HIV Monitoring

Annual report 2017

Annual report 2017, approved by the Stichting HIV Monitoring Governing Board on 23 May 2018

We would like to thank Inge Bartels, Daniela Bezemer, Ward van Bilsen, Sonia Boender, Arianne van der Doelen, Catriona Ester, Mireille Koenen, Amy Matser, Henk van Noort, Maria Prins, Ard van Sighem, Colette Smit, Melanie Sormani, Brenda Tuk, Yunka de Waart, Ferdinand Wit and Sima Zaheri for their contributions.

Requests for copies: The Annual Report is only published online and can be downloaded from our website: www.hiv-monitoring.nl. For further information please contact the Communications Department by email: shm-communicatie@amc.uva.nl or by telephone: +31 20 5664172.

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Foreword

In 2017, Stichting HIV Monitoring (SHM) continued its important task of monitoring the HIV epidemic in the Netherlands. Our solid and well-established collaboration with the 26 appointed HIV treatment centres in the Netherlands enables us to collect and analyse data on relevant health outcomes, including non-communicable co-morbidities and viral hepatitis co-infections, from people living with HIV in clinical care. Through these analyses, we are able to provide a truly representative and nationwide picture of the outcome of care for those living with HIV in the Netherlands. The outcomes of these analyses are described in detail in the 2017 HIV Monitoring Report, the key findings of which are included in this annual report.

As in previous years, individual treatment centres were provided with regular updates of their own centre-specific data throughout 2017. These centre-specific reports enable the centres to critically review and improve their performance where necessary and are also required for formal certification of the centres. In this way, we make a significant contribution to the quality of care provided to HIV-positive individuals in the Netherlands.

Scientific collaboration

SHM continues to be closely involved in various European and other more global HIV observational cohort collaborations, contributing in terms of both data and knowledge. It is only through such collaborations that the scientific community can address questions that cannot be answered by individual cohorts alone. Such collaborations are therefore vitally important in ensuring optimal care for people living with HIV and their findings regularly lead to modifications in HIV treatment guidelines.

Innovation

2017 was a year of innovation for Stichting HIV Monitoring. Across the organisation, various teams have worked relentlessly to develop a new data entry system tailored to our specific requirements. The new system, called DataCapTree, went live at the beginning of 2018 as planned, and should make the data collection process more efficient and future-proof.

Foreword

Another move towards improving data collection efficiency is the ongoing expansion of LabLink, the direct electronic link between hospital laboratories and SHM's database. In 2017, a LabLink connection was established at two more hospital sites, meaning we now receive laboratory data through LabLink from almost 70% of registered people with HIV. We look forward to further implementation of LabLink in the remaining hospitals in 2018.

Privacy

SHM is committed to safeguarding privacy and data security. In the run-up to the EU General Data Protection Regulation (EU-GDPR) that will come into force in May 2018, a great deal of 2017 was spent reviewing processes and ensuring we are ready for the new regulation. With the appointment of a data privacy officer and clear procedures now in place to safeguard data privacy, I am confident that SHM will enter 2018 well-prepared for the EU-GDPR.

Word of thanks

The important work carried out by SHM would not be possible without the tireless efforts of numerous people from different fields. I would therefore like to take this opportunity to thank all these individuals, in particular the SHM staff, the HIV treatment teams, the members of SHM's governing board, advisory board and working groups, and all those involved in the ATHENA cohort. Finally, I would like to extend my sincerest thanks and appreciation to all those living with HIV who are in clinical care for allowing us to capture their data, store blood samples, and learn how we may continue to improve their care.

Prof. Peter Reiss, MD, PhD
Director
Amsterdam, 23 May 2018

Message from the Governing Board Chair

As the new chair of Stichting HIV Monitoring's governing board, I am very excited to have been given the opportunity to be closely involved in an organisation that makes such an important contribution to HIV care in the Netherlands. It is therefore my privilege to present this year's annual report to you.

Stichting HIV Monitoring's work throughout 2017 continued to provide important insight into trends and changes in the HIV epidemic in the Netherlands. Moreover, by providing treatment centres with centre-specific reports, SHM facilitates the certification of these HIV treatment centres. As such, SHM helps to maintain and further improve the level of medical care provided to people living with HIV in the Netherlands.

SHM also contributes to a wider understanding of the HIV epidemic through ongoing involvement in national and international scientific research collaborations. The outcomes of such collaborative research can subsequently be used as the basis for treatment and healthcare policy guidelines.

2017 has been an important year for Stichting HIV Monitoring as the organisation continued to pursue its ambitious digitisation programme. One of the highlights of this programme was the development of a new, future-proof data entry system that went live at the beginning of 2018. This new system will make data collection more efficient and can also be adapted to future digital developments within treatment centres. In my capacity as chair of SHM's board, I am looking forward to accompanying SHM on the next stage of this digitisation journey.

SHM's invaluable work would not be possible without the efforts and contributions of many different people and I would therefore like to thank all the staff at SHM, the HIV healthcare professionals and, of course, the people living with HIV who are in clinical care. I would also like to express my appreciation to my fellow board members for their work on behalf of SHM. Finally, I would like to thank the outgoing chair, Dr Frank Kroon, for his commitment to leading the governing board during the past eight years.

Dr Marc van der Valk
Chair of the governing board
Amsterdam, 23 May 2018

In this year's report

Stichting HIV Monitoring in 2017

SHM in 2017

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About us

STICHTING HIV MONITORING

Stichting HIV Monitoring (SHM), the Dutch HIV monitoring foundation, was founded in 2001 and appointed by the Dutch minister of Health, Welfare and Sport as the executive organisation for the registration and monitoring of HIV-positive individuals in the Netherlands.

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-positive man, woman and child. In this way SHM is able to comprehensively map the HIV epidemic and HIV treatment outcomes in the Netherlands.

Since its founding, 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 individuals. 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 the designated HIV treatment centres in the Netherlands by either treatment centre staff or SHM data collectors in cooperation with the responsible HIV physician. Patient data are collected and entered into the registration database in a pseudonymised form for storage and analysis.

ABOUT US STICHTING HIV MONITORING

OUR MISSION

Our mission is to further the knowledge and understanding of all relevant aspects of HIV infection, including comorbidities and co-infections, such as viral hepatitis, in HIV-positive persons in care in the Netherlands.

Objectives

- To monitor and report trends in all aspects of HIV infection by collecting high-quality, nationwide data from HIV-positive persons in care.
- To inform all relevant stakeholders, including healthcare providers, government, researchers, and the community of people living with HIV, about national trends in all aspects of HIV infection, including comorbidities and co-infections (such as viral hepatitis), in HIV-positive persons in care in the Netherlands.
- To develop models that accurately predict future trends in the overall HIV epidemic and in the clinical course of HIV-positive persons in care in the Netherlands.
- To monitor and report on the quality of HIV treatment and care in the Netherlands, thereby contributing to the national HIV quality of care standards and formal certification of HIV treatment centres in the Netherlands.
- To contribute to national and international collaborative scientific research.
- To act as a national knowledge centre for information on trends in all relevant aspects of HIV infection and in the clinical course of HIV-positive persons in care in the Netherlands.

ABOUT US STICHTING HIV MONITORING

HIV TREATMENT CENTRES IN 2017

The monitoring of HIV-positive adults is a collaborative effort involving SHM and a total of 26 health institutes that are recognised by the Dutch minister of Health, Welfare and Sport as HIV treatment centres or subcentres. In addition, HIV-positive children and adolescents are monitored in four institutes that are recognised as paediatric HIV treatment centres.

SHM has contracts with each centre or subcentre for the collection of demographic, epidemiological, clinical, virological, immunological, and pharmacological data for HIV-positive individuals who are followed in one of these hospitals.

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-positive persons seen by HIV-treating physicians at the St. Elisabeth Hospital in Curaçao (SEHOS).

26 HIV treatment centres in the Netherlands

4 paediatric HIV treatment centres

ABOUT US STICHTING HIV MONITORING

HIV treatment centres

1	Noordwest Ziekenhuisgroep	Alkmaar
2	Flevoziekenhuis	Almere
3	Academic Medical Center of the University of Amsterdam (AMC-UvA)	Amsterdam
4	DC Klinieken Lairesse - Hiv Focus Centrum	Amsterdam
5	OLVG	Amsterdam
6	MC Slotervaart	Amsterdam
7	Medisch Centrum Jan van Goyen (MC Jan van Goyen)	Amsterdam
8	VUmc	Amsterdam
9	Rijnstate	Arnhem
10	HagaZiekenhuis (Leyweg site)	Den Haag
11	HMC (Haaglanden Medisch Centrum)	Den Haag
12	Catharina Ziekenhuis	Eindhoven
13	Medisch Spectrum Twente (MST)	Enschede
14	Admiraal De Ruyter Ziekenhuis	Goes
15	Universitair Medisch Centrum Groningen (UMCG)	Groningen
16	Spaarne Gasthuis	Haarlem
17	Medisch Centrum Leeuwarden (MCL)	Leeuwarden
18	Leids Universitair Medisch Centrum (LUMC)	Leiden
19	MC Zuiderzee	Lelystad
20	Maastricht UMC+ (MUMC+)	Maastricht
21	Radboudumc	Nijmegen
22	Erasmus MC	Rotterdam
23	Maasstad Ziekenhuis	Rotterdam
24	ETZ (Elisabeth-TweeSteden Ziekenhuis)	Tilburg
25	Universitair Medisch Centrum Utrecht (UMC Utrecht)	Utrecht
26	Isala	Zwolle

[Click on the hospital name to visit the hospital's website]

Centres for the treatment and monitoring of paediatric HIV:

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

ABOUT US STICHTING HIV MONITORING

OUR ORGANISATION

Governance and management

Governing board

Our governing board members represent academic and general hospitals, health insurers, the Dutch HIV Association (Hiv Vereniging), the Dutch Association of HIV-Treating Physicians (*Nederlandse Vereniging van HIV Behandelaren*, NVHB), the national organisation of Public Health Services (GGD GHO*R Nederland*), and the Academic Medical Center of the University of Amsterdam (AMC-UvA). The governing board convenes twice a year and its duties include approving SHM's budget and the content of the annual report; board members receive no remuneration for this work.

Governing board members in 2017

Name	Position	Representing	Affiliation
Dr M. van der Valk (as of November 2017)	Chair	Dutch Association of HIV-Treating Physicians (NVHB)	AMC-UvA, Amsterdam
Dr F.P. Kroon (until November 2017)	Chair	NVHB	LUMC, Leiden
Dr Y.T.H.P. van Duijnhoven	Secretary	GGD GHOR Nederland	GGD Amsterdam
P.W.D. Venhoeven	Treasurer		Alexander Monro Ziekenhuis, Bilthoven
P. Brokx	Member	Hiv Vereniging	Hiv Vereniging, Amsterdam
J. Crasborn	Member	Zorgverzekeraars Nederland	Achmea, Zeist
Prof. K. Jager (as of November 2017)	Member	AMC-UvA	AMC-UvA, Amsterdam
P.E. van der Meer	Member	Nederlandse Vereniging van Ziekenhuizen (NVZ)	Albert Schweizer Ziekenhuis, Dordrecht
Prof. K. Stronks (until November 2017)	Member	AMC-UvA	AMC-UvA, Amsterdam
Prof. M.M.E. Schneider	Member	Nederlandse Federatie Universitair Medische Centra (NFU)	UMC Utrecht, Utrecht

ABOUT US STICHTING HIV MONITORING

Advisory board

A scientific advisory board has been established by the governing board to provide governing board members and SHM's director with strategic advice regarding the registration and monitoring of data from HIV-positive individuals in care in the Netherlands, as well as the use of these data in research. The advisory board comprises national and international experts from the field and a representative of the *Hiv Vereniging*. The advisory board convenes once a year and receives no remuneration for this work.

Advisory board members in 2017

Name	Affiliation
Prof. D.R. Kuritzkes (Chair)	Brigham and Women's Hospital, MA, USA
Dr J. Arends (as of November 2017)	UMC Utrecht, Utrecht
Prof. M. Egger	University of Bern, Switzerland
Prof. T.B.H. Geijtenbeek	AMC-UvA, Amsterdam
Prof. B. Ledergerber	University Hospital Zurich, Switzerland
Prof. C. Sabin	University College, London, UK
P.J. Smit	Hiv Vereniging, Amsterdam
Dr M. van der Valk (until November 2017)	AMC-UvA, Amsterdam

ABOUT US STICHTING HIV MONITORING

Working groups

SHM has two working groups that advise the director on executive matters regarding research proposals involving data stored in our national HIV database:

- The SHM working group reviews general scientific research proposals.
- The hepatitis working group works together with the NVHB and assesses scientific research proposals that relate specifically to HIV/hepatitis co-infection.

Working group members in 2017

Name	Affiliation
Dr M.E. van der Ende (Chair)	Erasmus MC, Rotterdam
Prof. C.A.B. Boucher	Erasmus MC, Rotterdam
Dr F.C.M. van Leth	KNCV Tuberculosis Foundation, The Hague; AIGHD Amsterdam

Working group reviewers in 2017

Name	Affiliation
Dr N.K.T. Back	AMC-UvA, Amsterdam
Prof. K. Brinkman	OLVG, Amsterdam
Dr D.M. Burger	Radboudumc, Nijmegen
Dr E.C.J. Claas	LUMC, Leiden
Prof. Emer. G.J.J. Doornum	Erasmus MC, Rotterdam
Dr S.P.M. Geelen	UMC Utrecht-WKZ, Utrecht
Prof. A.I.M. Hoepelman	UMC Utrecht, Utrecht
Dr S. Jurriaans	AMC-UvA, Amsterdam
Prof. T.W. Kuijpers	AMC-UvA, Amsterdam
Dr W.J.G. Melchers	Radboudumc, Nijmegen
Prof. J.M. Prins	AMC-UvA, Amsterdam
Prof. P.H.M. Savelkoul	MUMC+, Maastricht
Dr R. Schuurman	UMC Utrecht, Utrecht
Dr H.G. Sprenger	UMCG, Groningen
Dr A.M.J. Wensing	UMC Utrecht, Utrecht

Hepatitis working group

Name	Affiliation
Dr J. Arends (Chair)	UMC Utrecht, Utrecht
Prof. K. Brinkman	OLVG, Amsterdam
Dr M.E. van der Ende (until May 2017)	Erasmus MC, Rotterdam
Prof. A.I.M. Hoepelman	UMC Utrecht, Utrecht
Dr. B. Rijnders (as of May 2017)	Erasmus MC, Rotterdam
Dr. C. Richter	Rijnstate, Arnhem
Dr J. Schinkel	AMC-UvA, Amsterdam
Dr E.F. Schippers	HagaZiekenhuis, Den Haag
Dr C. Smit	SHM, Amsterdam
Dr J. van der Meer	AMC-UvA, Amsterdam
Dr M. van der Valk	AMC-UvA, Amsterdam
Dr T.E.M.S. de Vries-Sluys	Erasmus MC, Rotterdam
Dr A. Vollaard	LUMC, Leiden

ABOUT US STICHTING HIV MONITORING

Management team

Our management team (MT) consists of the director (chair), the deputy director, the communications manager, and a senior researcher representing the Data Analysis, Reporting & Research Unit. The MT establishes SHM's strategic objectives by common agreement and is responsible for the day-to-day implementation of this strategy. The MT convenes once a week and is advised by the organisation's financial controller and human resources (HR) advisor.

