in given populations. Potential caveats to the robustness of our findings are that only half of all potential transmitters had a viral sequence sampled, and that half of those had their sequence sampled relatively late in the course of infection. We predict within these limitations that provision of oral, single-pill antiretrovirals to HIV-uninfected MSM is consistently associated with the largest short-term reductions of HIV incidence amongst MSM in the Netherlands. Several studies support our prediction that test-and-treat strategies are associated with a limited short-term impact on HIV incidence in this high-risk population. Changes in sexual risk behaviour over time or the long term impact of HIV prevention approaches on HIV incidence were not evaluated in this study. Many other countries have a similar HIV epidemic amongst MSM and comparable characteristics of treatment cascade. We expect our conclusions to be generalisable in similar settings, with the exception of countries where loss through the care cascade is more common.

Presentations in 2014

Sources of HIV-1 transmission in the ongoing, concentrated HIV epidemic among men having sex with men in the Netherlands between July 1996 and December 2010
Ratmann O, van Sighem A, Bezemer D, Gavryushkina A, Reiss P, de Wolf F, Fraser C and the ATHENA observational cohort.
Oral presentation at 8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment, Amsterdam, the Netherlands, 18 November 2014

Modest improvements to HIV treatment and care could prevent half of all new HIV infections among men having sex with men: a phylogenetic study
Ratmann O, van Sighem A, Bezemer D, Gavryushkina A, de Wolf F, Reiss P, Fraser C and the ATHENA observational cohort.
Poster presentation at HIV Dynamics and Evolution, Budapest, Hungary, May 11-16 2014

I12045 An HIV-1 genome-wide association study to identify viral determinants of HIV-1 plasma concentration

De Wolf F, Cornelissen M, Fraser C, Kellam P, Gall A, Gras L, van Sighem A, Boucher C, Schuurman R, Claas E, Bezemer D, Reiss P, Zaheri S, Hillebregt M

Date of approval: 16 September 2012

The first phase of the BEEHIVE collaboration (*Bridging the Epidemiology and Evolution of HIV in Europe*) included 1) testing the logistics of stored serum/plasma samples from patients selected for inclusion in the study of virulence factors associated with severity of infection, and 2) testing the efficacy of HIV-RNA isolation procedures

needed for whole genome sequencing. Procedures have been developed to support these logistics, and the most productive and efficient isolation procedures have been selected. The very first sequencing results were available at the end of 2012 and, at the same time, the study entered a second phase that continued in 2013. During this second phase, 593 samples from 5 associated virology laboratories in the Netherlands were located and transported. Viral RNA was isolated by the laboratory for Experimental Virology at the AMC in Amsterdam and was subsequently sent to the Wellcome Trust Sanger Institute where a number of whole genome sequences have successfully been obtained. Progress was made on developing a pipeline for generating whole HIV genomes from the short read output from the sequencing. Construction of a database holding clinical and sequence data was completed. Other international cohorts with samples obtained from individuals with a reliable estimate of moment of infection were invited to join BEEHIVE. A kick-off meeting was held in Greenwich, London, UK, 21-22 October 2014, with investigators from contributing cohorts and experts on phylogenetics and molecular evolution and epidemiology. In 2015, samples obtained from included patients will continue to be collected for RNA isolation and subsequent sequencing, after obtaining patient's informed consent and monitoring of seroconversion data.

I13032 Combined and comparative analysis of virulence trends across multiple cohorts

Gras L, de Wolf F, Herbeck J, Müller V

Date of approval: 25 May 2013

We have shown an increase over time in the HIV plasma concentration at viral setpoint. Monitoring of these changes is critical, since such an increase may be indicative for increasing HIV virulence, which in turn would have implications for the treatment and prevention of HIV/AIDS.

Virulence is defined as the severity of disease; the virulence of a pathogen may evolve within a host population as the rates of transmission and host death are balanced. HIV is a unique model system for the study of virulence evolution, as its recent origin and high evolutionary potential suggest that it has adapted to humans rapidly. Whether HIV virulence has evolved, or is evolving still, can inform our understanding about past and possible future patterns of the HIV/AIDS pandemic.

The HIV Virulence Trends Working Group has been established, within which large scale data analysis together with mathematical modelling aims to inquire about past virulence trends and to predict future virulence trends. The Working Group is an initiative of scientists from the University of Washington School of Medicine, Seattle and Eötvös Loránd University, Institute of Biology, Budapest. In order to accomplish the goal, the group will:

1) bring together a collaborative network of HIV cohorts representing US, Europe and Africa to create a database of relevant clinical and epidemiological information;
2) assess whether HIV virulence has changed over the course of the pandemic;
3) investigate whether variation in regional epidemiology explains discrepancies among previous HIV virulence studies;

4) use mathematical modelling to predict future trends of HIV virulence, considering the effect of potential interventions, e.g., the effect of widely-used HIV antiretroviral therapy. The results of this HIV Virulence Trends Working Group will inform public policy on past and future trends of HIV virulence.

A meeting at the National Evolutionary Synthesis Center in Durham, NC, USA was held on February 28 and March 1 2014 and a detailed analysis plan with input from all participating cohorts was drawn up. Individual cohorts have sent data to the MRC Clinical Trials Unit in London, which acts as the data centre. After quality checks, a combined dataset was put together. No analyses have yet been undertaken.

I13051 aMASE: advancing migrant access to health services in Europe (EuroCoord work package 14: migrants and HIV). Barriers for HIV prevention, testing and treatment service uptake by migrants in the Netherlands

Bil J, Prins M, Zuure F, Burns F, del Amo J

Date of approval: 22 July 2013

Background: migrants represent a significant group in the HIV epidemic across Europe. Many remain unaware of their HIV infection, and migrants are more likely to be diagnosed late. Existing HIV testing and prevention strategies targeting migrant populations need to be enhanced and new strategies developed for new and emerging migrant populations. This study is part of a European research project (aMASE-study within EuroCoord) which aims to prevent HIV infection, and improve diagnosis and prognosis of migrant populations living with HIV by providing evidence to support policy development at the European level. We aim to determine the likely country of HIV acquisition for migrant populations and identify barriers to HIV prevention, testing and treatment. In the Dutch study arm, we will focus on the identification of barriers faced by migrants living in the Netherlands.

Methods: Data will be collected through two surveys. The first survey targets HIV-infected migrants and HIV-infected native Dutch patients (reference group); recruitment will take place at the HIV clinic (i.e., clinical survey). The second survey targets migrants in general, irrespective of their HIV status, and will be disseminated via the Internet (i.e., community survey). All participants will self-complete a questionnaire. In addition to the questionnaire, the clinic survey will collect data about clinical indicators of HIV disease (data source: SHM).

The clinical survey is a multi-site study which takes place in nine European countries. In the Netherlands we aim to recruit at three sites; 1) Academic Medical Center of Amsterdam (AMC), 2) Onze Lieve Vrouwe Gasthuis (OLVG) in Amsterdam, 3) Medisch Centrum Haaglanden (MCH) in The Hague. In addition to the European study, in the Netherlands we will also collect data from native HIV-positive patients to compare the results with those found among the migrant patients. The community survey will be disseminated through non-governmental and community-based organisations in nine European countries including the Netherlands.

Results in 2014: In 2014, recruitment in the Netherlands of HIV-positive patients for the clinical survey took place at the AMC and

the OLVG. Recruitment in the AMC started in July 2013 and continued until the beginning of May 2014. Recruitment in the OLVG took place between August and November 2014. In total, 206 patients (92 migrants and 114 native Dutch) were included in both clinics. Across Europe, a total of 1,701 patients had been included at the time of writing (12 January 2015).

In 2013, the questionnaire for the community survey was developed together with the European partners. Dissemination of the community survey started in May 2014 and will continue until the end of March 2015. At the end of 2014, a total of 867 migrants were included in the European community survey (n=46 in the Netherlands).

Expected results for 2015: in 2015, recruitment for the clinical survey in the MCH will start and is expected to finish by the end of June 2015. Recruitment for the community survey will continue, using social media, community outreach activities, and advertisements. The European results and the results of the Dutch data for the clinical and community survey are expected to be presented by the end of 2015.

I13059 Clinical, immunological, virological and social outcomes of cART-treated HIV-infected children after transition into adult health care services (CLIVIA study)

Weijsenfeld A, Mutschelknauss M, Smit C, Pajker D, van der Knaap L, de Jonge H, Nauta N, Strik-Albers R

Date of approval: 7 October 2013

Participating HIV treatment centres: 17, including 4 paediatric HIV treatment centres.
Inclusion and data collection: January-December 2014. Of 78 patients, we have included a total of 59 patients. Data analyses: January- March 2015.

Manuscript preparation: March- May 2015.

I13061 Factors associated with time to HIV RNA suppression in women with HIV infection starting antiretroviral treatment during pregnancy

Mudrikova T, van Snippenburg W, Wensing A, Nellen J, Godfried M, Smit C

Date of approval: 11 July 2013

The analysis of the dataset is complete. The results of this analysis will be submitted as an abstract to the *13th European HIV & Hepatitis Workshop* which will be held on June 3-5, 2015.

A manuscript on the results of this analysis is in preparation and should be submitted for publication in the second half of 2015.

I13087 Dutch protease for hepatitis C in HIV-infected patients – study (DECIDE-study)

Arends J, Hoepelman A, Brinkman K, van der Meer J, van de Ende I, Richter C, Schippers E, de Vries-Sluijs D, Schinkel J, Smit C

Date of approval: 3 August 2013

The final article for the DECIDE study will be submitted to *HIV Medicine* in 2015.

Presentations in 2014

Good SVR12 rates in boceprevir or telaprevir triple therapy in both treatment-naive and -experienced patients with HIV/HCV co-infection in the Netherlands
Arends JE, van der Meer J, Posthouwer D, Kortmann W, van Assen S, Reiss P, van de Ende M, Brinkman K, Richter C, Hoepelman AIM, Smit C, van der Valk M, Schinkel J.
Poster presentation at 8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment, Amsterdam, the Netherlands, 18 November 2014

I13120 SPREAD Program 3.0 – Surveillance of transmission of HIV-1 drug resistance

Wensing AMJ, Boucher CAB, Brinkman K, Richter C, Bierman WFW, van der Ende ME, van Kasteren MEE, Hoepelman IM, van Sighem A

Date of approval: 19 May 2014

Data from patients newly-diagnosed in 2011-2013 in any of the six participating centres of the Netherlands have been received from SHM and have been incorporated in the European SPREAD cohort. The SPREAD cohort collects data from 28 European countries. Data collection for 2011-2013 has been completed for nearly all countries. Over 4,000 patients have been included for 2011-2013.

A data analysis team has been formed with participants from various European countries, and includes Dr A.M.J. Wensing and Prof. C. Boucher of the Netherlands. Data analysis will start when data submission and verification has been completed by all countries. First results are planned to be submitted to the European HIV & Hepatitis Meeting in June 2015. In addition to the European analysis, we are investigating whether we can perform an analysis on the Dutch dataset only. Ard van Sighem has been added to the Dutch SPREAD group.

I13153 Factors associated with late presentation and advanced disease of HIV in the Netherlands, 1996-2014

Op de Coul E, van Sighem A, Brinkman K, van der Ende M, Geerlings S, Reiss P for the ATHENA national observational HIV cohort

Date of approval: 17 December 2013

Article submission expected in February 2015.

Presentations in 2014

Factors associated with late presentation and advanced disease of HIV in the Netherlands, 1996-2014
Op de Coul E, van Sighem A, Brinkman K, van der Ende M, Geerlings S, Reiss P for the ATHENA national observational HIV cohort.
Oral presentation at 8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment, Amsterdam, the Netherlands, 18 November 2014

Factors associated with late presentation and advanced disease of HIV in the Netherlands
Op de Coul E, van Sighem A, Brinkman K, van der Ende M, Geerlings S, Reiss P for the ATHENA national observational HIV cohort.
Poster presentation at IUSTI 2014, St. Julian's, Malta, 18-20 September 2014

I14065 Incidence of hepatocellular carcinoma in HIV/HBV-coinfected patients: Implications for screening strategies

Wandeler G, Rauch A, Reiss P, Smit C, van der Valk M, Arends J

Date of approval: 4 May 2014

Background: hepatocellular carcinoma (HCC) is a leading cause of cancer-related death. Patients co-infected with HIV and HBV have a particularly high risk of developing HCC. In order to reduce cancer-related mortality, surveillance programs with ultrasonography with or without alpha-foetoprotein (AFP) every six months have been widely applied, despite scarce scientific evidence. However, the current screening recommendations are based on extrapolations from incidence estimates in untreated HIV mono-infected patients and might not be adequate for treated HIV/HBV co-infected individuals.

Study aims: to (1) give a detailed description of the demographic and clinical characteristics of HCC cases in HIV/HBV co-infected patients, (2) to assess the incidence of HCC according to antiretroviral therapy regimen, and (3) to evaluate whether there is evidence to support the current recommendations for HCC screening in HIV/HBV-coinfected patients.

Study design: descriptive statistics will be used to evaluate the demographic and clinical characteristics of HIV/HBV-infected patients who developed an HCC. The incidence of HCC in HIV/HBV co-infected patients will be compared between antiretroviral regimens (untreated, lamivudine-based ART and tenofovir-based ART) using time-to-event analyses.

There has been no progress in analyses yet. We are waiting for the final dataset from ATHENA to be used in the analyses.

I14067 Predictive value of cardiovascular risk equations in the HIV-infected population receiving care in the Dutch HIV treatment centres

Wit F, van Zoest R, Vaartjes I, Gras L, Arends J, Reiss P

Date of approval: 3 June 2014

Background: cardiovascular disease (CVD) is more prevalent among HIV-infected participants than in HIV-uninfected controls. The pathophysiological mechanism is thought to be multifactorial. The current Dutch cardiovascular risk management guidelines recommend risk assessment based on the SCORE risk equation. However, it is unknown whether the SCORE risk equation also accurately identifies HIV-infected patients at increased risk of CVD. The aim of our study is (1) to assess whether the SCORE risk equation correctly estimates the CVD risk of the HIV-infected population in the Netherlands, and (2) to compare various CVD risk equations in the HIV-infected population.

Methods: we received the SHM data set in June 2014. The population that will be used for the current analysis was selected using our predefined inclusion criteria. The baseline date has been defined for all study participants, and all variables have been labelled. The five risk equations we will evaluate in this project have been implemented in STATA syntax: SCORE-NL equation, D:A:D risk equation (reduced and full), Framingham risk equation, and Pooled

Cohort Risk Equation. In addition, the CVD endpoints have been defined and coded. At the moment we are identifying the proportion of missing values per variable and imputing these data in a correct manner.

Results: no results available, analysis ongoing.

Conclusions: no conclusion available, analysis ongoing.

l14082 HIV testing and counselling in general practices in the Netherlands

Op de Coul E, van den Broek I, Joore I, Reukers D, van Bergen J, van Sighem A

Date of approval: 20 August 2014

Presentations in 2014

Dutch GPs' adherence to national guidelines promoting risk based HIV testing: bridging database information with clinical practice
Reukers D, Joore I, van den Broek I, Op de Coul E, Donker G, van Bergen J.
Poster presentation at 8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment, Amsterdam, the Netherlands, 18 November 2014

l14087 Clinical experience with rilpivirine (KLIRI study)

Roelofsen E, Burger DM, Touw DJ, Gelinck LBS, Wilms EB

Date of approval: 28 October 2014

Ongoing

l14096 Primary and recurrent venous thromboembolism in HIV-1 (PREDICT study)

Borjas-Howard J, Rijnders BJS, Rokx C, Tichelaar YIGV, Verbon A, Meijer K

Date of approval: 21 August 2014

Ongoing

l14145 Evaluation of an evidence-based, internet-supported self-help program for people living with HIV suffering from mild to moderate depressive symptoms

Van Bergen J, Joore I, Op de Coul E, van Sighem A, Prins J, Geerlings S

Date of approval: 24 September 2014

Ongoing

l14157 Overlap between HIV and HCV networks among MSM with HIV/HCV coinfection

Vanhommerig J, Schinkel J, Bezemer D, van de Laar T, van Sighem A, Smit C, Prins M

Date of approval: 8 December 2014

Ongoing

Publications in 2014

HIV-1 transmission networks amongst men having sex with men and heterosexuals in Kenya
Bezemer D, Faria NR, Hassan AS, Hamers RL, Mutua G, Anzala O, Mandaliya KN, Cane PA, Berkley JA, Rinke de Wit TF, Wallis CL, Graham SM, Price MA, Coutinho R, Sanders EJ.
AIDS Res Hum Retroviruses. 2014 Feb;30(2):118-26. doi: 10.1089/AID.2013.0171. Epub 2013 Sep 17

A simplified combination antiretroviral therapy regimen enhances adherence, treatment satisfaction and quality of life: results of a randomized clinical trial
Langebeek N, Sprenger H, Gisolf E, Reiss P, Sprangers M, Legrand J, Richter C, Nieuwkerk P.
HIV Med. 2014 May;15(5):286-90. doi: 10.1111/hiv.12112. Epub 2013 Nov 11

Estimating HIV incidence from case-report data: method and an application in Colombia
Vesga JF, Cori A, van Sighem A, Hallett TB.
AIDS. 2014 Nov;28 Suppl 4:S489-96. doi: 10.1097/QAD.0000000000000466

Cross-sectional comparison of the prevalence of age-associated comorbidities and their risk factors between HIV-infected and uninfected individuals: the AGEhIV cohort study
Schouten J, Wit FW, Stolte IG, Kootstra NA, van der Valk M, Geerlings SE, Prins M, Reiss P; AGEhIV Cohort Study Group.
Clin Infect Dis. 2014 Dec 15;59(12):1787-97

Increased virological failure in naive HIV-1 patients taking lamivudine compared to emtricitabine in combination with tenofovir and efavirenz or nevirapine in the Dutch nationwide ATHENA cohort
Rokx C, Fibriani A, van de Vijver DA, Verbon A, Schutten M, Gras L, Rijnders BJ; On behalf of the ATHENA national observational cohort.
Clin Infect Dis. 2015 Jan 1;60(1):143-53. doi: 10.1093/cid/ciu763. Epub 2014 Oct 1

Low bone mineral density in patients with well-suppressed HIV infection: association with body weight, smoking, and prior advanced HIV disease
Kooij KW, Wit FW, Bisschop PH, Schouten J, Stolte IG, Prins M, van der Valk M, Prins JM, van Eck-Smit BL, Lips P, Reiss P; AGEhIV Cohort Study group.
J Infect Dis. 2015 Feb 15;211(4):539-48. doi: 10.1093/infdis/jiu499. Epub 2014 Sep 1