Management team members

Name	Position
P. Reiss	Director
S. Zaheri	Deputy director
A.I. van Sighem	Senior researcher
C.J. Ester	Communications manager

Director

SHM's director is appointed by, and reports to, the governing board. He is responsible for day-to-day operations and is primarily responsible for representing the organisation externally.

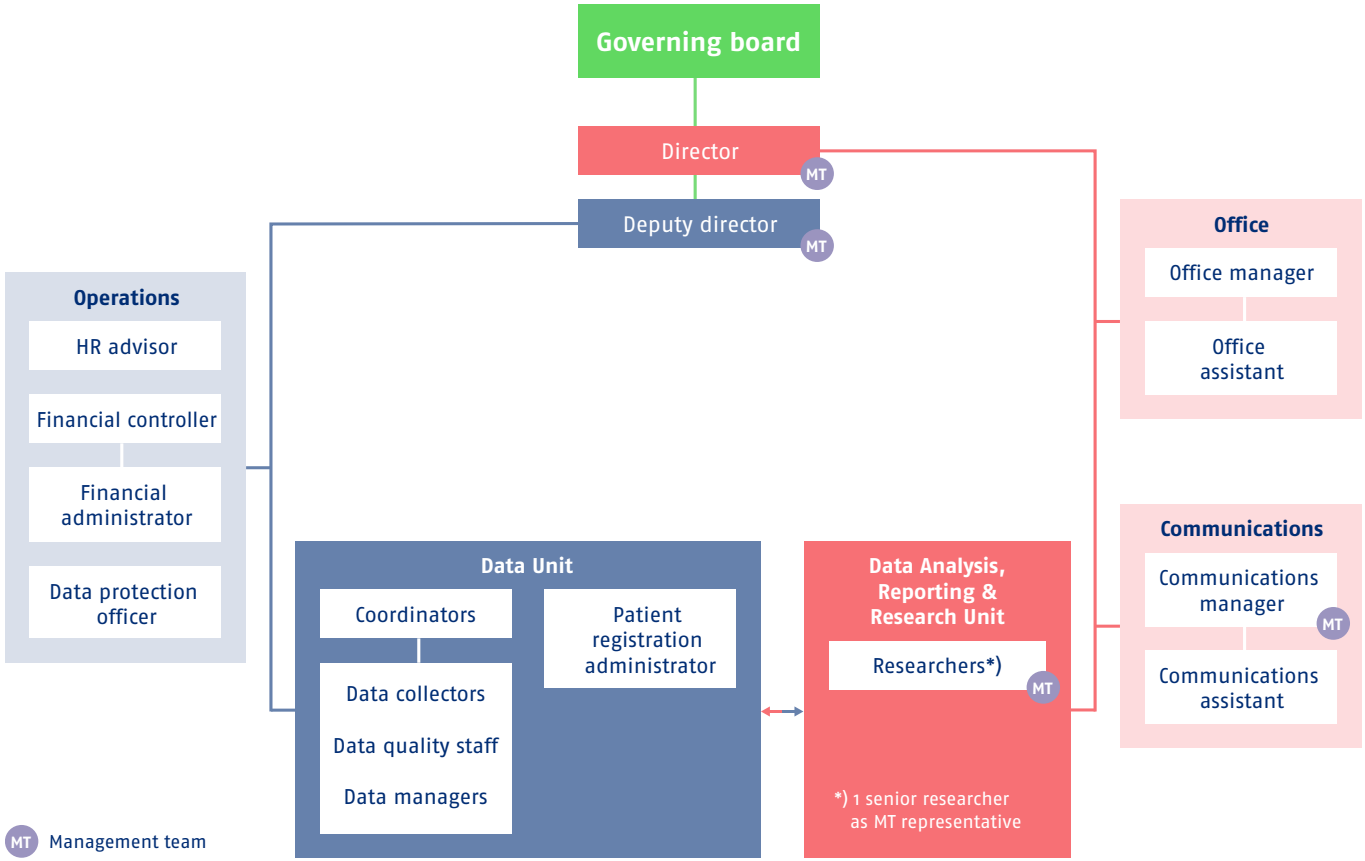
Deputy director

As of 1 June 2017, the manager of the Data Unit was appointed as deputy director. Acting on behalf of the director, the deputy director oversees:

- policy implementation within the Data Unit, HR and finance,
- company and data security,
- various essential processes, such as accommodation and office automation.

ABOUT US STICHTING HIV MONITORING

Stichting HIV Monitoring organisational chart.



ABOUT US STICHTING HIV MONITORING

Business units and support

We have two main business units that carry out our primary activities:

- Data Unit,
- Data Analysis, Reporting & Research Unit.

Data Unit

The Data Unit is led by the deputy director and comprises the following three departments: Patient Registration & Data Collection, Quality Control, Helpdesk & Protocol Management, and Data Management.

Within the Data Unit, the following five core activities are carried out:

- *Patient registration*: This involves the registration and de-registration of HIV-positive individuals. This administration system is used to assign a pseudonymised code to each registered individual.
- *Data collection and data entry*: This involves the collection of data from all individuals living with HIV who are being followed in one of the HIV treatment centres in the Netherlands.
- *Quality control*: This activity is carried out by data quality staff (data monitors) to safeguard the validity and reliability of the collected data entered into SHM's database.
- *Helpdesk and protocol management*: This involves keeping protocols up to date, and drafting regular helpdesk products such as mailings, protocol updates and FAQ sheets.
- *Data management*: This core activity is carried out by data managers and involves checking, cleaning, standardising, combining and documenting data. Some of these tasks are outsourced to the AMC's Clinical Research Unit (CRU) of the Clinical Epidemiology and Biostatistics Department and the AMC's general IT service (ADICT).

Data Analysis, Reporting & Research Unit

The Data Analysis, Reporting & Research Unit is led by our director and is staffed by researchers in the field of epidemiology, HIV medicine, statistics, mathematical modelling of HIV and modelling of transmission networks. Together, these researchers implement the HIV monitoring programme, the results of which are presented in our annual Monitoring Report. The researchers also contribute to publications involving analyses of SHM's data in peer-reviewed national and international scientific journals. In addition, the Data Analysis, Reporting & Research Unit supports and collaborates with researchers in the national HIV treatment centres.

The unit also collaborates with international research groups involved in comparable observational cohorts in the field of HIV epidemiology and treatment. Our researchers contribute to these collaborations both by setting up and carrying out scientific research.

ABOUT US STICHTING HIV MONITORING

Support

The primary activities of our management team are supported by the communications, HR, office and finance staff. The Communications Department, led by the communications manager, actively disseminates information about the HIV epidemic in the Netherlands and provides information about our activities through a wide variety of communication channels. The communications manager is also responsible for the annual reporting process, in close collaboration with our director and researchers. The communications manager and office manager report to the director, while the finance and HR staff report to the deputy director.

ABOUT US STICHTING HIV MONITORING

Staffing in 2017

In total, we had an average staffing level in 2017 of 37.5 full-time equivalents (FTEs). In addition, we cover the personnel costs for a total of 7.87 FTEs for data collectors and data entry staff who are employed by the HIV treatment centres rather than SHM.

SHM Personnel

Director
Prof. P. Reiss MD, PhD

Deputy director
S. Zaheri MSc

Data Analysis, Reporting & Research Unit

Researchers
D.O. Bezemer PhD
T.S. Boender PhD
A.I. van Sighem PhD
C. Smit PhD
F.W.N.M. Wit MD, PhD

Data Unit

Data management
M.M.J. Hillebregt MSc (coordinator)
A.S. de Jong MSc
T.J. Woudstra

Quality control, helpdesk & protocol management
S. Grivell MSc
(protocol & helpdesk coordinator)
A.M. Jansen MSc
(data quality staff coordinator)

Data quality staff
D. Bergsma MSc
R. Meijering MSc
M.S. Raethke MSc
T. Rutkens

Data protection officer
M.M.B. Tuk-Stuster

Patient registration & data collection
L.G.M. de Groot-Berndsen (coordinator)
M.M.B. Tuk-Stuster
(patient registration administrator)

Data collectors
M. van den Akker
Y.M. Bakker
M. Bezemer
E.J. Claessen (until 16 May 2017)
A. El Berkaoui
J. Geerlinks
R. Henstra-Regtop
J. Koops MSc
E.I. Kruijne
C.R.E. Lodewijk
E.G.A. Lucas
R. van der Meer MA
L. Munjishvili MA
F. Paling MSc
B.M. Peeck MSc
C.M.J. Ree
Y.M.C. Ruijs-Tiggelman
L. van de Sande MA
(until 28 February 2017)
M.J.C. Schoorl MSc
A.G. Timmerman MSc
(until 30 September 2017)
E.M. Tuijn-de Bruin
D.P. Veenenberg-Benschop
S. van der Vliet
S.J. Wisse MSc
E.C.M. Witte

Communications

C.J. Ester PhD
(communications manager)
M.J. Sormani
(communications assistant)

Human resources, finance & office

I. Bartels (HR advisor)
A. J.P. van der Doelen
(financial controller)
H.J.M. van Noort MSc
(financial administrator)
M.M.T. Koenen (office manager)
Y de Waart
(office, HR & finance assistant)

Data collection & quality control

A YEAR OF INNOVATION

Our Data Unit carries out five main activities:

- patient registration,
- data collection and data entry,
- quality control,
- helpdesk and protocol management,
- data management and reporting.

In addition to the above-mentioned core activities (discussed later in this chapter), the Data Unit is responsible for various projects designed to further improve both data quality and process efficiency. In 2017, priority was given to the following projects:

- **IT project 'LISA':** This project involves the replacement and concomitant improvement of our data entry system. The aims of this project are:
  - to minimise manual input,
  - to standardise and optimise data collection, data quality management and data processing,
  - to improve the infrastructure for information technology (IT).
- **LabLink:** The aim of this project is to expand hospital use of the automated link that allows laboratory data from hospital computer systems to be entered directly into the SHM database in a pseudonymised form.
- **Centralisation of data collection:** This project strives, where possible, to further centralise the collection of data by specially-trained staff employed by SHM.
- **Knowledge management:** This project aims to train and coach data collectors, data quality staff (data monitors) and data managers.
- **ISO 9001 and ISO 27001 certification:** This project was set up to implement the International Organization for Standardization (ISO) standards for quality and information security within SHM.

PROGRESS IN 2017

IT project 'LISA'

As described in our annual report for 2016, work has been underway to find a replacement for the Oracle Clinical data entry system. Following an intensive period of preparation that involved drawing up the statement of requirements, and carrying out market research, reference visits, cost negotiations, and legal checks, the proposal to develop and implement a LogicNets-based system was approved by the governing board in 2016.

The project, which involves a collaboration between LogicNets, ICT automatisering, SHM and the AMC's general ICT service (ADICT), was named 'LISA' and officially started on 24 May 2016.

DATA COLLECTION & QUALITY CONTROL A YEAR OF INNOVATION

The project fits well within our innovation programme initiated in 2013. Moreover, it offers new opportunities for ensuring our data collection process is even more efficient and ready for the future, particularly in view of IT developments surrounding electronic medical records in the HIV treatment centres.

The following aspects of the new system will contribute towards improving efficiency:

1. Protocol management: Data collection protocols will be integrated within the system, thereby reducing the maintenance and administrative workload associated with managing the protocols.
2. Manual data collection: The new data entry system is a decision-support system and allows information to be structured in protocols that have been programmed within the system. This should reduce the time spent on data collection.
3. Quality control: With the new system, we expect that certain manual quality checks will become unnecessary, since it will be possible to integrate these quality criteria into the primary data collection phase. In addition, the quality of the data collection will improve even further because data validation (currently carried out as random manual checks) will now become a fixed component of the data collection process for the entire patient population.
4. Data warehouse: As part of the LISA project, a new and more modern structure will be developed for the data warehouse to allow data to be imported from external sources. This approach enables us to prepare for future developments, for example importing more data directly from clinical data warehouses in HIV treatment centres.
5. Functional management: The new system should allow independent functional management by a number of our own staff. As a result, we will become less dependent on third-party support (currently provided by AMC).

LISA project: approach and progress in 2017

Following the official start of LISA, the project was organised according to the PRINCE2 approach. It was divided into eight manageable phases of 6 weeks, and the work packages in each phase were clearly defined and planned. Careful consideration was given to the dependencies between the different parties when planning the delivery of the products in each phase.

All the work packages contribute to the products planned for each phase. Globally, the work package tasks have been distributed as follows:

- SHM is responsible for the content, modelling of content in the data entry system and modelling of the system in the data warehouse. In addition, SHM is responsible for the data model and for the migration of historical data to the new data warehouse. SHM's activities in each phase comprise 2 weeks' preparation and 4 weeks' production, including testing the products.