Changes in HIV RNA and CD4 cell count following acute HCV infection in chronically HIV-infected individuals
Gras L, de Wolf F, Smit C, Prins M, van der Meer JT, Vanhommerig JW, Zwinderman AH, Schinkel J, Geskus RB; for the ATHENA national observational cohort and the MOSAIC study.
J Acquir Immune Defic Syndr. 2015 Apr 15;68(5):536-42. doi: 10.1097/QAI.0000000000000514

Publications related to collaborations

ART-CC

Immunodeficiency at the start of combination antiretroviral therapy in low-, middle-, and high-income countries
IeDEA and ART Cohort Collaborations.
J Acquir Immune Defic Syndr. 2014 Jan 1;65(1):e8-16.doi:10.1097/QAI.0b012e3182a39979

Sex differences in overall and cause-specific mortality among HIV-infected adults on antiretroviral therapy in Europe, Canada and the US
The Antiretroviral Therapy Cohort Collaboration (ART-CC).
Antivir Ther. 2014 Mar 27. doi: 10.3851/IMP2768. [Epub ahead of print]

Impact on life expectancy of HIV-1 positive individuals of CD4+ cell count and viral load response to antiretroviral therapy
May MT, Gompels M, Delpech V, Porter K, Orkin C, Kegg S, Hay P, Johnson M, Palfreeman A, Gilson R, Chadwick D, Martin F, Hill T, Walsh J, Post F, Fisher M, Ainsworth J, Jose S, Leen C, Nelson M, Anderson J, Sabin C; UK Collaborative HIV (UK CHIC) Study.
AIDS. 2014 May 15;28(8):1193-202. doi: 10.1097/QAD.0000000000000243

Long-term mortality in HIV-positive individuals virally suppressed for more than three years with incomplete CD4 recovery
Engsig FN, Zangerle R, Katsarou O, Dabis F, Reiss P, Gill J, Porter K, Sabin C, Riordan A, Fätkenheuer G, Gutiérrez F, Raffi F, Kirk O, Mary-Krause M, Stephan C, de Olalla PG, Guest J, Samji H, Castagna A, Monforte AD, Skaletz-Rorowski A, Ramos J, Lapadula G, Mussini C, Force L, Meyer L, Lampe F, Boufassa F, Bucher HC, De Wit S, Burkholder GA, Teira R, Justice AC, Sterling TR, Crane H, Gerstoft J, Grarup J, May M, Chêne G, Ingle SM, Sterne J, Obel N; The Antiretroviral Therapy Cohort Collaboration (ART-CC) and the Collaboration of Observational HIV Research Europe (COHERE) in EuroCoord.
Clin Infect Dis. 2014 May;58(9):1312-21. doi: 10.1093/cid/ciu038. Epub 2014 Jan 22

Cohort profile: antiretroviral therapy cohort collaboration (ART-CC)
May MT, Ingle SM, Costagliola D, Justice AC, de Wolf F, Cavassini M, D'Arminio Monforte A, Casabona J, Hogg RS, Mocroft A, Lampe FC, Dabis F, Fätkenheuer G, Sterling TR, del Amo J, Gill MJ, Crane HM, Saag MS, Guest J, Brodt HR, Sterne JA; Antiretroviral Cohort Collaboration.
Int J Epidemiol. 2014 Jun;43(3):691-702. doi: 10.1093/ije/dyt010. Epub 2013 Apr 18

Prognosis of children with HIV-1 infection starting antiretroviral therapy in Southern Africa: a collaborative analysis of treatment programs
Davies MA, May M, Bolton-Moore C, Chimbetete C, Eley B, Garone D, Giddy J, Moultrie H, Ndirangu J, Phiri S, Rabie H, Technau KG, Wood R, Boulle A, Egger M, Keiser O; IeDEA Southern Africa Collaboration.
Pediatr Infect Dis J. 2014 Jun;33(6):608-16. doi: 10.1097/INF.0000000000000214

Impact of risk factors for specific causes of death in the first and subsequent years of antiretroviral therapy among HIV-infected patients
Ingle SM, May MT, Gill MJ, Mugavero MJ, Lewden C, Abgrall S, Fätkenheuer G, Reiss P, Saag MS, Manzardo C, Grabar S, Bruyand M, Moore D, Mocroft A, Sterling TR, D'Arminio Monforte A, Hernando V, Teira R, Guest J, Cavassini M, Crane HM, Sterne JA; Antiretroviral Therapy Cohort Collaboration.
Clin Infect Dis. 2014 Jul 15;59(2):287-97. doi: 10.1093/cid/ciu261. Epub 2014 Apr 24

Mortality in patients with HIV-1 infection starting antiretroviral therapy in South Africa, Europe, or North America: a collaborative analysis of prospective studies
Boulle A, Schomaker M, May MT, Hogg RS, Shepherd BE, Monge S, Keiser O, Lampe FC, Giddy J, Ndirangu J, Garone D, Fox M, Ingle SM, Reiss P, Dabis F, Costagliola D, Castagna A, Ehren K, Campbell C, Gill M, Saag M, Justice AC, Guest J, Crane HM, Egger M, Sterne JA.
PLoS Med. 2014 Sep 9;11(9):e1001718. doi: 10.1371/journal.pmed.1001718. eCollection 2014

Smoking and life expectancy among HIV-infected individuals on antiretroviral therapy in Europe and North America: The ART Cohort Collaboration
Helleberg M, May MT, Ingle SM, Dabis F, Reiss P, Fätkenheuer G, Costagliola D, d'Arminio A, Cavassini M, Smith C, Justice AC, Gill J, Sterne JA, Obel N.
AIDS. 2015 Jan 14;29(2):221-9. doi: 10.1097/QAD.0000000000000540.

CASCADE

Blunted response to combination antiretroviral therapy in HIV elite controllers: an international HIV controller collaboration
Boufassa F, Lechenadec J, Meyer L, Costagliola D, Hunt PW, Pereyra F, Deeks S, Pancino G, Taulera O, Lichterfeld M, Delobel P, Saez-Cirion A, Lambotte O; ANRS CO18 HIV Controllers Cohort, the Cascade Collaboration in Eurocoord, the SCOPE Cohort and the International HIV Controllers Study.
PLoS One. 2014 Jan 17;9(1):e85516. doi: 10.1371/journal.pone.0085516. eCollection 2014

An evaluation of HIV elite controller definitions within a large seroconverter cohort collaboration
Olson AD, Meyer L, Prins M, Thiebaut R, Gurdasani D, Guiguet M, Chaix ML, Amornkul P, Babiker A, Sandhu MS, Porter K; for C.A.S.C.A.D.E. Collaboration in EuroCoord.
PLoS One. 2014 Jan 28;9(1):e86719. doi: 10.1371/journal.pone.0086719. eCollection 2014

High percentage of recent HIV infection leading to onward transmission in Odessa, Ukraine, associated with young adults
Simmons R, Semenenko I, Tolpina M, Tereschenko R, Kotlik L, Zasyptka L, Murphy G, McKinney E, Copas A, Malyuta R, Porter K; CASCADE collaboration in EuroCoord.
AIDS Behav. 2014 Feb;18(2):411-8. doi: 10.1007/s10461-013-0518-9

Evaluation of rapid progressors in HIV infection as an extreme phenotype
Olson AD, Guiguet M, Zangerle R, Gill J, Perez-Hoyos S, Lodi S, Ghosn J, Dorrucci M, Johnson A, Sannes M, Moreno S, Porter K; for CASCADE Collaboration in EuroCoord.
J Acquir Immune Defic Syndr. 2014 Sep 1;67(1):15-21. doi: 10.1097/QAI.0000000000000240

Temporal trends in prognostic markers of HIV-1 virulence and transmissibility: an observational cohort study
Pantazis N, Porter K, Costagliola D, De Luca A, Ghosn J, Guiguet M, Johnson A, Kelleher A, Morrison C, Thiebaut R, Wittkop L, Touloumi G, for the CASCADE Collaboration in EuroCoord.
Lancet HIV 2014. doi:10.1016/S2352-3018(14)00002-2

COHERE

Long-term mortality in HIV positive individuals virally suppressed for more than three years with incomplete CD4 recovery

Engsig FN, Zangerle R, Katsarou O, Dabis F, Reiss P, Gill J, Porter K, Sabin C, Riordan A, Fätkenheuer G, Gutiérrez F, Raffi F, Kirk O, Mary-Krause M, Stephan C, de Olalla PG, Guest J, Samji H, Castagna A, Monforte AD, Skaletz-Rorowski A, Ramos J, Lapadula G, Mussini C, Force L, Meyer L, Lampe F, Boufassa F, Bucher HC, De Wit S, Burkholder GA, Teira R, Justice AC, Sterling TR, Crane H, Gerstoft J, Grarup J, May M, Chêne G, Ingle SM, Sterne J, Obel N; The Antiretroviral Therapy Cohort Collaboration (ART-CC) and the Collaboration of Observational HIV Research Europe (COHERE) in EuroCoord.
Clin Infect Dis. 2014 May;58(9):1312-21. doi: 10.1093/cid/ciu038. Epub 2014 Jan 22

Factors associated with short-term changes in HIV viral load and CD4(+) cell count in antiretroviral-naive individuals

Natural History Project Working Group for the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) in EuroCoord.
AIDS. 2014 Jun 1;28(9):1351-6. doi: 10.1097/QAD.0000000000000224

Delayed HIV diagnosis and initiation of antiretroviral therapy: inequalities by educational level, COHERE in EuroCoord

Socio-economic Inequalities and HIV Writing Group for Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) in EuroCoord.
AIDS. 2014 Sep 24;28(15):2297-306. doi: 10.1097/QAD.0000000000000410

Impact of body weight on virological and immunological responses to efavirenz-containing regimens in HIV-infected, treatment-naive adults

Marzolini C, Sabin C, Raffi F, Siccardi M, Mussini C, Launay O, Burger D, Roca B, Fehr J, Bonora S, Mocroft A, Obel N, Dauchy FA, Zangerle R, Gogos C, Gianotti N, Ammassari A, Torti C, Ghosn J, Chêne G, Grarup J, Battegay M; for the Efavirenz, Obesity Project Team the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) in EuroCoord.
AIDS. 2015 Jan 14;29(2):193-200. doi: 10.1097/QAD.0000000000000530

D:A:D

Predictors of advanced chronic kidney disease and end-stage renal disease in HIV-positive persons

Ryom L, Mocroft A, Kirk O, Ross M, Reiss P, Fux CA, Morlat P, Moranne O, Smith C, El-Sadr W, Law M, Lundgren JD.
AIDS. 2014 Jan 14;28(2):187-99. doi: 10.1097/QAD.0000000000000042

Development of a definition for rapid progression (RP) of renal function in HIV-positive persons: the D:A:D study

Kamara DA, Ryom L, Ross M, Kirk O, Reiss P, Morlat P, Moranne O, Fux CA, Mocroft A, Sabin C, Lundgren JD, Smith CJ; D:A:D study Group.
BMC Nephrol. 2014 Mar 25;15:51. doi: 10.1186/1471-2369-15-51

Increased risk of cardiovascular disease (CVD) with age in HIV-positive men: a comparison of the D:A:D CVD risk equation and general population CVD risk equations

Petoumenos K, Reiss P, Ryom L, Rickenbach M, Sabin C, El-Sadr W, d'Arminio Monforte A,

Phillips A, De Wit S, Kirk O, Dabis F, Pradier C, Lundgren J, Law M; D:A:D study group.
HIV Med. 2014 May 19. doi: 10.1111/hiv.12162. [Epub ahead of print]

Trends in underlying causes of death in people with HIV from 1999-2011 (D:A:D): a multicohort collaboration
Smith CJ, Ryom L, Weber R, Morlat P, Pradier C, Reiss P, Kowalska JD, de Wit S, Law M, el Sadr W, Kirk O, Friis-Moller N, Monforte Ad, Phillips AN, Sabin CA, Lundgren JD, D:A:D Study Group.
Lancet. 2014 Jul 19;384(9939):241-8. doi: 10.1016/S0140-6736(14)60604-8

A clinically useful risk-score for chronic kidney disease in HIV infection
Mocroft A, Lundgren J, Ross M, Law M, Reiss P, Kirk O, Smith C, Wentworth D, Heuhaus J, Fux C, Moranne O, Morlat P, Johnson M, Ryom L; Data on Adverse Events (D:A:D) study group, the Royal Free Hospital Clinic Cohort and the INSIGHT study group.
J Int AIDS Soc. 2014 Nov 2;17(4 Suppl 3):19514

EPPICC

Post-licensing safety of fosamprenavir in HIV-infected children in Europe
Judd A, Duong T, Galli L, Goetghebuer T, Ene L, Julian AN, Ramos Amador JT, Pimenta JM, Thorne C, Giaquinto C; European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC) study group in EuroCoord.
Pharmacoepidemiol Drug Saf. 2014 Mar; 23(3):321-5

EuroSIDA

Short- and long-term mortality and causes of death in HIV/tuberculosis patients in Europe
Podlekareva DN, Panteleev AM, Grint D, Post FA, Miro JM, Bruyand M, Furrer H, Obel N, Girardi E, Vasilenko A, Losso MH, Arenas-Pinto A, Caylá J,Rakhmanova A, Zeltina I, Werlinrud AM, Lundgren JD, Mocroft A, Kirk O; HIV/TB study group.
Eur Respir J. 2014 Jan;43(1):166-77. doi: 10.1183/09031936.00138712. Epub 2013 Jun 13

Predictors of advanced chronic kidney disease and end-stage renal disease in HIV-positive persons
Ryom L, Mocroft A, Kirk O, Ross M, Reiss P, Fux CA, Morlat P, Moranne O, Smith C, El-Sadr W, Law M, Lundgren JD.
AIDS. 2014 Jan 14;28(2):187-99. doi: 10.1097/QAD.0000000000000042

Immuno-virological discordance and the risk of non-AIDS and AIDS events in a large observational cohort of HIV patients in Europe
Zoufaly A, Cozzi-Lepri A, Reekie J, Kirk O, Lundgren J, Reiss P, Jevtovic D, Machala L, Zangerle R, Mocroft A, Van Lunzen J; EuroSIDA in EuroCoord.
PLoS One. 2014 Jan 31;9(1):e87160. doi: 10.1371/journal.pone.0087160. eCollection 2014

Increased incidence of antiretroviral drug discontinuation among patients with viremic HCV coinfection and high hyaluronic acid, a marker of liver fibrosis
Grint D, Peters L, Rockstroh JK, de Wit S, Mitsura VM, Knysz B, Pedersen C, Kirk O, Lundgren JD, Mocroft A; EuroSIDA in EuroCoord.
AIDS. 2014 Feb 20;28(4):577-87. doi: 10.1097/QAD.0000000000000069

Deteriorating renal function and clinical outcomes in HIV-positive persons
Mocroft A, Ryom L, Begovac J, Monforte AD, Vassilenko A, Gatell J, Florence E, Ormaasen V, Kirk O, Lundgren JD; EuroSIDA in EuroCOORD.
AIDS. 2014 Mar 13;28(5):727-37. doi: 10.1097/QAD.0000000000000134

A comparison of estimated glomerular filtration rates using Cockcroft-Gault and the Chronic Kidney Disease Epidemiology Collaboration estimating equations in HIV infection
Mocroft A, Ryom L, Reiss P, Furrer H, D'Arminio Monforte A, Gatell J, de Wit S, Beniowski M, Lundgren J, Kirk O; for EuroSIDA in EuroCOORD.
HIV Med. 2014 Mar;15(3):144-52. doi: 10.1111/hiv.12095. Epub 2013 Oct 3

Development of a definition for Rapid Progression (RP) of renal function in HIV-positive persons: the D:A:D study
Kamara DA, Ryom L, Ross M, Kirk O, Reiss P, Morlat P, Moranne O, Fux CA, Mocroft A, Sabin C, Lundgren JD, Smith CJ; D:A:D study Group.
BMC Nephrol. 2014 Mar 25;15:51. doi: 10.1186/1471-2369-15-51

High rate of hepatitis C virus (HCV) recurrence in HIV-infected individuals with spontaneous HCV RNA clearance
Peters L, Mocroft A, Soriano V, Rockstroh J, Kirkby N, Reiss P, Katlama C, Zakharova N, Flisiak R, Lundgren J; for EuroSIDA in EuroCoord.
HIV Med. 2014 May 11. doi: 10.1111/hiv.12160. [Epub ahead of print]

Increased risk of cardiovascular disease (CVD) with age in HIV-positive men: a comparison of the D:A:D CVD risk equation and general population CVD risk equations
Petoumenos K, Reiss P, Ryom L, Rickenbach M, Sabin C, El-Sadr W, d'Arminio Monforte A, Phillips A, De Wit S, Kirk O, Dabis F, Pradier C, Lundgren J, Law M; D:A:D study group.
HIV Med. 2014 May 19. doi: 10.1111/hiv.12162. [Epub ahead of print]

Factors associated with short-term changes in HIV viral load and CD4(+) cell count in antiretroviral-naive individuals
Natural History Project Working Group for the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) in EuroCoord.
AIDS. 2014 Jun 1;28(9):1351-6. doi: 10.1097/QAD.0000000000000224

Prognostic value of vitamin D level for all-cause mortality, and association with inflammatory markers, in HIV-infected persons
Shepherd L, Souberbielle JC, Bastard JP, Fellahi S, Capeau J, Reekie J, Reiss P, Blaxhult A, Bickel M, Leen C, Kirk O, Lundgren JD, Mocroft A, Viard JP; On behalf of EuroSIDA in EuroCOORD.
J Infect Dis. 2014 Jul 15;210(2):234-43. doi: 10.1093/infdis/jiu074. Epub 2014 Feb 3

Impact of risk factors for specific causes of death in the first and subsequent years of antiretroviral therapy among HIV-infected patients
Ingle SM, May MT, Gill MJ, Mugavero MJ, Lewden C, Abgrall S, Fätkenheuer G, Reiss PR, Saag MS, Manzardo C, Grabar S, Bruyand M, Moore D, Mocroft A, Sterling TR, D'Arminio Monforte A, Hernando V, Teira R, Guest J, Cavassini M, Crane HM, Sterne JA; Antiretroviral Therapy Cohort Collaboration.

Clin Infect Dis. 2014 Jul 15;59(2):287-97. doi: 10.1093/cid/ciu261. Epub 2014 Apr 24

A survey of ATRIPLA use in clinical practice as first-line therapy in HIV-positive persons in Europe

Mocroft A, Reiss P, Rakhmanova A, Banhegyi D, Phillips AN, De Wit S, Ristola M, Lundgren JD, Grarup J, Kirk O; for EuroSIDA in EuroCOORD.