DATA COLLECTION & QUALITY CONTROL A YEAR OF INNOVATION

February 2018: DataCapTree launch with 36 data collection protocols

- ICT Automatisering and LogicNets are responsible for the design, development and installation of the data entry application. They are also responsible for training and coaching SHM staff in modelling the data entry application.
- ADICT is responsible for building the IT infrastructure required for the data warehouse, the data entry application, and the application required for authentication and authorisation of all end users.

To ensure that the project runs smoothly, various project teams have been set up within SHM. In 2017, the protocol team continued converting current data collection protocols into decision tree structures. The team has built the decision trees as efficiently as possible to ensure that there are no unnecessary steps or queries. In 2017, all decision trees were identified, designed and conceptually tested. The researchers responsible for carrying out data analyses within SHM have been given the task of assessing and approving the decision trees on the basis of each person's field of expertise. During the eight phases of the project, the approved protocols were constructed in LogicNets and re-tested by the end users (i.e., data collectors, data quality staff and researchers).

In 2017, seven phases of the project were successfully completed. The end of 2017 marked the start of an intensive testing phase, during which a total of 120 pre-defined system requirements were tested with 905 test plans. These test plans were designed and implemented by various test groups that included protocol builders, data collectors, data quality staff and researchers. These groups also used scenarios to test the content of the protocols. If, after testing, a protocol was approved and accepted by all the test groups, it was prepared for production. However, if a protocol was not accepted by all the test groups, the groups presented their findings to the protocol group so that the latter could amend and adapt the protocol in question.

Data collection in Oracle Clinical will terminate on 31 December 2017. During January 2018, the data collectors will be given training centrally at the SHM head office and locally at their own places of work. The new system, which will be named DataCapTree, is expected to go live on 5 February 2018 and data collection will then start with 36 tested and accepted protocols. During 2018, the remaining protocols will go into production, following test and acceptance by all test groups.

In the second half of 2018, we will carry out an evaluation and impact assessment. Depending on the outcome of this assessment, an update of the system may be scheduled for the end of 2018/early 2019. Moreover, when necessary, we will carry out functional adjustments and/or expansions during the course of 2018.

DATA COLLECTION & QUALITY CONTROL A YEAR OF INNOVATION

LabLink in
14
HIV treatment centres

LabLink

LabLink is part of our innovation programme that was launched in 2013 to automate data collection as much as possible and, as such, minimise manual data collection. It is the name given to the interface implemented at an HIV treatment centre that allows laboratory data to be collected electronically wherever possible and entered directly into our data warehouse.

Using LabLink, HIV-related laboratory data are selected from hospital information systems and sent to SHM in a pseudonymised form. These data are then entered into SHM's data warehouse by ADICT. In 2012, a standard LabLink protocol was developed in collaboration with the AMC's Clinical Research Unit (CRU) and ADICT for sending laboratory results as HL7 messages (an international standard for electronic data exchange between healthcare information systems). All HIV treatment centres with LabLink now send data to SHM according to this standard.

For the pseudonymisation of LabLink data, each hospital maintains a LabLink-specific overview of those individuals who are in care, have left care or have objected to data collection. Laboratory results are only collected for those individuals who are in care and who have not lodged an objection to their data being collected.

For each laboratory result, the following data are required:

- pseudonym,
- date of sample collection,
- test carried out,
- result,
- unit,
- material code,
- assay code,
- normal values.

Expansion of LabLink in 2017

In 2013, all HIV treatment centres were informed about LabLink and sent the standard LabLink protocol so that they could investigate how LabLink could be implemented within their existing IT infrastructure. Between 2013 and 2017, LabLink was set up in 14 hospitals. Further expansion of LabLink to other hospitals and sites was continued in 2017 and resulted in LabLink going live in the OLVG West site and DC Klinieken Lairesse-Hiv Focus Centrum in 2017. In addition, during 2017 preparations were undertaken to set up LabLink in the Rijnstate hospital in Arnhem. LabLink could not yet be set up in the remaining hospitals due to our prioritisation of the LISA project during 2017, as well as the ongoing implementation of electronic medical record systems and other IT priorities within the hospitals.

DATA COLLECTION & QUALITY CONTROL A YEAR OF INNOVATION

LabLink status in HIV treatment centres.

- *Hospitals that transmit laboratory data through LabLink or other automated link.*
- *Hospitals that are in the process of implementing LabLink.*
- *Hospitals that are awaiting decision on whether to implement LabLink or that have postponed LabLink due to other ongoing projects.*

Numbers on map correspond to treatment centre list on page 11.

In total, 14 HIV treatment centres now use LabLink and, together, deliver electronic laboratory results from 69% of the individuals followed by SHM. This figure is expected to rise substantially in 2018 once LabLink has been implemented in those hospitals that are coupled to the OLVG laboratory computer system (MC Jan van Goyen, Flevoziekenhuis and MC Zuiderzee) and in those where the first steps towards LabLink implementation have already been taken. Finally, in 2017, the AMC continued to transfer results directly to SHM from its laboratory computer system using an internal LabLink connection made possible because SHM uses the AMC IT network.

Harmonisation of LabLink data

In 2012, the CRU developed a LabLink 'mapping tool' in Microsoft Access. This tool receives and standardises ('harmonises') laboratory results from different treatment centres with different terminology. In 2017, 2,797 combinations of laboratory terms and accompanying samples were harmonised using this tool.

Centralisation of data collection

The collection of data from all individuals who are in care at an HIV treatment centre in the Netherlands is carried out by data collectors, all of whom are trained and coached by SHM. Most data collectors are centrally employed by SHM, while a smaller number remain locally employed by the HIV treatment centre. Our experience has shown that centralisation of data collection,

DATA COLLECTION & QUALITY CONTROL A YEAR OF INNOVATION

which involves the mobile deployment of specially trained staff employed by SHM (central data collectors), is more effective in terms of achieving efficient, timely, and high-quality data collection. We therefore encourage centralisation wherever possible. In line with this strategy, data collection was centralised at both the OLVG West site and Medisch Spectrum Twente in 2017.

In 2017, our central data collectors also provided assistance to local data collectors in UMC Utrecht, Spaarne Gasthuis, ETZ (Elisabeth-TweeSteden Ziekenhuis), and Erasmus MC to ensure that data collection in these HIV treatment centres remained up to date and to resolve discrepancies in the data. In addition, central data collectors collected prospective and retrospective data on hepatitis from hospitals throughout the country and entered these data into SHM's database. Finally, the central data collectors were involved in collecting additional data from a number of HIV treatment centres as part of a national collaboration entitled the NOVA study (part of the H-TEAM project), thereby creating more data analysis opportunities for the researchers involved.

Knowledge management

In 2017, we trained five new data collectors, with specific training on relevant medical information relating to HIV, data collection protocols, and the data entry system. In addition, individual coaching was provided to existing data collectors and a review day was held on 26 June 2017 for all data collectors. This review day focused on the new data entry system, DataCapTree.

Data collectors were also informed about the regulations regarding privacy and were given a refresher training on specific medical conditions they may come across when collecting data.

In 2017, we also provided structural assistance to the data collector in Curaçao, providing her with tailored training and an introduction to DataCapTree. This assistance and training took place both at our head office in Amsterdam and remotely.

ISO 9001 and ISO 27001 certification

We work with pseudonymised patient information and treat this information with the utmost care. To ensure that we can continue to protect patients' privacy in the current digital landscape, we plan to expand our existing PDCA-based quality management system by acquiring ISO 9001 and ISO 27001 certification.

ISO 9001 certification comprises requirements for a general quality management system, while ISO 27001 is a standard that is fully focused on the security of company information and confidential information made available to the organisation. This standard also includes the Dutch NEN 7510 standard ('Information security in health care'), which is an instrument for managing and continually improving security. Our goals for information security are fully compliant with the requirements set out by the ISO 27001

standard, current legislation (including the EU General Data Protection Regulation [GDPR] that will come into force on 25 May 2018), and the agreements regarding personal data protection as defined in the individual contracts between SHM and HIV treatment centres.

During 2017, priority was given to preparing for the GDPR. In addition, internal audits were carried out in 2017 as a step towards the ISO 9001 and ISO 27001 certification; external audits will be scheduled in 2018.

STRUCTURAL ACTIVITIES

Patient registration

Patient registration involves registering and de-registering patients in the registration system, and is carried out separately from the data collection activity. Patient registration takes place centrally because of the need to generate a unique number under which all subsequent data are stored and processed. This approach provides a clear separation between privacy-sensitive data stored in the registration database and the pseudonymised data stored in the national database.

In 2017, 1,724 individuals were registered and 769 individuals were de-registered. These numbers include new diagnoses and de-registration due to death of an individual, as well as registration and de-registration due to an individual moving to another HIV treatment centre or abroad. In addition, validity and reliability checks were carried out on patient registration data on a monthly basis. These checks resulted in 576 amendments.

Data collection and data entry

Manual collection of data from individuals followed in the HIV treatment centres in the Netherlands is carried out by data collectors. They collect data straight from either paper or electronic medical records and, based on data collection protocols, standardise, code and enter the data into SHM's data entry system.

Data collection progress

Table 1 presents the percentage of patients in treatment centres with a backlog in data collection. Backlog is calculated on the basis of the difference between the predicted time from the most recent patient visit to the subsequent visit and the actual time between these visits. The predicted time is based on the frequency of visits in the year prior to the last visit. A distinction is made between an estimated backlog of more than 365 days (long-term backlog) and one of fewer than 365 days (short-term backlog) between the predicted time and actual time between visits, whereby a difference of 180 days or less is not considered a backlog.

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DATA COLLECTION & QUALITY CONTROL A YEAR OF INNOVATION

The average short-term backlog in 2017 was low for most centres and, at 4%, was 1% less than in 2016. The average long-term backlog in data collection in 2017 remained 0%. These are good results given that, in 2017, 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 and were closely involved in testing protocols for the LISA project. Another factor that has contributed to this outcome is the ongoing training of data collectors in efficient data collection, where individual patient reports and standard data queries are used to monitor backlogs and establish priorities. The backlog is expected to improve further once DataCapTree comes into use.

DATA COLLECTION & QUALITY CONTROL A YEAR OF INNOVATION

Table 1: Percentage of individuals followed in each treatment centre with an average data collection backlog of more, and less, than 365 days.

		>365 days		<365 days	
HIV treatment centre	**Site**	**2017**	**2016**	**2017**	**2016**
Noordwest Ziekenhuisgroep	Alkmaar	0%	0%	2%	3%
Flevoziekenhuis	Almere	0%	0%	3%	8%
AMC-UvA	Amsterdam	0%	1%	3%	4%
DC Klinieken Lairesse – Hiv Focus Centrum	Amsterdam	0%	0%	3%	5%
MC Jan van Goyen	Amsterdam	0%	0%	5%	5%
OLVG	Amsterdam	1%	1%	4%	1%
MC Slotervaart	Amsterdam	1%	0%	1%	3%
VUmc	Amsterdam	0%	1%	6%	1%
Rijnstate	Arnhem	0%	1%	8%	5%
HagaZiekenhuis (Leyweg)	Den Haag	0%	0%	0%	9%
HMC	Den Haag	1%	0%	7%	0%
Catharina Ziekenhuis	Eindhoven	0%	0%	2%	6%
MST	Enschede	0%	1%	0%	5%
Admiraal De Ruyter Ziekenhuis	Goes	1%	0%	4%	0%
UMCG	Groningen	0%	0%	6%	9%
Spaarne Gasthuis	Haarlem	0%	1%	6%	11%
MCL	Leeuwarden	0%	0%	3%	6%
LUMC	Leiden	0%	0%	3%	5%
MC Zuiderzee	Lelystad	0%	0%	5%	7%
MUMC+	Maastricht	0%	0%	4%	8%
Radboudumc	Nijmegen	0%	0%	15%	12%
Erasmus MC	Rotterdam	1%	3%	4%	8%
Maasstad Ziekenhuis	Rotterdam	0%	0%	1%	1%
ETZ	Tilburg	0%	1%	0%	1%
UMC Utrecht	Utrecht	1%	1%	9%	12%
Isala	Zwolle	1%	0%	1%	6%
Average		**0%**	**0%**	**4%**	**5%**

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DATA COLLECTION & QUALITY CONTROL A YEAR OF INNOVATION

Quality control

In the 16 years since our foundation, we have developed extensive and valuable expertise for monitoring and maintaining data quality. In particular, as the number of patients being followed over a prolonged period of time has grown, data quality control efforts have become more demanding and complex. For example, data obtained electronically (i.e., through LabLink) require a different quality control approach to those collected manually, which are checked and improved by means of both manual and automated checks.

Manual quality control

Manual quality checks were carried out as usual in 2017 by our data quality staff, albeit to a lesser extent than in previous years due to additional time demands placed on these staff by the LISA project. As a result, quality checks focussed on cause of death in deceased patients, including a check of baseline data. During 2017, data from 100 deceased patients were checked. In addition, priority was given to data on endpoint-defined comorbidities. This resulted in quality checks on 170 endpoints. Finally, as well as carrying out cause-of-death quality checks, causes of death were also reclassified and validated based on the CoDe (Coding Causes of Death in HIV) classification.

As part of the LISA project and in preparation for the migration of data collected up to 31 December 2017 into DataCapTree, data collectors carried out additional checks to improve the quality of the migration data and to amend these migration data so that they met the requirements of the new data entry system. These extra quality checks focussed on the following data:

- HIV history: recent infections and acute symptoms,
- CDC events: inaccurate or missing start date, missing classification,
- side effects: inaccurate or missing start date,
- antiretroviral medication: inaccurate start/stop date,
- comedication: comedication without code,
- laboratory data: mapping of LabLink data,
- liver radiology data: inconsistencies in hepatocellular carcinoma data,
- pregnancies: linking birth data to pregnancy data.

As a result of these checks, a total of 2,043 additional discrepancies in data were solved in 2017 compared to the previous year.

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LabLink quality control

Both automated and manual checks, developed in 2013, were carried out on the LabLink data in 2017. One-off checks for acceptance of new LabLink connections with a laboratory were carried out on data in an acceptance test environment, while structural checks on LabLink data were performed three times on LabLink data in the production environment.

The LabLink data were specifically checked for the following points:

- anonymisation of HL7 messages from within the HIV treatment centre,
- completeness of the HIV treatment centre's patient population for 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 a comparison with laboratory results in the electronic medical records (carried out by the data collectors).