Infection. 2014 Aug;42(4):757-62. doi: 10.1007/s15010-014-0630-4. Epub 2014 Jun 6

Delayed HIV diagnosis and initiation of antiretroviral therapy: inequalities by educational level, COHERE in EuroCoord

Socio-economic Inequalities and HIV Writing Group for Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) in EuroCoord.

AIDS. 2014 Sep 24;28(15):2297-306. doi: 10.1097/QAD.0000000000000410

The effects of HIV-1 subtype and ethnicity on CD4 decline in antiretroviral naive patients: a Canadian-European collaborative cohort study

Klein MB, Young J, Dunn D, Ledergerber B, Sabin C, Cozzi-Lepri A, Dabis F, Harrigan R, Tan DH, Walmsley S, Gill J, Cooper C, Scherrer AU, Mocroft A, Hogg RS, Smaill F; Canadian-European Clade Collaboration.

CMAJ Open. 2014 Oct 1;2(4):E318-29. doi: 10.9778/cmajo.20140017. eCollection 2014

HIV and hepatitis C co-infection in Europe, Israel and Argentina: a EuroSIDA perspective

Peters L, Mocroft A, Lundgren J, Grint D, Kirk O, Rockstroh J.

BMC Infect Dis. 2014;14 Suppl 6:S13. doi: 10.1186/1471-2334-14-S6-S13. Epub 2014 Sep 19

HIV-CAUSAL

Antiretroviral penetration into the CNS and incidence of AIDS-defining neurologic conditions

Caniglia EC, Cain LE, Justice A, Tate J, Logan R, Sabin C, Winston A, van Sighem A, Miro JM, Podzamczer D, Olson A, Arribas JR, Moreno S, Meyer L, Del Romero J, Dabis F, Bucher HC, Wandeler G, Vourli G, Skoutelis A, Lanoy E, Gasnault J, Costagliola D, Hernán MA; HIV-CAUSAL Collaboration.

Neurology. 2014 Jul 8;83(2):134-41. doi: 10.1212/WNL.0000000000000564. Epub 2014 Jun 6

Opportunistic infections and AIDS malignancies early after initiating combination antiretroviral therapy in high-income countries

HIV-CAUSAL Collaboration.

AIDS. 2014 Oct 23;28(16):2461-73. doi: 10.1097/QAD.0000000000000456

RDI

An update to the HIV-TRePS system: the development of new computational models that do not require a genotype to predict HIV treatment outcomes

Revell AD, Wang D, Wood R, Morrow C, Tempelman H, Hamers R, Alvarez-Uria G, Streinu-Cercel A, Ene L, Wensing A, Reiss P, van Sighem AI, Nelson M, Emery S, Montaner JS, Lane HC, Larder BA; on behalf of the RDI Study Group.

J Antimicrob Chemother. 2014 Apr;69(4):1104-10. doi: 10.1093/jac/dkt447. Epub 2013 Nov 24

A comparison of computational models with and without genotyping for prediction of response to second-line HIV therapy
Revell A, Boyd M, Wang D, Emery S, Gazzard B, Reiss P, van Sighem A, Montaner J, Lane H, Larder B.
HIV Med. 2014 Aug;15(7):442-8. doi: 10.1111/hiv.12156. Epub 2014 Apr 15

Other printed materials

Sexually transmitted infections, including HIV, in the Netherlands in 2013
van Aar F, Koedijk FDH, van den Broek IVF, Op de Coul ELM, Soetens LC, Woestenberg PJ, Heijne JCM, van Sighem AI, Nielen MMJ, van Benthem BHB.
RIVM Rapport number: 150002005/2014; ISBN 978-90-6960-272-1

Hart- en vaatziekten in Nederland 2014, cijfers over kwaliteit van leven, ziekte en sterfte [Cardiovascular disease in the Netherlands 2014, figures on quality of life, morbidity and mortality]
Bots ML, van Dis I, Koopman C, Vaartjes I, Visseren FLJ.
Hartstichting, ISBN 978-90-75131-76-5

Nederlandse vertegenwoordiging tijdens CROI 2014 [Dutch representation at CROI 2014]
van Sighem AI.
HIV Bulletin, Special CROI, 20140002005

Presentations in 2014

Oral presentations

Ongoing HIV-1 subtype B transmission networks in the Netherlands
Bezemer D, Ratmann O, van Sighem A, Dutilh B, Faria N, van den Hengel R, Gras L, Reiss P, de Wolf F, Fraser C, and the ATHENA observational cohort.
21st Conference on Retroviruses and Opportunistic Infections, Boston, USA, 3-6 March 2014

Resurgence of HIV amongst MSM in Switzerland?
van Sighem, A.
Institut für Sozial- und Präventivmedizin
ISPM, Bern, Switzerland, 20 March 2014

CD4 cell count dynamics in HIV-1 and HIV-2 seroprevalent patients while naive for antiretroviral treatment, a multicohort study
Wittkop L.
18th Workshop on HIV Observational Databases (IWHOD), Sitges, Spain, 26-28 March 2014

Estimating HIV incidence and diagnosis rates amongst men who have sex with men in the Netherlands
van Sighem A.
18th Workshop on HIV Observational Databases (IWHOD), Sitges, Spain, 26-28 March 2014

Estimation of size and characteristics of HIV-positive populations using an individual-based stochastic simulation model of HIV progression and effects of ART
Nakagawa F.
18th Workshop on HIV Observational Databases (IWHOD), Sitges, Spain, 26-28 March 2014

Immediate versus CD4-based initiation of antiretroviral treatment in AIDS-free individuals recently diagnosed with HIV in high-income countries
Lodi S.
18th Workshop on HIV Observational Databases (IWHOD), Sitges, Spain, 26-28 March 2014

Post 10-year prognosis of those who started ART between 1996-1999
Trickey A.
18th Workshop on HIV Observational Databases (IWHOD), Sitges, Spain, 26-28 March 2014

When to switch antiretroviral therapy following virologic failure on a first-line regimen
Cain L; on behalf of ART-CC, CNICS and HIV-CAUSAL.
18th Workshop on HIV Observational Databases (IWHOD), Sitges, Spain, 26-28 March 2014

Drivers of ongoing HIV transmission among men having sex with men despite access to care and high treatment coverage in the Netherlands
Ratmann O.
21st Annual HIV Dynamics & Evolution, Tucson, USA, 7-10 May 2014

Long-established HIV-1 subtype B transmission networks persist through transmission to next generations of MSM in the Netherlands
Bezemer D.
21st Annual HIV Dynamics & Evolution, Tucson, USA, 7-10 May 2014

The HIV treatment response prediction system – using the experience of treating tens of thousands of patients to guide optimal drug selection
Revell AD, Wang D, Reiss P, van Sighem A, Hamers R, Morrow C, Gazzard B, Montaner JS, Lane HC, Larder BA on behalf of the global RDI study group.
HIV Drug Therapy in the Americas, Rio de Janeiro, Brazil, 8-10 May 2014

Modelling HIV incidence and the undiagnosed fraction
van Sighem A, Quinten C, Cowan S, Nakagawa F, Pharris A.
STI and HIV Network Meeting, Dubrovnik, Croatia, 20-22 May 2014

Meer testen en sneller op therapie – De gevolgen voor de HIV-epidemie onder MSM in Nederland [The effect of more frequent testing and earlier treatment on the HIV epidemic amongst MSM]
van den Hengel R.
RIVM/CIb Expert meeting SOA HIV, Bilthoven, the Netherlands, 27 June 2014

A clinically useful risk-score for chronic kidney disease in HIV infection
Mocroft A, Lundgren J, Ross M, Law M, Preiss P, Kirk O, Smith C, Wentworth D, Heuhaus J, Fux C, Moranne O, Morlat P, Johnson M, Ryom L.
HIV Drug Therapy Glasgow, Glasgow, UK, 2-6 November 2014

Lack of association between use of efavirenz and death from suicide: evidence from the D:A:D study
Smith C, Ryom L, Monforte A, Reiss P, Mocroft A, El-Sadr W, Weber R, Law M, Sabin C, Lundgren J.
HIV Drug Therapy Glasgow, Glasgow, UK, 2-6 November 2014

More virological failure with lamivudine than emtricitabine in efavirenz and nevirapine regimens in the Dutch nationwide HIV cohort
Rokx C, Fibriani A, van de Vijver D, Verbon A, Schutten M, Gras L, Rijnders B.
HIV Drug Therapy Glasgow, Glasgow, UK, 2-6 November 2014

Predictive value of prostate-specific antigen for prostate cancer: a nested case-control study in EuroSIDA
Shepherd L, Borges Al, Ravn L, Harvey R, Viard J, Bower M, Grulich A, Silverberg M, De Wit S, Kirk O, Lundgren J, Mocroft A.
HIV Drug Therapy Glasgow, Glasgow, UK, 2-6 November 2014

Regional differences in self-reported HIV care and management in the EuroSIDA study
Laut K, Mocroft A, Lazarus J, Reiss P, Rockstroh J, Karpov I, Rakhmanova A, Knysz B, Moreno S, Gargalianos P, Lundgren J, Kirk O.
HIV Drug Therapy Glasgow, Glasgow, UK, 2-6 November 2014

'Test-and-treat' in the Netherlands
Van Sighem AI, Gras LAJ, Op de Coul ELM, Bezemer DO, Agtmael MA, de Bree G, Reiss P; on behalf of the ATHENA national observational HIV cohort.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