Helpdesk and protocol management

This activity, carried out by a number of our data quality staff, is designed to ensure the data collection protocols are kept up to date and to provide content-based input for staff training, with the aim of further improving the quality of our database.

During 2017, the helpdesk received 145 queries from data collectors, 111 of which could be resolved immediately by the responsible data quality staff member. In some cases, these queries resulted in protocol changes. These helpdesk-driven protocol changes were included in the overall revision of medically-based protocols that was carried out in 2017 for the LISA project.

In 2017, our helpdesk staff also developed training material for the DataCapTree training days provided to data collectors in January 2018.

111
queries resolved by the data collectors' helpdesk in 2017

DATA COLLECTION & QUALITY CONTROL A YEAR OF INNOVATION

Data management and reporting

Data warehousing and data processing

Our 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 SHM database on the previous day and with data sent by treatment centres via LabLink. 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.

To ensure that our data warehouse is ready to link with the new data entry system, DataCapTree, the structure of the data warehouse was changed in 2017. The new structure is based on the protocols integrated within DataCapTree and will take the form of a relational database (Microsoft SQL server).

Within DataCapTree, there are 2,192 general answer options and 1,241 protocol-specific options. The answer options in DataCapTree are user-friendly and clearly formulated for the data collectors to minimise data entry errors. Moreover, each answer option used in the protocols has been assigned a unique identification number to facilitate storage in the data warehouse.

The protocols in the DataCapTree database make it possible for records in the data warehouse tables to be created, changed or updated in real time. As soon as a data collector selects 'Send' in a protocol, the collected data are stored in the data warehouse. This is an improvement compared with the previous situation where entered data were refreshed overnight in the data warehouse, with a one-day delay.

A data freeze is carried out twice a year, after which the raw data tables from the data warehouse are processed to yield tables suitable for data analysis. This involves cleaning, clustering, and coding the data according to the standard protocols of various national and international collaborations and the Anatomical Therapeutic Chemical (ATC) classification. In 2017, these data processing steps resulted in data sets for use by our researchers, for centre-specific reports, and for the Co-morbidity and Ageing with HIV (AGEhIV) study and the NOVA study. In addition, data processing and data set generation was carried out for two international collaborations, EPPICC and BEEHIVE.

Patient-specific reports, graphs and queries

Each centre has access to Microsoft Report Builder, in which treatment teams can view and download for use reports, graphs and queries relating to raw data from their own patients. In 2017, these reports, graphs and other standard data queries were maintained, further developed where needed, and optimised.

DATA COLLECTION & QUALITY CONTROL A YEAR OF INNOVATION

Centre-specific reports

Standard reports for each centre are presented twice a year on a password-protected area of our website. These centre-specific reports are intended to provide treatment teams in the treatment centres with an overview of developments, trends and issues within their own patient populations compared to the national average. These centre-specific reports were updated and made available to the HIV treatment centres twice during the course of 2017.

Logo for our new data entry system, DataCapTree.

Registration

OF HIV-POSITIVE INDIVIDUALS IN 2017

GENERAL

Up to and including 31 December 2017, a cumulative total of 26,576 people living with HIV were registered by Stichting HIV Monitoring (SHM) (Table 2), of whom 1,102 were newly-registered in 2017 (Table 3). In total, 259 individuals were registered at an HIV treatment centre specialised in HIV care for children and adolescents.

Further clinical data were collected for 25,987 (97.8%) of the registered individuals. The remaining 589 (2.2%) persons objected to the collection of their data. Of the 1,102 people who were newly registered in 2017, 65 (6.0%) were registered as objecting to data collection.

In 2017, data were collected from 19,984 (77%) individuals. Of the 6,093 (23%) individuals with no data collected in 2017, 2,819 had died before 2017, 1,567 had moved abroad and 1,707 had disappeared from care for an unknown reason. Of the individuals who had ever been registered as objecting to data collection, 67 were known to have died prior to 2017 and 2 had moved abroad.

Box 1: Definitions of infection, diagnosis, entry into care, and registration

Infection	The moment an individual acquires an HIV infection. The time of infection is often unknown.
Diagnosis	The moment an individual is newly diagnosed with an HIV infection. The time of diagnosis can be weeks, months, or years after infection.
Entry into care	The moment an HIV-positive individual is first seen for care in an HIV treatment centre, which usually is within a few weeks of HIV diagnosis.
Registration	The moment an HIV-positive individual in care is notified to SHM by their treating HIV physician or nurse and registered in the SHM database. Registration is usually within a few months of entering care, but can take longer. Collection of demographic and clinical data from the time of HIV diagnosis can only be done after an HIV-positive individual is registered with SHM.

REGISTRATION OF HIV-POSITIVE INDIVIDUALS IN 2017

ADULTS

Of the 25,987 individuals registered up to and including 2017 and for whom further clinical data were collected, 25,527 were adults at the time of registration: 20,723 (81%) men and 4,804 (19%) women.

In 2017, there were 1,015 adults who were newly-registered and for whom clinical data were collected. These comprised 871 (86%) men and 144 (14%) women.

CHILDREN

Of the 25,987 persons registered as of 31 December 2017, 460 (2%) were children or adolescents at the time of registration. This group consisted of 217 (47%) boys and 243 (53%) girls. In 2017, 22 children and adolescents (16 children aged between 0 and 12 years and 6 adolescents aged 13-17 years) were newly registered, comprising 10 boys and 12 girls.

PREGNANT WOMEN

Up to and including 31 December 2017, 3,380 pregnancies were registered in a total of 1,854 women living with HIV. HIV was diagnosed before the start of the pregnancy in 58% of the first pregnancies and during the pregnancy in 42%.

During 2016 and 2017, 228 pregnancies were registered, 91 of which were first pregnancies. In 30% of these first pregnancies, HIV was diagnosed during the pregnancy.

228
pregnancies registered in women living with HIV during 2016 & 2017

REGISTRATION OF HIV-POSITIVE INDIVIDUALS IN 2017

Table 2: Total number of HIV-positive individuals registered by SHM as of 31 December 2017, according to most recent HIV treatment centres.

		Total		Alive		Deceased		Objection[a]		Data in 2017[b]		No data in 2017			
												Deceased before 2017[c]		Other reasons[d]	
HIV treatment centre	**Location**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Adults															
Noordwest Ziekenhuisgroep	Alkmaar	386	1.5	348	90.2	38	9.8	6	1.6	308	79.8	33	8.5	45	11.7
Flevoziekenhuis	Almere	227	0.9	213	93.8	14	6.2	4	1.8	199	87.7	10	4.4	18	7.9
AMC-UvA	Amsterdam	2,851	10.8	2,418	84.8	433	15.2	12	0.4	2,024	71.0	403	14.1	424	14.9
DC Klinieken Lairesse - Hiv Focus Centrum	Amsterdam	873	3.3	865	99.1	8	0.9	5	0.6	853	97.7	5	0.6	15	1.7
MC Jan van Goyen	Amsterdam	324	1.2	282	87.0	42	13.0	3	0.9	216	66.7	42	13.0	66	20.4
OLVG	Amsterdam	4,008	15.2	3,507	87.5	501	12.5	164	4.1	2,930	73.1	490	12.2	588	14.7
MC Slotervaart	Amsterdam	864	3.3	697	80.7	167	19.3	12	1.4	596	69.0	160	18.5	108	12.5
VUmc	Amsterdam	704	2.7	608	86.4	96	13.6	19	2.7	486	69.0	94	13.4	124	17.6
Rijnstate	Arnhem	896	3.4	806	90.0	90	10.0	3	0.3	719	80.2	83	9.3	94	10.5
HagaZiekenhuis (Leyweg)	Den Haag	781	3.0	671	85.9	110	14.1	32	4.1	515	65.9	108	13.8	158	20.2
HMC	Den Haag	1,150	4.4	1,054	91.7	96	8.3	43	3.7	865	75.2	90	7.8	195	17.0
Catharina Ziekenhuis	Eindhoven	738	2.8	690	93.5	48	6.5	7	0.9	583	79.0	47	6.4	108	14.6
MST	Enschede	637	2.4	520	81.6	117	18.4	5	0.8	395	62.0	114	17.9	128	20.1
Admiraal De Ruyter Ziekenhuis	Goes	216	0.8	200	92.6	16	7.4	3	1.4	160	74.1	16	7.4	40	18.5
UMCG	Groningen	1,012	3.8	903	89.2	109	10.8	48	4.7	782	77.3	100	9.9	130	12.8
Spaarne Gasthuis	Haarlem	526	2.0	468	89.0	58	11.0	5	1.0	402	76.4	57	10.8	67	12.7
MCL	Leeuwarden	324	1.2	291	89.8	33	10.2	0	0.0	258	79.6	32	9.9	34	10.5
LUMC	Leiden	746	2.8	670	89.8	76	10.2	39	5.2	557	74.7	70	9.4	119	16.0
MC Zuiderzee	Lelystad	97	0.4	96	99.0	1	1.0	1	1.0	85	87.6	1	1.0	11	11.3
MUMC+	Maastricht	993	3.8	838	84.4	155	15.6	5	0.5	714	71.9	146	14.7	133	13.4
Radboudumc	Nijmegen	811	3.1	709	87.4	102	12.6	30	3.7	654	80.6	91	11.2	66	8.1

[a] *Objection: consent not given for collection of clinical data.*
[b] *Data in 2017: registered by SHM in 2017, or deceased during 2017, or last contact with an HIV treatment centre during 2017.*
[c] *No data in 2017 – deceased before 2017: individuals who are not included in 'data in 2017' and who had died before 2017.*
[d] *No data in 2017 – other reasons: individuals who are not included in 'data in 2017' because they moved abroad before 2017 or because they had no contact with their HIV treatment centre in 2017 for an unknown reason.*

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[Continued on page 36]

REGISTRATION OF HIV-POSITIVE INDIVIDUALS IN 2017

Table 2: Continued.

HIV treatment centre	Location	Total n	Total %	Alive n	Alive %	Deceased n	Deceased %	Objection[a] n	Objection[a] %	Data in 2017[b] n	Data in 2017[b] %	No data in 2017: Deceased before 2017[c] n	No data in 2017: Deceased before 2017[c] %	No data in 2017: Other reasons[d] n	No data in 2017: Other reasons[d] %
Adults (continued)															
Erasmus MC	Rotterdam	2,743	10.4	2,410	87.9	333	12.1	14	0.5	2,010	73.3	316	11.5	417	15.2
Maasstad Ziekenhuis	Rotterdam	830	3.2	773	93.1	57	6.9	12	1.4	693	83.5	55	6.6	82	9.9
ETZ	Tilburg	1,234	4.7	1,146	92.9	88	7.1	21	1.7	983	79.7	85	6.9	166	13.5
UMC Utrecht	Utrecht	1,803	6.9	1,607	89.1	196	10.9	68	3.8	1,373	76.2	195	10.8	235	13.0
Isala	Zwolle	543	2.1	500	92.1	43	7.9	25	4.6	417	76.8	40	7.4	86	15.8
Total		**26,317**	**100.0**	**23,290**	**88.5**	**3,027**	**11.5**	**586**	**2.2**	**19,777**	**75.1**	**2,883**	**11.0**	**3,657**	**13.9**
Paediatric															
EKZ, AMC-UvA	Amsterdam	71	27.4	71	100.0	0	0.0	1	1.4	65	91.5	0	0.0	6	8.5
BKZ, UMCG	Groningen	28	10.8	28	100.0	0	0.0	0	0.0	26	92.9	0	0.0	2	7.1
Erasmus MC-Sophia Kinderziekenhuis	Rotterdam	89	34.4	86	96.6	3	3.4	0	0.0	58	65.2	2	2.2	29	32.6
WKZ, UMC Utrecht	Utrecht	71	27.4	70	98.6	1	1.4	2	2.8	58	81.7	1	1.4	12	16.9
Total		**259**	**100.0**	**255**	**98.5**	**4**	**1.5**	**3**	**1.2**	**207**	**79.9**	**3**	**1.2**	**49**	**18.9**
Curaçao															
SEHOS	Willemstad	1,078	98.6	911	84.5	167	15.5	1	0.1	651	60.4	165	15.3	262	24.3
SEHOS kinderkliniek	Willemstad	15	1.4	5	33.3	10	66.7	0	0.0	0	0.0	10	66.7	5	33.3
Total Curaçao		**1,093**	**100.0**	**916**	**83.8**	**177**	**16.2**	**1**	**0.1**	**651**	**59.6**	**175**	**16.0**	**267**	**24.4**

[a] *Objection: consent not given for collection of clinical data.*
[b] *Data in 2017: registered by SHM in 2017, or deceased during 2017, or last contact with an HIV treatment centre during 2017.*
[c] *No data in 2017 – deceased before 2017: individuals who are not included in 'data in 2017' and who had died before 2017.*
[d] *No data in 2017 – other reasons: individuals who are not included in 'data in 2017' because they moved abroad before 2017 or because they had no contact with their HIV treatment centre in 2017 for an unknown reason.*

Download Table 2

REGISTRATION OF HIV-POSITIVE INDIVIDUALS IN 2017

Table 3: Total number of people who were first registered by SHM in 2017, according to HIV treatment centre.