An update on HIV in the Netherlands
Reiss P.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Cerebral structural and microstructural differences between perinatally HIV-infected children and healthy controls
Cohen S, Caan MAW, Scherpbier HJ, Kuijpers TW, Reiss, Majoie CBLM, Pajkrt D.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Factors associated with late presentation and advanced disease of HIV in the Netherlands, 1996-2014
Op de Coul ELM, van Sighem AI, Brinkman K, van Benthem BH, van der Ende ME, Geerlings S, Reiss P.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

HIV infection is independently associated with frailty in middle-aged HIV-infected individuals compared to uninfected controls
Kooij KW, Wit FWNM, Schouten J, van der Valk M, Stolte I, Reiss P.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Majority of HIV/HCV co-infected patients currently in care in the Netherlands have not yet or not successfully been treated for HCV
Smit C, Arends JE, van der Valk, M, Brinkman K, Ammerlaan H, Arend S, Reiss P, Richter C.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Risk factors for sexual transmission of hepatitis C virus: results from the MOSAIC cohort
Vanhommerig JW, Lambers FAE, Schinkel J, Arends JE, Lauw FN, Brinkman K, Gras LAJ, Rijnders B, van der Meer JTM, Prins M.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Sources of HIV-1 transmission in the ongoing, concentrated HIV epidemic among men having sex with men in the Netherlands between July 1996 and December 2010
Ratmann, O, Sighem, A van, Bezemer, D, Gavryushkina, A, Reiss, P, Wolf, F de, Fraser, C.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Poster presentations

Association between dideoxynucleoside analogues (d-drugs) and End-Stage Liver Disease (ESLD)
Ryom L on behalf of DAD.
21st Conference on Retroviruses and Opportunistic Infections, Boston, USA, 3-6 March 2014

Cumulative viral load predicts all-cause and AIDS-related mortality after initiation of ART
Mugavero M, Westfall A, Gill J, Saag M, Abgrall S, Fatkenheuer G, Reiss P, Ingle S, May M, Sterne J on behalf of the ART-CC.
21st Conference on Retroviruses and Opportunistic Infections, Boston, USA, 3-6 March 2014

Current first-line regimens are effective in patients with single transmitted TAM
van Nispen tot Pannerden CMF, El Barzouhi A, van Sighem AI, Prins JM, Jurriaans S, Back NK, Brinkman K, Boucher CA, van der Ende ME, Schutten M.
21st Conference on Retroviruses and Opportunistic Infections, Boston, USA, 3-6 March 2014

Estimating the size of the undiagnosed HIV population in the Netherlands by disease stage
van Sighem A, Nakagawa F, Bezemer D, De Angelis D, Op de Coul E, Egger M, de Wolf F, Fraser C, Phillips A.
21st Conference on Retroviruses and Opportunistic Infections, Boston, USA, 3-6 March 2014

Impact of low-level viremia on clinical and virological outcomes in treated HIV infected patients
Vandenhende MA, Ingle S, May M, Cavassini M, Mocroft A, Reiss P, Tate J, Crane H, Sterne J, Chêne G on behalf of the ART-CC.
21st Conference on Retroviruses and Opportunistic Infections, Boston, USA, 3-6 March 2014

Impact of smoking on life expectancy among HIV-infected individuals: The ART Cohort Collaboration
Helleberg M, May MT, Sterne JAC & Obel N for ART-CC.
21st Conference on Retroviruses and Opportunistic Infections, Boston, USA, 3-6 March 2014

Is there continued evidence for an association between abacavir and myocardial infarction risk?
Sabin C on behalf of D:A:D.
21st Conference on Retroviruses and Opportunistic Infections, Boston, USA, 3-6 March 2014

Kaposi sarcoma in the era of combination antiretroviral therapy
Wyss N, Egger M, Bohlius J, on behalf of the Malignancy Working Group for COHERE in EuroCoord.
21st Conference on Retroviruses and Opportunistic Infections, Boston, USA, 3-6 March 2014

Predictors of progression, stabilisation or improvement of eGFR after chronic renal impairment
Ryom L, on behalf of D:A:D.
21st Conference on Retroviruses and Opportunistic Infections, Boston, USA, 3-6 March 2014

The clinical impact of viral load copy years in antiretroviral-naive HIV seroconverters
Van der Heiden M, Zoufaly A, Sabin C, van Lunzen J, Stellbrink H, Gunsenheimer-Bartmeyer B, Vanhems P, Perez-Hoyos S, Chêne G, Hamouda O, on behalf of CASCADE.
21st Conference on Retroviruses and Opportunistic Infections, Boston, USA, 3-6 March 2014

Value of viremia copy years in deciding optimal timing of ART initiation in adults with HIV
Olson A, Walker A, Suthar A, Sabin C, Bucher H, Jarrin I, Moreno S, Perez-Hoyos S, Porter K, Deborah F, CASCADE Collaboration in EuroCoord.
21st Conference on Retroviruses and Opportunistic Infections, Boston, USA, 3-6 March 2014

Accounting for misclassification bias in multivariable models using weighting by positive predictive values: case study on whether the association between injection drug use (IDU) and mortality is explained by differential rates of hepatitis C virus (HCV) infection
May M, Justice A, on behalf of ART-CC.
18th Workshop on HIV Observational Databases (IWHOD), Sitges, Spain, 26-28 March 2014

Starting cART in antiretroviral-naive HIV-1–infected patients presenting with cryptococcal meningitis
Ingle S, Miro JM, Furrer H, Justice A, Saag M, Manzardo C, Esteve A, Sterne J, May M on behalf of COHERE, CNICS and NA-ACCORD.
18th Workshop on HIV Observational Databases (IWHOD), Sitges, Spain, 26-28 March 2014

Cascade of HIV care in the Netherlands from 2002 to 2013
Engelhard EAN, Smit C, van Sighem AI, Reiss P, Brinkman K, Geerlings SE, on behalf of the Q-HIV and the ATHENA National Observational Cohort Study Groups.
WEON 2014, Leiden, the Netherlands, 5 June 2014

Improved weighted darunavir genotypic mutation score predicting treatment response for HIV-1 subtype B and non-B infected patients receiving darunavir in a salvage regimen
De Luca A, Flandre P, Castagna A, Ceccherini-Silberstein F, Cozzi-Lepri A, Churchill D, De Wit S, Dunn D, Fuchs W, Garcia F, Günthard H, Imaz A, Kordossis T, Mussini C, Obel N, Roca B, Santoro MM, Schuelter E, Torti C, van Sighem A, Wensing AM, Wittkop L, Zangerle R, Zazzi M, Descamps D, on behalf of CHAIN and COHERE in Eurocoord working group.
International Workshop on Antiviral Drug Resistance: Meeting the Global Challenge, Berlin, Germany, 3-7 July 2014

Clinical implication of an aging HIV-population: multi-morbidity, polypharmacy and drug-drug interactions
Smit M, Brinkman K, Geerlings S, Smit C, Thyagarajan K, van Sighem A, de Wolf F, Hallett TB.
20th International AIDS Conference, Melbourne, Australia, 20-25 July

Factors associated with late presentation and advanced disease of HIV in the Netherlands
Op de Coul E, van Sighem A, Brinkman K, van der Ende M, Geerlings S, Reiss P, for the ATHENA national observational HIV cohort.
XXVIII IUSTI, St. Julian's, Malta, 18-20 September 2014

Insight into the HIV prevalence and the undiagnosed HIV population in the Netherlands
Schreuder I, Op de Coul ELM, Conti S, van Sighem AI, De Angelis D, van Veen MG, Xiridou M, Heijne JCM.
XXVIII IUSTI, St. Julian's, Malta, 18-20 September 2014

Long term effectiveness of once-daily unboosted atazanavir plus abacavir/lamivudine as a switch strategy in subjects with virological suppression
Llibre J, Cozzi-Lepri A, Valencia La Rosa J, Pedersen C, Ristola M, Losso M, Mocroft A, Mitsura V, Ormaasen V, Maltez F, Beniowski M, Paredes R.
HIV Drug Therapy Glasgow, Glasgow, UK, 2-6 November 2014

Patients' willingness to take separate component antiretroviral therapy regimens for HIV in The Netherlands
Engelhard E, Smit C, Vervoort S, Kroon F, Brinkman K, Nieuwkerk P, Reiss P, Geerlings S.
HIV Drug Therapy Glasgow, Glasgow, UK, 2-6 November 2014

The prevalence and predictive value of dipstick urine protein (DUP) in HIV-positive persons in Europe
Mocroft A, Ryom L, Lapadula G, Reiss P, Blaxhult A, Furrer H, Kutsyna G, Gatell J, Begovac J, Kirk O, Lundgren J.
HIV Drug Therapy Glasgow, Glasgow, UK, 2-6 November 2014