HIV treatment centre	Location	Total n	Total %	Alive n	Alive %	Deceased n	Deceased %	Objection[a] n	Objection[a] %
Adults									
Noordwest Ziekenhuisgroep	Alkmaar	23	2.1	22	95.7	1	4.3	1	4.3
Flevoziekenhuis	Almere	15	1.4	15	100.0	0	0.0	1	6.7
AMC-UvA	Amsterdam	94	8.7	78	83.0	16	17.0	1	1.1
DC Klinieken Lairesse - Hiv Focus Centrum	Amsterdam	26	2.4	26	100.0	0	0.0	2	7.7
MC Jan van Goyen	Amsterdam	15	1.4	15	100.0	0	0.0	0	0.0
OLVG	Amsterdam	109	10.1	108	99.1	1	0.9	2	1.8
MC Slotervaart	Amsterdam	11	1.0	11	100.0	0	0.0	1	9.1
VUmc	Amsterdam	43	4.0	43	100.0	0	0.0	8	18.6
Rijnstate	Arnhem	48	4.4	47	97.9	1	2.1	0	0.0
HagaZiekenhuis (Leyweg)	Den Haag	26	2.4	26	100.0	0	0.0	0	0.0
HMC	Den Haag	39	3.6	39	100.0	0	0.0	0	0.0
Catharina Ziekenhuis	Eindhoven	37	3.4	37	100.0	0	0.0	1	2.7
MST	Enschede	26	2.4	26	100.0	0	0.0	3	11.5
Admiraal De Ruyter Ziekenhuis	Goes	9	0.8	9	100.0	0	0.0	0	0.0
UMCG	Groningen	62	5.7	61	98.4	1	1.6	19	30.2
Spaarne Gasthuis	Haarlem	16	1.5	16	100.0	0	0.0	2	12.5
MCL	Leeuwarden	16	1.5	16	100.0	0	0.0	0	0.0
LUMC	Leiden	25	2.3	23	92.0	2	8.0	0	0.0
MC Zuiderzee	Lelystad	11	1.0	11	100.0	0	0.0	0	0.0
Maastricht UMC+	Maastricht	61	5.6	60	98.4	1	1.6	0	0.0
Radboudumc	Nijmegen	42	3.9	37	88.1	5	11.9	10	23.8
Erasmus MC	Rotterdam	108	10.0	107	99.1	1	0.9	0	0.0
Maasstad Ziekenhuis	Rotterdam	49	4.5	49	100.0	0	0.0	2	4.1
ETZ	Tilburg	64	5.9	64	100.0	0	0.0	3	4.7
UMC Utrecht	Utrecht	67	6.2	67	100.0	0	0.0	2	3.0
Isala	Zwolle	40	3.7	40	100.0	0	0.0	7	17.5
Total		***1,082**	**100.0**	**1,053**	**97.3**	**29**	**2.7**	**65**	**6.0**

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

* *Includes 2 of the 22 children/adolescents newly-registered in 2017.*

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[Continued on page 38]

REGISTRATION OF HIV-POSITIVE INDIVIDUALS IN 2017

Table 3: Continued.

HIV treatment centre	Location	Total n	Total %	Alive n	Alive %	Deceased n	Deceased %	Objection[a] n	Objection[a] %
Paediatric									
EKZ, AMC-UvA	Amsterdam	4	20.0	4	100.0	0	0.0	0	0.0
BKZ, UMCG	Groningen	2	10.0	2	100.0	0	0.0	0	0.0
Erasmus MC-Sophia Kinderziekenhuis	Rotterdam	12	60.0	12	100.0	0	0.0	0	0.0
WKZ, UMC Utrecht	Utrecht	2	10.0	2	100.0	0	0.0	0	0.0
Total		**20**	**100.0**	**20**	**100.0**	**0**	**0.0**	**0**	**0.0**
Curaçao									
SEHOS	Willemstad	54	100.0	53	98.1	1	1.9	0	0.0

Download Table 3

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

* *Includes 2 of the 22 children/adolescents newly-registered in 2017.*

Of the HIV-positive people monitored by SHM:

6% had a chronic HCV co-infection

2% had an acute HCV co-infection

6% had a chronic HBV co-infection

REGISTRATION OF HIV-POSITIVE INDIVIDUALS IN 2017

HIV SEQUENCE DATA

Up until the end of 2017, 14,348 reverse transcriptase and/or protease sequences and 155 integrase gene sequences had been included in the SHM database. To date, three laboratories have submitted sequences for 2017. These sequences are used to examine resistance to treatment regimens and to investigate possible HIV transmission networks.

HEPATITIS B AND HEPATITIS C CO-INFECTION

Up to and including 31 December 2017, 1,457 (6%) of the monitored HIV-positive individuals were found to have a chronic HCV co-infection, while 491 (2%) were found to have an initial acute HCV co-infection. Of these 491 individuals, 22 were first diagnosed with HCV in 2017, 6 of whom were newly registered with SHM in 2017.

In 2017, chronic HBV co-infection was detected in 1,622 (6%) of the monitored HIV-positive individuals. HBV was first diagnosed in 2017 in 24 of these individuals, 15 of whom were newly registered with SHM in 2017.

In 2017 SHM registered 11 cases of liver fibrosis, 10 liver cirrhosis events and 1 case of hepatocellular carcinoma.

SAMPLE COLLECTION AND STORAGE

Since the start of the AIDS Therapy Evaluation in the Netherlands (ATHENA) project in 1996, an estimated total of 536,410 plasma samples from people 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 epidemiology research into resistance development over time and for research 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-POSITIVE INDIVIDUALS IN CURAÇAO

The registration and monitoring of HIV-positive persons being followed in the St. Elisabeth Hospital in Willemstad, Curaçao, was continued during 2017. In total, 1,093 individuals were registered, of whom 54 were newly registered in 2017.

HIV in the Netherlands

KEY FINDINGS FROM OUR 2017 HIV MONITORING REPORT

This chapter provides a summary of the key findings from the latest HIV Monitoring Report that was published on 17 November 2017. Highlights from the report were also presented at the annual Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment on 21 November 2017. The full report is available on our website.

Download 2017 HIV Monitoring Report

THE HIV EPIDEMIC IN THE NETHERLANDS IN 2016

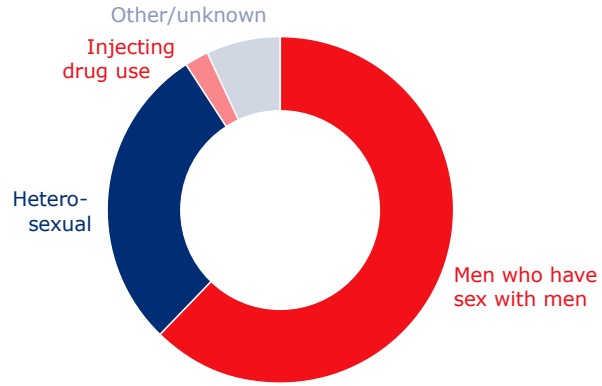
Fewer new HIV diagnoses in 2016

Since 2008 there has been a decreasing trend in the annual number of new HIV diagnoses to below 900 new diagnoses in recent years. This decreasing trend continued in 2016. The projected number of diagnoses for 2016 is 816, although this may change as registration of HIV diagnoses for 2016 has not yet been finalised.

Majority of new diagnoses were in men who have sex with men

In 2016, the majority (67%) of newly-diagnosed infections were in men who have sex with men (MSM), while 25% were acquired through heterosexual contact and around 8% through other or unknown modes of transmission.

Figure 1: Route of HIV transmission in the full population in HIV care in the Netherlands in 2016.



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HIV IN THE NETHERLANDS KEY FINDINGS

People newly-diagnosed with HIV rapidly receive specialised care

Over 95% of people newly-diagnosed with HIV entered specialised HIV care within 6 weeks after diagnosis. This rate was more or less the same regardless of where the diagnosis was made (i.e., hospital, general practice, sexually transmitted infections clinic, or other test location).

HIV testing is becoming more common

The rates of testing for HIV appear to be increasing in the Netherlands. This conclusion is based on the following observations. Firstly, our data show that the proportion of individuals with a previously negative HIV test has increased (71% of MSM, 32% of other men and 40% of women diagnosed in 2016 had a reported previous negative test). In addition, the proportion of individuals who are diagnosed with HIV relatively early in their infection (including during primary HIV infection) continues to increase, particularly among MSM. This is reflected in the CD4 count at diagnosis gradually having risen over time to a median of 380 cells/mm^3 in 2016.

Earlier diagnosis for MSM in Amsterdam

It is interesting to note that MSM in Amsterdam are now generally being diagnosed earlier in infection than elsewhere in the Netherlands; this may be a preliminary indicator of the effectiveness of the H-TEAM project that is underway in Amsterdam.

Late presentation for care remains a problem

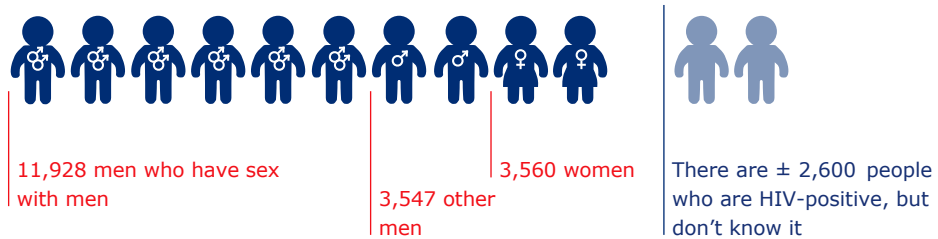
Despite the observed earlier diagnosis among certain groups, many people still present late for care, i.e. with an already impaired immune system (CD4 count below 350 cells/mm^3) or even AIDS; in 2016, this was the case for 37% of MSM, 63% of other men and 43% of women.

HIV IN THE NETHERLANDS KEY FINDINGS

How many people were in HIV care in 2016?

As of 31 December 2016, a total of 19,035 people living with HIV in the Netherlands (18,824 adults and 211 children and adolescents) were known to be in care in one of the 26 adult or 4 paediatric HIV treatment centres.

***Figure 2:** Number of people living with HIV and in care in the Netherlands in 2016.*



CONTINUUM OF HIV CARE IN 2016: '89-92-95'

One of the goals of HIV treatment is to achieve viral suppression. The key steps that need to be achieved to reach viral suppression are illustrated in a continuum of HIV care. A continuum of care also gives a measure of progress towards achieving the UNAIDS 90-90-90 goals for HIV care by 2020.

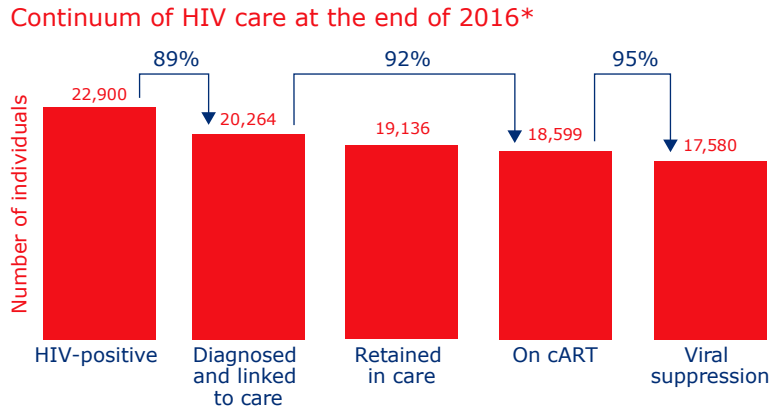
The continuum of care for the Netherlands shows we are making good progress in reaching these goals (89-92-95 in 2016, see *Figure 3*):

- By the end of 2016, 22,900 individuals were estimated to be living with HIV, of whom 2,600 were still undiagnosed.
- In total, 20,264 individuals (**89%** of the total number estimated to be living with HIV) had been diagnosed, linked to care, and registered by SHM.
- Of the individuals who had been diagnosed, linked to care, and registered by SHM, the majority (n=18,599; **92%**), had started combination antiretroviral therapy (cART), and 17,580 of those (**95%**) had achieved viral suppression, irrespective of treatment.

This means that overall, 77% of the total estimated population living with HIV and 87% of those diagnosed and ever linked to care had a suppressed viral load.

HIV IN THE NETHERLANDS KEY FINDINGS

Figure 3: Continuum of HIV care for the total estimated HIV-positive population in the Netherlands by the end of 2016, based on UNAIDS 90-90-90 goals for 2020: 89-92-95.



*Corrected for lag in registration with SHM.

Need for transdisciplinary strategies

The figures for the Netherlands are impressive compared with other parts of the world. Nonetheless, in 2016 there were around 800 new diagnoses and an estimated 2,600 people who remained undiagnosed. To achieve a significant decline in these numbers, novel transdisciplinary strategies are needed to simultaneously reduce the likelihood of HIV transmission in key populations at risk, identify individuals with HIV infection early, rapidly link all people living with HIV to care, and immediately offer them the possibility of starting combination antiretroviral therapy.

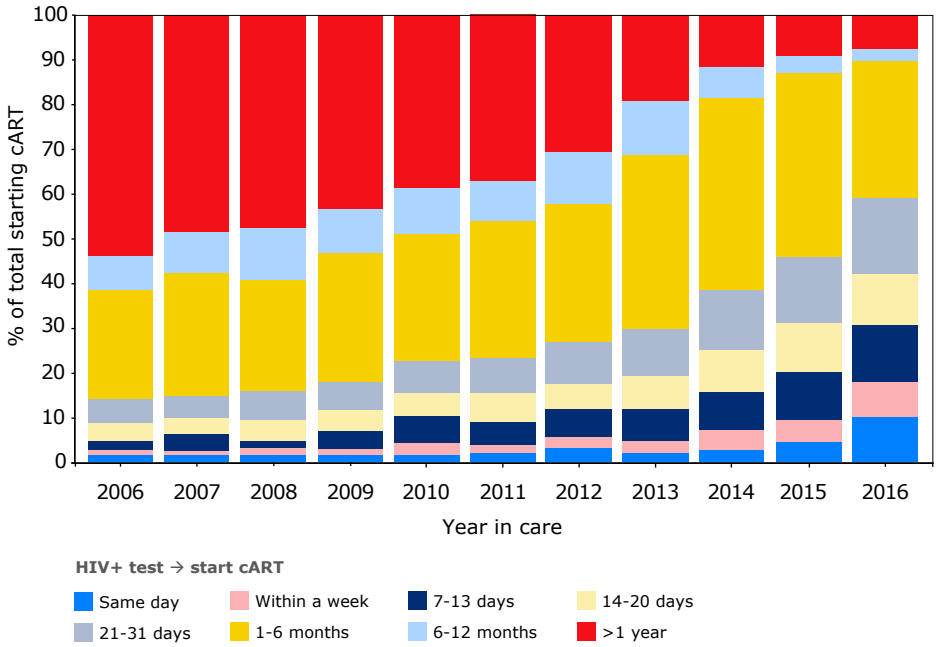
HIV IN THE NETHERLANDS KEY FINDINGS

COMBINATION ANTIRETROVIRAL THERAPY IN ADULTS

In 2016, most people started HIV treatment within a month of diagnosis

People are increasingly starting cART sooner after being diagnosed with HIV. Of those starting cART in 2016 more than half did so within one month, and more than 90 percent within 6 months after diagnosis (*Figure 4*). Importantly, this was the case irrespective of the CD4 cell count at diagnosis.