Accentuated CD8+ T-cell senescence is associated with both calendar age and CD8+ T-cell activation in long-term treated HIV-1-infected patients
Cobos Jiménez VCJ, Wit FWNM, Joerink M, Maurer I, Harskamp AH, Schouten J, Prins M, Reiss P, van Leeuwen EMM, Kootstra NA.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Changing patterns of undiagnosed HIV infection in the Netherlands: who benefits most from intensified HIV test and treat policies?
Op de Coul ELM, Schreuder I, Conti S, Van Sighem A, De Angelis D, Xiridou M, Van Veen M, Heijne JCM.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Consequences of increased testing and earlier start of therapy on the HIV epidemic among MSM in the Netherlands
Van den Hengel, R, Bezemer DO, Zwinderman AH, de Wolf F, van Sighem AI.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Dutch GPs' adherence to national guidelines promoting HIV testing in populations at higher risk for HIV: bridging database information with clinical practice
Reukers DFM, Joore IKCW, van Bergen JEAM, Op de Coul ELM, Donker GA, van Sighem AI, Barth RE, van den Broek IV.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Estimating the size of the undiagnosed HIV population in the Netherlands by disease stage
Van Sighem AI, Nakagawa F, Bezemer DO, De Angelis D, Op de Coul ELM, Egger M, de Wolf F, Fraser C, Phillips AN.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Good SVR12 rates in boceprevir or telaprevir triple therapy in both treatment-naive and -experienced patients with HIV/ HCV coinfection in the Netherlands
Arends JE, van der Meer JTM, Posthouwer D, Kortmann W, van Assen S, Reiss P, van de Ende M, Brinkman K, Richter C, Hoepelman AIM, Smit C, van der Valk M, Schinkel J.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Health-related quality of life in perinatally HIV-infected children in the Netherlands
Ter Stege JA, Cohen S, Weijsenfeld AM, van der Plas A, Kuijpers TW, Reiss P, Haverman L, Pajkrt D.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Higher prevalence of hypertension in HIV-infected individuals partially explained by increased waist-hip ratio rather than BMI, other traditional risk factors or markers of systemic inflammation
Van Zoest RA, Wit FW, Kooij KW, van der Valk, M, Schouten J, Stolte IG, Kootstra NA, Wiersinga WJ, Prins M, van den Born BJH, Reiss P.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Patients' willingness to take separate component antiretroviral therapy regimens for HIV in the Netherlands
Engelhard E, Smit C, Vervoort S, Kroon F, Brinkman K, Nieuwkerk P, Reiss P, Geerlings S.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Poorer cognitive performance in perinatally HIV-infected children as compared to healthy socioeconomically matched controls
Cohen S, ter Stege JA, Geurtsen GJ, Scherpbier HJ, Kuijpers TW, Reiss P, Schmand B, Pajkrt D.

8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Prevalence and determinants of insufficient work ability in older HIV-positive and HIV-negative workers
Möller LM, Brands R, Sluiter JK, Schouten J, Wit FW, Reiss P, Prins M, Stolte IG.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

The aging HIV-infected population: quantifying the future challenges of HIV clinical care and exploring possible interventions
Smit M, Brinkman K, Geerlings SE, Smit C, Thyagarajan K, van Sighem AI, de Wolf F, Hallett TB.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Virological responses to lamivudine and emtricitabine in combination with tenofovir and efavirenz, nevirapine or boosted protease inhibitors in the nationwide ATHENA Cohort
Rokx C, Fibriani A, van de Vijver DAMC, Verbon A, Schutten M, Gras LAJ, Rijnders BJA, on behalf of the ATHENA National Observational Cohort, SHM.
8th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2014, Amsterdam, the Netherlands, 18 November 2014

Appendix 1: Composition of SHM

SHM board

Name	Position	Representing	Affiliation
Dr F.P. Kroon	Chair	*Nederlandse Vereniging HIV Behandelaren*	LUMC
Dr J.S.A. Fennema	Secretary	*GGD Nederland*	GGD Amsterdam
Dr P.W.D. Venhoeven	Treasurer		Prinses Maxima Centre for Paediatric Oncology
Prof. K. Stronks	Member	AMC-UvA	AMC-UvA
L.J.M. Elsenburg	Member	*HIV Vereniging Nederland*	HIV Focus Centrum
Dr R.J.M. Hopstaken	Member	*Nederlandse Federatie Universitair Medische Centra (NFU)*	AMC-UvA
P.E. van der Meer	Member	*Nederlandse Farmaceutische Zorggroep (NFZ)*	OLVG
J. Crasborn	Member	*Zorgvezekeraars Nederland*	Achmea

SHM advisory board

Name	Affiliation
Prof. D.R. Kuritzkes (chair)	Brigham and Women's Hospital, Section of Retroviral Therapeutics, Boston, MA, USA
Prof. R.M. Anderson	Imperial College, Faculty of Medicine, Dept. of Infectious Disease Epidemiology, London, UK
Prof. G. Chêne	Université Victor Segalen, Bordeaux, France
Prof. M. Egger	University of Bern, Zwitserland; University of Bristol, UK
Prof. dr. T.B.H. Geijtenbeek	AMC-UvA, Dept. Experimental Immunology, Amsterdam
P.J. Smit	HIV Vereniging Nederland, Amsterdam
Dr M. van der Valk	NVHB chair, AMC-UvA, Dept. Internal Medicine, Amsterdam

SHM working group

Members

Name	Affiliation
Dr M.E. van der Ende (Chair)	Erasmus MC, Dept. of Internal Medicine, Rotterdam
Prof. C.A.B. Boucher	Erasmus MC, Dept. of Internal Medicine, Rotterdam
Dr F.C.M. van Leth	KNCV Tuberculosis Foundation, The Hague; AIGHD Amsterdam
Dr W.M.C. Mulder	HIV Vereniging Nederland, Amsterdam

Reviewers

Name	Affiliation
Dr N.K.T. Back	AMC-UvA, Clinical Virology Laboratory, Amsterdam
Prof. K. Brinkman	OLVG, Dept. of Internal Medicine, Amsterdam
Dr D.M. Burger (Pharmacology subgroup)	Radboudumc, Dept. of Clinical Pharmacology, Nijmegen
Dr E.C.J. Claas	LUMC, Clinical Virology Laboratory, Leiden
Prof. G.J.J. van Doornum	Erasmus MC, Dept. of Virology, Rotterdam (Emeritus)
Dr S.P.M. Geelen	UMC Utrecht-WKZ, Dept. of Paediatrics, Utrecht
Prof. A.I.M. Hoepelman	UMC Utrecht, Dept. of Virology, Utrecht
Dr S. Jurriaans	AMC-UvA, Clinical Virology Laboratory, Amsterdam
Dr P.P. Koopmans	Radboudumc, Dept. of Internal Medicine, Nijmegen
Prof. A.C.M. Kroes	LUMC, Clinical Virology Laboratory, Leiden
Prof. T.W. Kuijpers	AMC-UvA, Dept. of Paediatrics, Amsterdam
Dr W.J.G. Melchers	Radboudumc, Dept. of Medical Microbiology, Nijmegen
Prof. J.M. Prins	AMC-UvA, Dept. of Internal Medicine, Amsterdam
Prof. P.H.M. Savelkoul	MUMC+, Dept. of Internal Medicine, Maastricht
Dr R. Schuurman	UMC Utrecht, Dept. of Virology, Utrecht
Dr H.G. Sprenger	UMCG, Dept. of Internal Medicine, Groningen
Dr A.M.J. Wensing	UMC Utrecht, Dept. of Virology, Utrecht

Hepatitis working group

Name	Affiliation
Dr C. Richter (Chair)	Rijnstate, Dept. of Internal Medicine, Arnhem
Dr C. Smit	Stichting HIV Monitoring, Amsterdam
Prof. K. Brinkman	OLVG, Dept. of Internal Medicine, Amsterdam
Prof. A.I.M. Hoepelman	UMC Utrecht, Dept. of Virology, Utrecht
Dr J. Arends	UMC Utrecht, Dept. of Internal Medicine, Utrecht
Dr M.E. van der Ende	Erasmus MC, Dept. of Internal Medicine, Rotterdam
Dr T.E.M.S. de Vries-Sluys	Erasmus MC, Dept. of Internal Medicine, Rotterdam
Dr M. van der Valk	AMC-UvA, Dept. of Internal Medicine, Amsterdam
Dr J. van der Meer	AMC-UvA, Dept. of Internal Medicine, Amsterdam
Dr J. Schinkel	AMC-UvA, Clinical Virology Laboratory, Amsterdam
Dr E.F. Schippers	HagaZiekenhuis, Dept. of Internal Medicine, Den Haag
Dr M. Schutten	Erasmus MC, Dept. of Clinical Virology, Rotterdam

SHM personnel

Position	Name
Director	Prof. P. Reiss MD
Analysis	
Senior researchers	D.O. Bezemer PhD
	L.A.J. Gras MSc
	A.I. van Sighem PhD
	C. Smit PhD
PhD candidates	E. Engelhard MSc (external)
	R. van den Hengel MSc
Patient Data & Quality Control	
Manager	S. Zaheri MSc
Registration	M.M.B. Tuk-Stuster
	R.F. Beard (until 1 June 2014)
Data collectors coordinator	L.G.M. de Groot-Berndsen
Data collectors	M. van den Akker
	Y.M. Bakker
	M. Broekhoven-van Kruijne
	E.J. Claessen
	R. Henstra-Regtop
	E.I. Kruijne
	C.R.E. Lodewijk
	R. Meijering MSc
	L. Munjishvili
	B.M. Peeck
	M.J.C. Rademaker MSc
	C.M.J. Ree
	Y.M.C. Ruijs-Tiggelman
	T. Rutkens
	M.J.C. Schoorl MSc
	E.M. Tuijn-de Bruin
	D.P. Veenenberg-Benschop
	T.J. Woudstra
	B. de Zeeuw MSc (until 31 March 2014)
	N.N. Hamid (until 31 July 2014)

Data management coordinator	M.M.J. Hillebregt MSc
Data monitors	M.M.Z. Berkhout MSc R. van den Boogaard MSc S. Grivell MSc P.T. Hoekstra-Mevius MSc A.M. Jansen MSc V. Kimmel MSc A. de Lang PhD Y.M. Tong MSc N.J. Wijnstok MSc (until 31 August 2014) B. Lascaris MSc (until 31 December 2014)
Assistant data monitors	D. Bergsma MSc A.S. de Jong MSc M.S. Raethke MSc
Office	
Human resources, office & finance manager	D. de Boer
Office and secretariat	I. Bartels-Koster M.M.T. Koenen
Personnel & administration	I.H.M. de Boer H.J.M. van Noort MSc
Communications	
	C.J. Ester PhD M.J. Sormani M.R. van der Linde (until 1 November 2014)

Appendix 2: Terminology & definitions

Acute infection
Any infection that begins suddenly, with intense or severe symptoms, is called acute (or primary). If the illness lasts more than a couple of weeks, it is called chronic.