Figure 4: Time between HIV diagnosis and starting combination antiretroviral therapy (cART) for those starting cART between 2006–2016.



HIV IN THE NETHERLANDS KEY FINDINGS

In 2016
94%
of people started cART within 6 months of diagnosis

People are increasingly starting treatment with a less impaired immune system

People are increasingly starting cART at higher CD4 counts. The proportion of people with a CD4 count of 500 cells/mm^3 or above and who had begun cART within 6 months of diagnosis rose from 87% in 2015 to 94% in 2016.

What was the most common initial regimen in 2016?

Three-quarters of people started on an integrase inhibitor-containing regimen in 2016, with abacavir/lamivudine/dolutegravir and tenofovir alafenamide/emtricitabine/cobicistat-boosted elvitegravir being the most frequently prescribed initial regimens.

Toxicity is the main reason for changing treatment

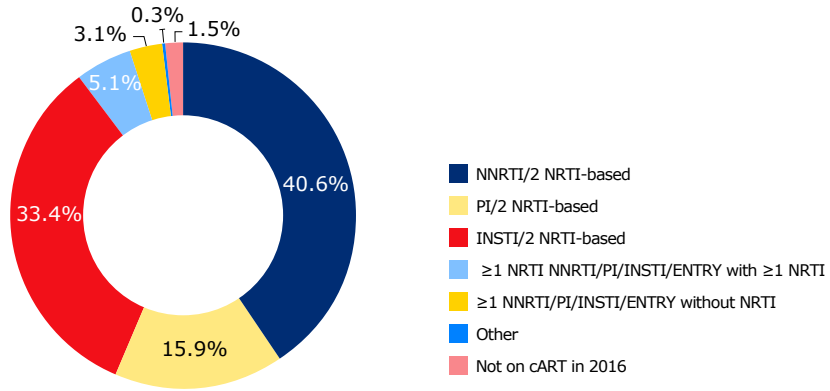
As in previous years, toxicity continued to be a main reason for discontinuing or switching the initial regimen during the first year of treatment. Toxicity-related discontinuations were often central nervous system-related, gastrointestinal, hepatic, or medication-related skin rash. Other, more recent, important reasons for discontinuation or regimen switch during the first year of treatment include regimen simplification or the availability of new drugs. Nonetheless, the time spent on the initial cART regimen has continued to increase over the years.

HIV IN THE NETHERLANDS KEY FINDINGS

Which cART regimens were most used in 2016?

Among all HIV-positive individuals in care and on treatment in 2016, the majority received a cART regimen based on two nucleoside reverse transcriptase inhibitors (NRTIs), combined with a non-NRTI (NNRTI, 41%), an integrase inhibitor (33%) or a protease inhibitor (16%) (*Figure 5*). The most commonly-prescribed regimens in 2016 were abacavir/lamivudine/dolutegravir (15%) and tenofovir disoproxil fumarate/emtricitabine combined with efavirenz (15%) or nevirapine (11%).

Figure 5: Combination antiretroviral therapy (cART) use in 2016 among HIV-positive individuals who ever started cART.



Legend: cART=combination antiretroviral therapy; ENTRY=entry inhibitor; INSTI=integrase inhibitor; NRTI=nucleoside reverse transcriptase inhibitor; NNRTI=non-NRTI; PI=protease inhibitor.

HIV IN THE NETHERLANDS KEY FINDINGS

Integrase inhibitor-based cART used increasingly frequently

Since its introduction a few years ago, integrase inhibitor-based cART has been implemented on a large scale in the Netherlands: in 2016, 39% of all adults in care and on cART received an integrase inhibitor, compared to 27% in 2015. While two-thirds of the population on cART in 2016 received a backbone consisting of tenofovir disoproxil fumarate/emtricitabine, the availability of new fixed-dose combinations has led to an increase in the use of abacavir/lamivudine and tenofovir alafenamide/emtricitabine.

Excellent virological response, including in long-term survivors

Both short-term and long-term viral suppression rates remain high and continue to improve. Of all adults in care and on cART in 2016, 97% had an undetectable viral load (<200 copies/ml). Individuals who had been diagnosed with HIV before 1990 and who remained in care and on cART in 2016 (i.e., long-term survivors) had equally high levels of viral suppression.

Changing cART landscape

Following revised HIV treatment guidelines, prompt cART initiation has continued to become more common in 2016. In recent years, the introduction of new integrase inhibitor-based once-daily fixed-dose combinations has changed the landscape of cART use in the Netherlands. All currently-recommended regimens are durable.

HIV IN THE NETHERLANDS KEY FINDINGS

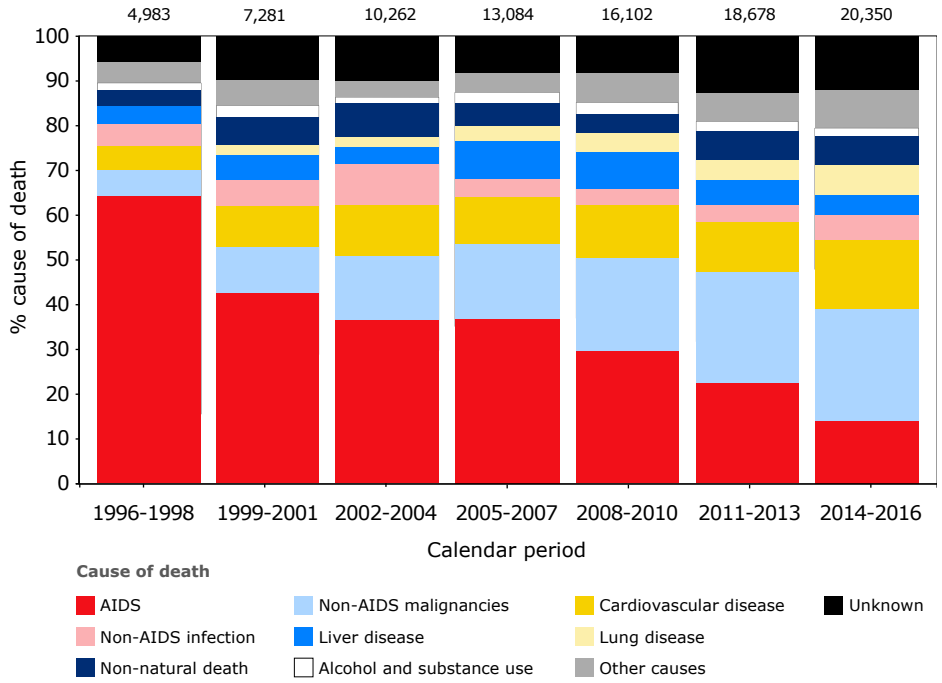
MORBIDITY AND MORTALITY

Sustained decline in AIDS-related death

Mortality remains low in HIV-positive individuals in care in the Netherlands. There has been a sustained decline in the risk of death from AIDS, with a shift towards death from non-AIDS comorbidities, including non-AIDS-defining malignancies (NADM), cardiovascular disease (CVD) and chronic liver disease (*Figure 6*).

In particular, the number and proportion of individuals dying of AIDS continues to decrease. Those cases of AIDS-related death that do occur are largely driven by late presentation and late entry into care, which once again stresses the importance of identifying and linking individuals to care earlier in the course of the infection.

Figure 6: Relative changes in cause of death in different calendar periods since the introduction of combination antiretroviral therapy (cART) in the Netherlands. Numbers above each bar represent the number of people at risk during that calendar period.

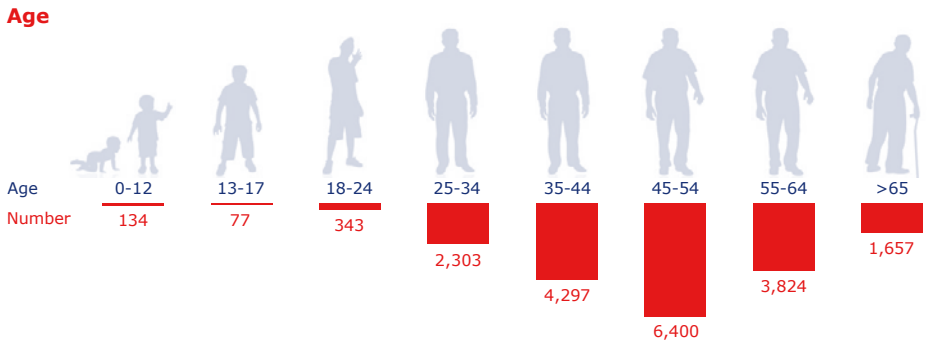


HIV IN THE NETHERLANDS KEY FINDINGS

Ageing and comorbidities

A substantial proportion of those people who were newly-diagnosed with HIV and entered HIV care in 2016 were older individuals; 27% were 50 years or older. At the same time, the overall population of people with HIV in care in the Netherlands also continues to age, with 46% currently older than 50 years compared with 39% in 2013 (*Figure 7*).

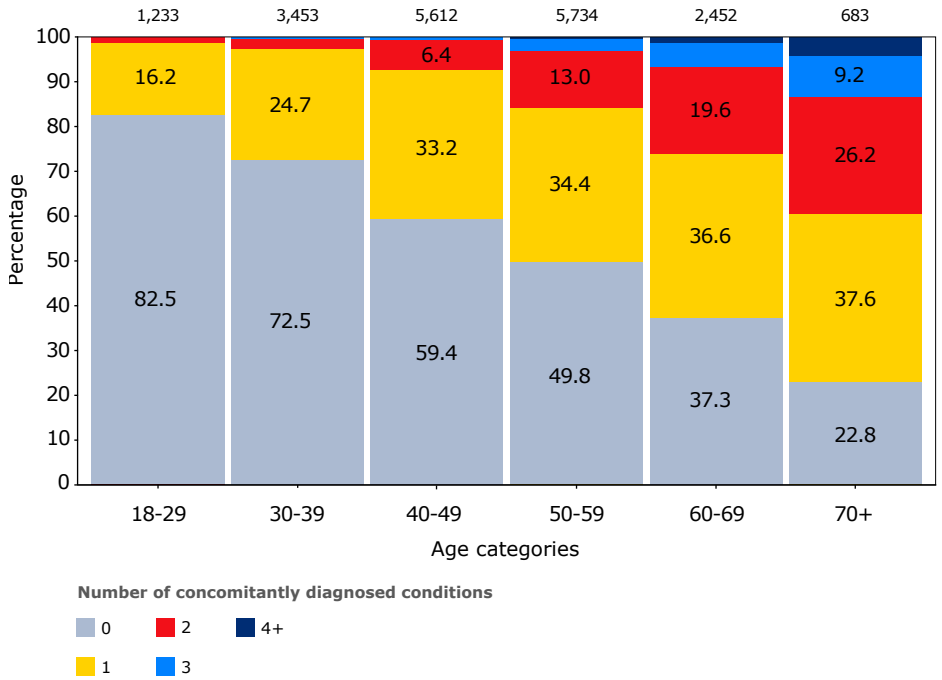
Figure 7: Age distribution of people living with HIV and in care in the Netherlands in 2016.



HIV IN THE NETHERLANDS KEY FINDINGS

As in the general population, older age was an important risk factor for comorbidities such as cardiovascular disease and non-AIDS malignancies. Of particular concern is the increasing proportion of individuals with multiple comorbidities, the risk of which appears to be increased in those with HIV (*Figure 8*).

Figure 8: *Prevalence of non-HIV/AIDS multimorbidity in adults in HIV care in 2016. Numbers on top of the bars represent the number of individuals contributing data to that age category.*



HIV IN THE NETHERLANDS KEY FINDINGS

Improved cardiovascular risk management

Despite the increasing age of the HIV-positive population, the proportion at high or very high cardiovascular risk only increased slightly over the period 2000-2016. This suggests that cardiovascular risk management may have improved over time. Significant room for further improvement remains, however, given the suboptimal use of statin therapy, antihypertensive therapy and antiplatelet therapy as secondary prevention following a myocardial infarction or ischaemic stroke, and the low uptake of these medications in the prevention of primary cardiovascular disease in high-risk individuals.

Non-AIDS malignancies

The most common non-AIDS malignancies are lung, anal, gastrointestinal, prostate, and head and neck cancers, and Hodgkin's lymphoma. Although the incidence rate of non-AIDS malignancies in the Netherlands has remained stable over time, the number of deaths due to these malignancies has increased. However, when taking the increasing age of the HIV-positive population into account, we did observe a decline in the risk of new non-AIDS malignancies in men, including anal cancer. This may be the result of a reduction in risk factors such as smoking, as well as expanded screening and treatment for early stages of anal cancer, together with a higher proportion of individuals living with higher CD4 cell counts in more recent years.

Improved awareness of risk factors may reduce comorbidity

Resilient ageing in people living with HIV with a lower comorbidity burden can be achieved by increasing awareness of the role of modifiable and often lifestyle-related risk factors among both physicians and the people living with HIV themselves. This is particularly relevant for older individuals and those with increased risk of comorbidity, and applies not only to conditions such as cardiovascular disease and diabetes mellitus, but also to cancer, chronic kidney disease, and loss of bone mineral density.

HIV IN THE NETHERLANDS KEY FINDINGS

HEPATITIS B AND C VIRUS CO-INFECTIONS

Hepatitis B and C virus screening is now universal

Hepatitis C virus (HCV) and hepatitis B virus (HBV) co-infections are far more prevalent in HIV-positive individuals than in the general Dutch population due to shared routes of transmission with HIV. Screening for HCV and HBV co-infection is part of the standard of HIV care in the Netherlands and, as a result, the presence or absence of these coinfections is documented for virtually all HIV-positive individuals.

Hepatitis C virus co-infection

Approximately 12% of all individuals monitored by SHM had evidence of ever having been exposed to HCV, 6% were documented as being chronically infected with HCV, and 2% were documented as having an acute HCV infection. Most individuals with HCV infection were male and from the Netherlands or other European countries.

Hepatitis B virus co-infection

The prevalence of HBV has decreased over time as a result of increased HBV vaccination rates, together with the HBV-prophylactic effect of tenofovir in HIV treatment. Six percent of individuals ever in care were found to have chronic HBV infection.

HBV vaccination remains a priority

An estimated 30% of HIV-positive individuals overall and 18% of MSM had not been exposed to HBV and had not been successfully vaccinated and therefore may remain at risk of acquiring HBV. These findings illustrate the importance of continuing our efforts to increase successful HBV vaccination rates in this subgroup, particularly in those who are not receiving a tenofovir-containing antiretroviral regimen.

HIV IN THE NETHERLANDS KEY FINDINGS

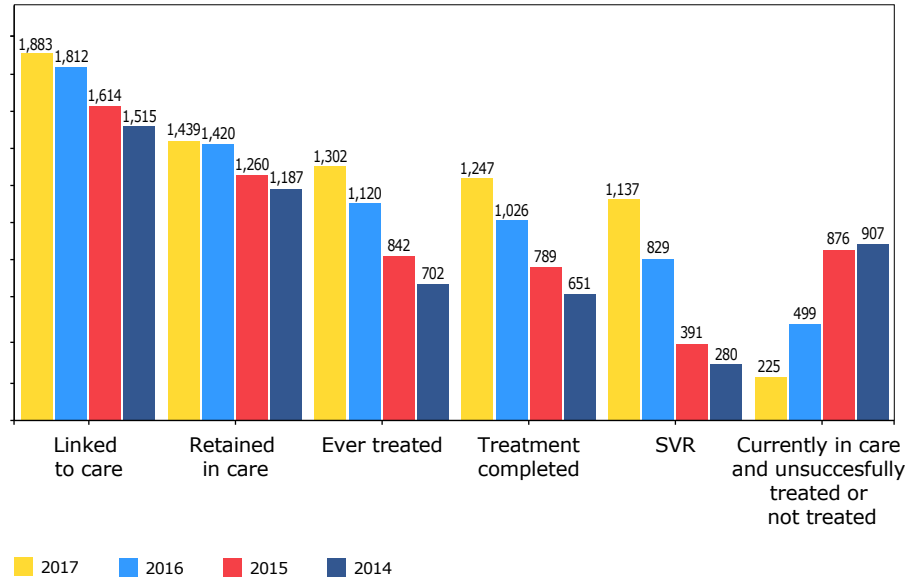
Risk of dying from HCV or HBV co-infection is decreasing

Overall, HIV-positive individuals with HCV or HBV co-infection remain at increased risk of liver-related morbidity and mortality. However, in people diagnosed with chronic HCV or HBV after 2000 (following introduction of tenofovir), there has been a significant reduction in the risk of liver-related death. For those with chronic HBV infection, this is likely a result of increasingly effective HBV treatment through the use of tenofovir-containing cART.

Successful HCV treatment with direct-acting antivirals

Our data clearly show that, with the advent of novel direct-acting antiviral agents (DAAs) since 2014, pegylated interferon-containing regimens have largely been replaced in clinical practice by a variety of DAAs. Moreover, as a result, the large majority of HIV-positive individuals with HCV co-infection have received treatment for HCV. By 2017, over 750 individuals had received, or were receiving, treatment with novel DAAs. Of all people treated with DAAs, 97% achieved a sustained virological response and had no evidence of an active HCV infection. These developments have resulted in fewer HCV co-infected individuals still requiring treatment compared with last year's report (225 as of May 2017 versus 499 as of August 2016), in spite of an increase in the total number of individuals who have ever had HCV co-infection and were in care (1,439 as of May 2017 versus 1,420 as of August 2016) (*Figure 9*).

Figure 9: Hepatitis C virus continuum of care.



Legend: SVR=sustained virological response.

HIV IN THE NETHERLANDS KEY FINDINGS

Successful HCV treatment prevents HCV transmission

Successful treatment of HCV may also prevent onward HCV transmission. Evidence for declining HCV transmission is based on the lower number of acute HCV infections observed in the past year and the rapid decline in prevalence of active HCV infections, with prevalence in MSM declining to less than 1.5% in 2016. Nonetheless, despite a drop in the re-infection rate in most recent years, cases of HCV re-infection following successful treatment are still being reported, indicating that HCV transmission is still taking place.

Regular HCV screening among MSM recommended

Over time, the rapidly expanding availability of DAA regimens for HCV, together with optimised screening for HCV co-infection, is expected to limit the impact of HCV co-infection on long-term liver-related morbidity and mortality; however, this effect should be monitored. To reduce new HCV infections among the key affected population of MSM, regular screening for HCV among successfully-treated individuals is recommended for early detection of HCV re-infections, in combination with preventive behavioural interventions.

HIV IN PREGNANT WOMEN AND IN CHILDREN

Perinatal transmission has become extremely rare

The number of pregnancies in women living with HIV in the Netherlands has declined over time. The proportion of women with an undetectable viral load on cART at the time of delivery, the most important factor in preventing vertical transmission of HIV, has increased considerably and is now close to 100%. Together with universal first-trimester screening for HIV in pregnant women, this has made perinatal transmission of HIV extremely rare in the Netherlands.

To ensure zero vertical transmissions of HIV, there is a need for continued vigilance for HIV infections during pregnancy.

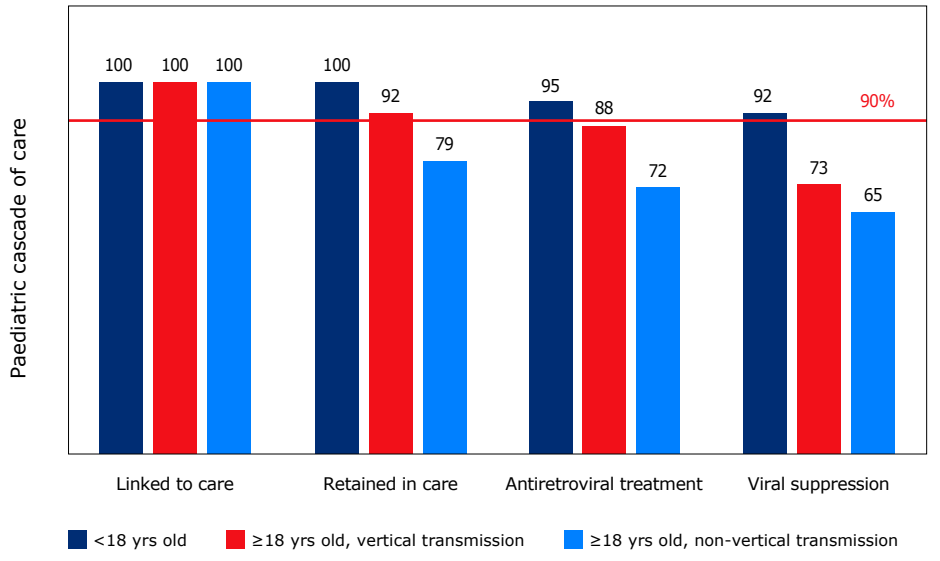
HIV IN THE NETHERLANDS KEY FINDINGS

Favourable outcomes for HIV-positive children

Of the 590 children diagnosed with HIV before the age of 18 years and ever registered by SHM, the majority (80%) are still in care. Of those who were registered before 18 years of age and who are currently in care, 115 (24%) acquired HIV in their country of birth and were subsequently adopted by Dutch parents.

There is a high retention-in-care rate among children currently under 18 years of age. Outcomes for children who are receiving cART are favourable, with a low mortality rate and good long-term immunological responses to treatment (*Figure 10*).

Figure 10: *Cascade of care by age and route of HIV acquisition, as of 31 December 2016. Numbers on top of the bars indicate the proportion of individuals.*



HIV IN THE NETHERLANDS KEY FINDINGS

Poorer viral suppression around transition to adult care

Of those individuals who were originally registered as a child and were still in care in 2016, 57% were older than 18 years of age on 31 December 2016. Of those children moving from paediatric to adult care, 30% did not have suppressed viraemia at the time of transition, suggesting challenges for these adolescents with respect to adherence to treatment around the time of transition to adult care.

Once in adult care, young adults were also less likely to have an undetectable viral load at their most recent clinic visit, and those with non-vertically-acquired HIV were more likely to be lost to follow up.

Optimisation of long-term care for young people
The large number of adolescents who have inadequately-suppressed viraemia at the time of transitioning to adult care illustrates that long-term care for this particularly vulnerable and difficult-to-manage group of young individuals clearly needs to be further optimised.

QUALITY OF CARE

High overall retention in care

The quality of care provided in Dutch adult HIV treatment centres was explored using indicators based on the national guidelines issued by the Dutch Association of HIV-Treating Physicians. Overall, retention in care was found to be high in most HIV treatment centres in the Netherlands, although it was lower for people from non-Dutch origin.

Earlier start of cART and high rates of viral suppression

In addition, across most centres, people are starting cART sooner after entering care, confirming that most centres are following the guideline to offer cART to everyone with newly-diagnosed HIV regardless of CD4 count. However, there are some centres in which this policy could be improved further for people who enter care with CD4 cell counts above 350 cells/mm^3.

Viral suppression rates in the first 6 months on cART, as well as during longer term use of cART, were high across all centres regardless of the number of people in care at a particular centre.

HIV IN THE NETHERLANDS KEY FINDINGS

Heterogeneity between centres in repeat HCV screening

Greater heterogeneity was observed in repeat HCV screening in MSM. This variation is due to a difference in screening policy, with some centres screening partly on the basis of elevated liver enzymes. Given that HCV transmission still occurs, continued monitoring of (repeat) HCV screening rates is certainly warranted.

HIV IN CURAÇAO

In recent years, individuals with HIV in care at the St Elisabeth Hospital in Willemstad in Curaçao appear to be diagnosed increasingly earlier in their infection, as shown by a declining proportion of individuals presenting late for care. As a consequence, cART is being started at increasingly higher CD4 cell counts. However, although early start of treatment appears to be possible, long-term continuous follow up should be guaranteed to optimise the effect of treatment.

Amsterdam Cohort Studies

The Amsterdam Cohort Studies (ACS) on HIV and AIDS started in 1984 among men who have sex with men (MSM) and were expanded in 1985 to include people who use drugs. 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 MSM and in men and women who use drugs. 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 further extended with prospective testing for STI and human papillomavirus infection.

From the outset, research within the ACS has taken a multidisciplinary approach. The collaborating institutes within the ACS framework are the Public Health Service of Amsterdam (*Geneeskundige en Gezondheidsdienst Amsterdam*; GGD Amsterdam), the Academic Medical Center of the University of Amsterdam, MC Jan van Goyen, Sanquin Blood Supply Foundation, DC Klinieken Lairesse - 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). The scientific studies are funded separately by external sources.

Following consultation with the ACS's scientific advisory group in 2015, follow up of people who use drugs ended in 2016 due to the absence of new HIV and hepatitis C infections in preceding years. In 2016, 182 end-of-study interviews were held. During the 31 years of follow up, 1,680 people who use drugs took part in the study and made a combined total of 28,011 visits to the ACS.

In line with the plan presented to the International Scientific Advisory Committee, which issued a positive evaluation of the ACS in 2013, expansion of the group of HIV-negative participants in the MSM cohort was initiated in 2015. The aim is to have expanded the ACS to a total of 750 HIV-negative MSM in active follow up by the end of 2018. In 2017, an online recruitment campaign was developed and special efforts were made to recruit younger MSM (below 30 years of age). In 2017, 60 new participants were included in the ACS.

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AMSTERDAM COHORT STUDIES

In addition to the large group of HIV-negative MSM, the ACS also follow a group of HIV-positive MSM. This follow up takes place primarily through the regular HIV medical care and through monitoring by SHM. In addition to the standard medical care, samples are collected and stored for specific immunological and virological studies. These samples are collected from HIV seroconverters who acquired HIV during the ACS follow up and from some of the individuals who were already HIV-positive at inclusion in the ACS. In addition, body material from the HIV-negative men is also collected and stored as part of the ACS.

As of 31 December 2017, 2,809 MSM had ever participated in the ACS. Since the start of the ACS, these MSM have made 59,024 study visits. In 2017, 711 MSM, 57 of whom were HIV-positive, had made a study visit to the GGD. The preliminary HIV incidence within the ACS in 2017 was 0.48 per 100 person years, with an absolute number of 2 HIV diagnoses in that year.

60
new ACS participants in 2017

711
MSM had a study visit in 2017

Communication activities

The HIV Monitoring Report 2017.

Stichting HIV Monitoring actively disseminates information about its activities through a wide variety of communication channels. In doing so, we aim to provide relevant information to people living with HIV, their healthcare providers, researchers, other health care professionals, the media and other interested parties. This chapter provides an overview of the main communication activities undertaken in 2017.

EXTERNAL COMMUNICATION ACTIVITIES

HIV Monitoring Report 2017: HIV Infection in the Netherlands

Each year, we publish our HIV Monitoring Report just before 1 December, World AIDS Day. The Monitoring Report is written by SHM researchers in close collaboration with a small group of reviewers consisting of HIV treating physicians and experts in public health, whose in-depth knowledge on relevant chapter topics is highly valuable in shaping the content of the chapters.

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. In addition, the Monitoring Report describes trends in HIV-related and non-AIDS-related morbidity and mortality, and includes a chapter dedicated to viral hepatitis. Finally, the 2017 Monitoring Report included a chapter on quality of care in the HIV treatment centres in the Netherlands. The main findings from the 2017 Monitoring Report are described in an earlier section of this annual report (*HIV in the Netherlands in 2017: Key findings from our latest HIV Monitoring Report*) and were also presented at the 11th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) by our director, Peter Reiss.

Distribution of 2017 HIV Monitoring Report

The 2017 HIV Monitoring Report was distributed as an online PDF on our website. In addition, all figures and tables were made available in the form of a downloadable PowerPoint presentation on our website. The report's Summary and Recommendations section was also printed in both Dutch and English and distributed to stakeholders, together with an updated infographics factsheet. In addition, the printed Summary and Recommendations was included in the conference bags at NCHIV and at the national conference on sexually transmitted diseases and HIV (Nationaal Congres Soa*Hiv*Seks) held on 1 December 2017.