Adherence
Adherence measures how faithfully a person takes all antiretroviral medications at the right time. Poor adherence is one of the main reasons antiretroviral combinations fail.

AIDS
Acquired Immunodeficiency Syndrome. A disease caused by a retrovirus, HIV (human immunodeficiency virus), and characterized by failure of the immune system to protect against infections and certain cancers.

Antibody
An immune system protein formed in response to invading disease agents such as viruses, fungi, bacteria, and parasites. Usually antibodies defend the body against invading disease agents, however, the HIV antibody does not give such protection.

Antigen
An invading substance that may be the target of antibodies.

Antiretroviral treatment (ART)
A treatment that may prevent HIV from further damaging the immune system by blocking or hampering the reproduction of the HIV virus.

Antiviral
A substance that stops or suppresses the reproduction of a virus.

ATHENA
AIDS Therapy Evaluation in the Netherlands project (ATHENA). Stichting HIV Monitoring was founded in 2001 as a result of the successful ATHENA project.

Baseline
An initial measurement used as the basis for future comparison. For people infected with HIV, baseline testing includes CD4 count, viral load (HIV RNA), and resistance testing. Baseline test results are used to guide HIV treatment choices and monitor effectiveness of antiretroviral therapy (ART).

cART
Combination antiretroviral treatment.

CD4 cell
CD4+ T-lymphocyte, or T4-cell or T-helper cell. A white blood cell that plays a vital role within the immune system and can be infected by the HIV virus. In the course of the HIV infection the number of CD4 cells may drop from normal levels (+ 500 per mm^3) to dangerously low levels (fewer than 200 CD4 cells per mm^3 of blood).

CDC
US Centers for Disease Control and Prevention.

CIb
Centre for Infectious Disease Control Netherlands, National Institute for Public Health and Environment (*www.rivm.nl/cib*).

CLB
Central Laboratory for the Blood Transfusion Service (*Centraal Laboratorium van Bloedtransfusiedienst*).

Co-infection
When a person has two or more infections at the same time. For example, a person infected with HIV may be co-infected with hepatitis C (HCV) or tuberculosis (TB) or both.

Comorbidity
When a person has two or more diseases or conditions at the same time. For example, a person with high blood pressure may also have heart disease.

Cross-resistance
After a person becomes resistant to one particular drug, they may develop resistance to similar drugs, without ever having been exposed to these drugs. This is known as cross-resistance.

DNA
Deoxyribonucleic acid. A complex protein that carries genetic information. HIV can insert itself into the DNA molecules inside human cells and establish dormant infection.

Epidemiology
The study of the distribution, causes, and clinical characteristics of disease or health status in a population.

Genotype
The genotype is the underlying genetic makeup of an organism.

GGD
Dutch public health service (*www.ggd.nl*).

HAART
Highly Active Antiretroviral Therapy, also known as combination antiretroviral therapy (cART).

Half-life
The time it takes a drug to lose half its original concentration or activity after being introduced into the body. Drug half-life is considered when determining drug dosing.

Hepatic
Pertaining to the liver.

Hepatitis B virus (HBV)
A viral infection that affects the liver and is transmitted only through blood-to-blood and sexual contact.

Hepatitis C virus (HCV)
A viral infection that is transmitted primarily by blood and blood products, as in blood transfusions or intravenous drug use, and sometimes through sexual contact.

HIV
Human Immunodeficiency Virus; the virus that causes the Acquired Immunodeficiency Syndrome (AIDS). HIV attacks and destroys the immune system by entering and destroying the cells that control and support the immune response system.

HIV Type 1 (HIV-1)
The HIV type responsible for the majority of HIV infections worldwide.

HIV Type 2 (HIV-2)
A virus very similar to HIV-1 that has been found to cause immune suppression. HIV-2 infections are found primarily in Africa.

HIV Vereniging Nederland
Dutch HIV patients' association (*http://www.hivnet.org*).

Immunologic failure
A type of HIV treatment failure. There is no consensus on the definition of immunologic failure. However, some experts define immunologic failure as the failure to achieve and maintain adequate CD4 counts despite viral suppression.

Interferon
Interferons are naturally-occurring proteins (cytokines) produced by immune cells in response to an antigen, usually a virus. Although they don't directly kill viral cells, they boost the immune response by signalling neighbouring cells into action and inhibiting the growth of malignant cells. There are three types of interferons: alpha, beta, and gamma. Laboratory-made interferons are used to treat certain cancers and opportunistic infections. Addition of polyethylene glycol to interferons prolongs the half-life of interferon. Pegylated interferon alpha is used to treat chronic hepatitis C infection.

Mono-infection
When a person has only one infection.

Mortality
Mortality rate is a measure of the frequency of occurrence of death among a defined population during a specified time period.

MSM
Men who have sex with men.

Nederlandse Federatie Universitair Medische Centra (NFU)
Netherlands Federation of University Medical Centres.

Non-AIDS events
Diseases and clinical events that are not related to AIDS (i.e. that are not listed as being associated with AIDS by the Centers for Disease Control and Prevention) and include conditions such as malignancies, end-stage renal disease, liver failure, pancreatitis, cardiovascular disease.

Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)
Antiretroviral (ARV) HIV drug class. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) bind to and block HIV reverse transcriptase (an HIV enzyme). HIV uses reverse transcriptase to convert its RNA into DNA (reverse transcription). Blocking reverse transcriptase and reverse transcription prevents HIV from replicating.

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Nucleotide
A building block of nucleic acids. DNA and RNA are nucleic acids.

Nucleotide Reverse Transcriptase Inhibitor
A type of antiretroviral (ARV) HIV drug. Nucleotide reverse transcriptase inhibitors interfere with the HIV life cycle in the same way as NRTIs. Both block reverse transcription and therefore nucleotide reverse transcriptase inhibitors are included in the NRTI drug class.

NVHB
Dutch Association of HIV-Treating Physicians (*Nederlandse Vereniging van HIV Behandelaren*)

Person year
A measure of time used in medical studies. A single person year is 1 year lived by 1 person.

Perinatal transmission
Perinatal transmission of HIV refers to the passage of HIV from an infected mother to her child during pregnancy, labour and delivery, or breastfeeding (through breast milk).

Protease
A type of enzyme that breaks down proteins into smaller proteins or smaller protein units, such as peptides or amino acids. HIV protease cuts up large precursor proteins into smaller proteins. These smaller proteins combine with HIV's genetic material to form a new HIV virus. Protease inhibitors (PIs) prevent HIV from replicating by blocking protease.

Protease Inhibitor (PI)
Antiretroviral (ARV) HIV drug class. Protease inhibitors (PIs) block protease (an HIV enzyme). This prevents new HIV from forming.

Retrovirus
A class of viruses which includes HIV. Retroviruses are so named because they carry their genetic information in RNA rather than DNA, and the RNA information must be translated "backwards" into DNA.

Reverse transcriptase
After infecting a cell, HIV uses an enzyme called reverse transcriptase to convert its RNA into DNA and then replicates itself using the cell's machinery.

Ribavirin
A type of nucleoside inhibitor prescribed for the treatment of hepatitis C in combination with an interferon. Ribavirin stops the hepatitis C virus from spreading by interfering with the synthesis of viral RNA.

RIVM
Dutch National Institute for Public Health and the Environment (*www.rivm.nl*).

Seroconversion
The change from an absence of HIV antibodies in the blood to the presence of those antibodies.

SHM
Stichting HIV Monitoring (the Dutch HIV monitoring foundation, *www.hiv-monitoring.nl*).

Sustained virologic response or sustained viral suppression
The continuous, long-term suppression of a person's viral load (HIV RNA), generally to undetectable levels, as the result of treatment with antiretroviral (ARV) drugs.

Tolerability
The extent to which a drug's side effects can be tolerated by the patient.

Viraemia
The presence of a virus in the blood.

Virologic failure
A type of HIV treatment failure. Virologic failure occurs when antiretroviral therapy (ART) fails to suppress and sustain a person's viral load to less than 200 copies/mL. Factors that can contribute to virologic failure include drug resistance, drug toxicity, and poor treatment adherence.

Viral load
The number of HIV particles in a millilitre of blood or another body fluid, such as semen or cerebrospinal fluid.

Viral suppression or virologic control
When antiretroviral therapy (ART) reduces a person's viral load (HIV RNA) to an undetectable level. Viral suppression does not mean a person is cured; HIV still remains in the body.

VWS
Dutch Ministry of Health, Welfare and Sport (*www.rijksoverheid.nl*).

Some of the above definitions were taken from www.aidsinfo.nih.gov/