Scientific output

In addition to the yearly Monitoring Report, SHM also contributes to the understanding of the HIV/AIDS epidemic and the effect of antiretroviral treatment on the course of HIV infection and co-infections/co-morbidities through research projects and scientific publications. In 2017, SHM's ATHENA cohort data were included in 62 publications in peer-reviewed national and

COMMUNICATION ACTIVITIES

international scientific journals and 53 oral and poster presentations at international and national peer-reviewed conferences, workshops and meetings. A full overview of the scientific output is included in a later section of this report.

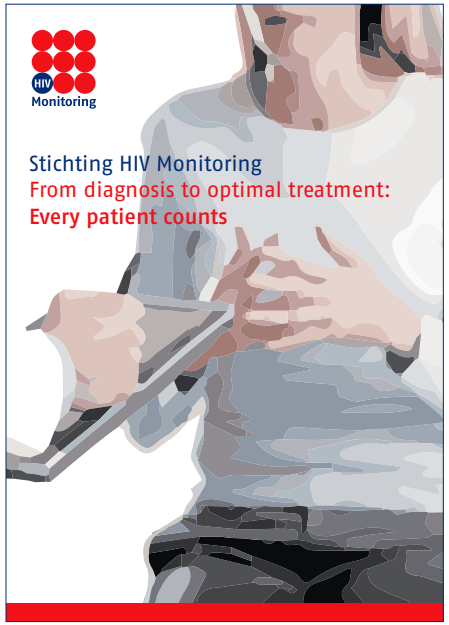
2016 annual report

Our 2016 annual report was published online in May 2017. In addition to an overview of the organisational structure, the annual report provided a detailed overview of the data collection and quality control activities undertaken in 2016 and a summary of the population registered in SHM's database as of 31 December 2016. The annual report also comprised a list of SHM's national and international collaborations, progress reports on research involving SHM's data, and a comprehensive overview of the resulting scientific output. Finally, the annual report included the financial report on our activities in 2016.

eNewsletter

The eNewsletter was sent out three times in 2017 and remains well read, with average open rates of 34% and 30% for the Dutch and English-language newsletters, respectively. In 2017, the eNewsletters 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. The 2017 newsletters also contained the *Spotlight on SHM research* item, showcasing a recent publication involving SHM data. Finally, in November 2017, the English-language newsletter was also published in print format and distributed at NCHIV 2017. All newsletters are archived on the website and can be accessed via a direct link on the homepage.

SHM's patient leaflet.



Patient leaflet and factsheet

Our patient leaflet provides a simple explanation of our activities and data collection process. Produced in both Dutch and English, this leaflet illustrates how coded data provided by people living with HIV in the Netherlands help to drive further improvements in HIV care through national and international research. The leaflet is accompanied by a factsheet insert that uses infographics to summarise the key figures from the latest Monitoring Report. Both the leaflet and the factsheet are intended for distribution to new patients by HIV treating physicians and HIV nurse consultants, and are well-received by the HIV treatment centres.

As well as being distributed with the printed Monitoring Report Summary and Recommendations to our stakeholders, the updated infographics factsheet was also included in conference bags at NCHIV 2017 and at the *Soa*Hiv*Seks* conference. In addition, copies of the updated factsheet and revised patient leaflet were sent to all treatment centres for distribution to new patients. The leaflets and insert are also available for download on our website.

COMMUNICATION ACTIVITIES

SHM researcher, Ard van Sighem, giving a talk in Istanbul earlier this year.

SHM website

During the course of 2017, our website was updated on an ongoing basis. For example, news items about SHM or relevant to the field of HIV treatment and research were placed on the homepage at regular intervals, along with updates about the latest research projects, presentations and publications involving our data. The website also provides an up-to-date list of treatment centres.

Events

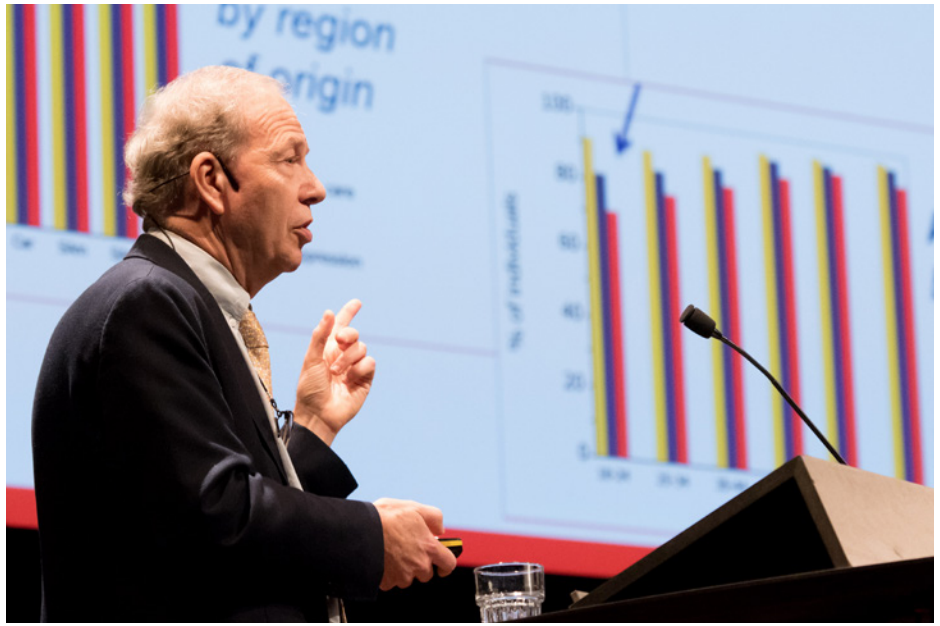
In 2017, our researchers and collaborators presented their work with SHM data at various international and national conferences and meetings. While further information on these presentations can be found later in this report, two Netherlands-based events are described in more detail below.

Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV)

In 2017, SHM organised the 11th annual Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV), in collaboration with the Centre for Infectious Disease Control Netherlands of the National Institute for Public Health and the Environment (RIVM-CIb), the Aidsfonds, the Amsterdam Institute for Global Health and Development (AIGHD)/ Department of Global Health of the Academic Medical Center of the University of Amsterdam (AMC-UvA) and the Dutch Association of HIV-Treating Physicians (NVHB).

NCHIV 2017 was well-attended, with a little under 300 participants. During the course of the day, there were 21 presentations, including an update on the HIV epidemic in the Netherlands by SHM director Peter Reiss and four plenary talks by pre-eminent guest speakers on topics such as HIV-related issues in migrant populations, long-working formulations for HIV treatment and prevention, how HIV infiltrates the immune system and the approach to ending the HIV epidemic in New York. The remaining 16 talks comprised oral abstract

COMMUNICATION ACTIVITIES



Our director, Peter Reiss, presenting the latest HIV figures at NCHIV 2017.

presentations on the pathogenesis, epidemiology, prevention and treatment of HIV and HIV/HCV co-infection. During the lunchtime poster session, 46 posters were presented for viewing. The lunch break also included an oral poster discussion session, entitled *Reaching and serving key populations*. During this session, there were five short oral presentations of selected posters, followed by an interactive discussion.

World AIDS Day

On World AIDS Day, 1 December 2017, Stichting HIV Monitoring was present at the *Soa*Hiv*Seks* conference, with a stand providing information about SHM's activities.

INTERNAL COMMUNICATION ACTIVITIES

Intranet

This externally-accessible, password-protected platform provides a central point of information for all our employees, with up-to-date contact details, HR documents, standard templates, and internal news and meetings. In addition, during 2017, regular updates were posted on the progress of the replacement data entry database (DataCapTree) and information and useful tips were shared regarding data protection.

Internal newsletter

In 2017, the internal Dutch-language newsletter, entitled *SHM Positive: a collection of all the internal news*, was published four times. It continues to provide a channel through which all employees, including those working outside the SHM offices in Amsterdam, can get to know new colleagues and stay up to date with internal developments, relevant issues such as privacy legislation, and upcoming events.

COMMUNICATION ACTIVITIES

*SHM at Soa*Hiv*Seks.*

Internal meetings

An internal meeting for all SHM employees is held on a bi-monthly basis. During this meeting, any internal developments are discussed and staff are brought up to date on recent scientific developments relevant to SHM's work, either by an invited speaker or one of our researchers. Scientific topics covered in 2017 included reasons for stopping dolutegravir or elvitegravir, quality of HIV care and the implementation of HIV treatment guidelines, and highlights of various conferences throughout the year, such as CROI, IWHOD and IAS 2017. During 2017, the internal meetings also included information on SHM's privacy policy and HR-related issues, in addition to regular updates on the progress of the project to replace the Oracle Clinical data entry database.

Our collaborations in 2017

Stichting HIV Monitoring (SHM) participates in both national and international scientific research collaborations. An overview of these collaborations is provided below.

NATIONAL COLLABORATIONS

AMC–UvA

SHM collaborates with the Academic Medical Center (AMC) of the University of Amsterdam (UvA) on various projects. Led by Prof. Peter Reiss (department of Global Health and division of Infectious Diseases at the AMC-UvA, and director of SHM), the *Co-morbidity and Ageing with HIV* (AGEhIV) cohort study aims to assess the incidence and prevalence of a broad range of comorbidities and known risk factors for these comorbidities in HIV-positive individuals compared with HIV-negative individuals.

Another collaboration closely associated with the AGE$_h$IV cohort study, is the COBRA (*Comorbidity 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 comorbidity 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 comorbidities. The results obtained from this research may be used to inform and adapt national and international guidelines for prevention and management of comorbidities in ageing HIV-positive individuals. COBRA's EU funding formally ended March 1, 2017, but scientific productivity based on collected data and biomaterial will continue during the coming years.

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/ department of Global Health at the AMC-UvA. The project is a multidisciplinary and interdisciplinary collaboration that aims to reduce the number of new HIV infections in Amsterdam and involves various stakeholders from preventative and curative HIV care and from other target groups (see the H-TEAM website for full list of participating organisations).

RIVM–CIb

The Centre for Infectious Disease Control Netherlands of the National Institute for Public Health and the Environment (*Centrum Infectieziektenbestrijding, Rijksinstituut voor Volksgezondheid en Milieu*; RIVM-CIb) coordinates the control of infectious diseases, including 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

OUR COLLABORATIONS IN 2017

hepatitis B virus (HBV) and hepatitis C virus (HCV), as well as infectious diseases such as tuberculosis. For the purpose of national HIV surveillance work carried out by the RIVM-CIb and to fulfil RIVM-CIb's reporting requirements to the European Centre for Disease Prevention and Control (ECDC), the RIVM-CIb and SHM regularly exchange data collected through SHM's framework.

GGD Amsterdam

SHM contributes to the *MSM Observational Study of Acute Infection with Hepatitis C* (MOSAIC) 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 study aims to look at how this group contributes to the transmission of HIV, to explore the driving factors of the HCV epidemic and HIV's role in this epidemic, 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 are primarily funded through the RIVM-CIb. Since 2015, ACS funding has been included in the structural institute grant awarded to SHM by the ministry of Health, Welfare and Sport through the RIVM-CIb.

Finally, the GGD participated in the aMASE study, which was part of EuroCoord. This study aimed to identify barriers that migrant communities face when accessing healthcare, so that HIV prevention, diagnosis and prognosis may be improved in migrants in Europe. SHM provided clinical data required for the Netherlands' part of the study.

aMASE was part of EuroCoord, the collaboration that encompassed all EU-funded cohort studies in the field of HIV and that ended in 2015. For the time being, scientific productivity within aMASE is continuing based on the last available joint dataset.

Pilot registration and monitoring of hepatitis C mono-infection

The National Hepatitis Plan (RIVM report 2016-0166) adopted in 2016 aims to enhance initiatives regarding viral hepatitis control in the Netherlands according to five themes. One of these themes is improved surveillance and monitoring of HBV and HCV to gain insight into the cascade of care. The Dutch Society for Internal Medicine (*Nederlandse Internisten Vereniging*, NIV) and the Dutch Association of Gastroenterologists and Hepatologists (*Nederlandse Vereniging Van Maag-Darm-Leverartsen*, NVMDL) established a steering committee that elected to work together with SHM to implement such a monitoring system. A working group was subsequently established, comprising representatives from NIV, NVMDL, the Dutch Association of

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OUR COLLABORATIONS IN 2017

HIV-Treating Physicians (NVHB) and SHM. As a first step, the working group has agreed to set up a pilot registration of individuals who are in care with a hepatitis C mono-infection and who have received direct-acting antiviral treatment. During 2017, the working group established the scope and implementation process of this pilot registration, which will take place at a select number of clinical centres. In 2017, SHM took the necessary preparatory measures for the pilot project, which is expected to start in the second or third quarter of 2018.

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 was to use the scientific strengths of each collaboration to ensure that the best, most competitive research was performed. EuroCoord formed a large, integrated network with a common virtual database, which currently contains data from more than 250,000 HIV-positive individuals from many different settings within and outside Europe. EuroCoord's multidisciplinary approach has allowed HIV research into a number of key areas aimed at improving the management and quality of life of HIV-positive individuals, while also exploring differences within subgroups.

EuroCoord was funded for a period of 5 years from 2011 onwards as part of the European Commission's 7th Framework Programme. Funding for EuroCoord and associated collaborations (see below) therefore ceased on 31 December 2015. Some of its associated collaborations (in particular, EPPICC and EuroSIDA) have succeeded in continuing parts of their research agendas through alternative funding mechanisms.

COHERE

The *Collaboration of Observational HIV Epidemiological Research in Europe* (COHERE) is a unique collaboration of 33 cohorts in Europe that aims to conduct epidemiological research on the prognosis and outcome of HIV-positive populations from across Europe, including children, pregnant mothers, and other adults.

COHERE was part of EuroCoord, the collaboration that encompassed all EU-funded cohort studies in the field of HIV and that ended in 2015. For the time being, scientific productivity continues based on the last available joint dataset.

Papers published by COHERE in 2017

OUR COLLABORATIONS IN 2017

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 was to monitor the course of HIV infection from the time of infection onwards. The Amsterdam Cohort Studies (ACS) participated in this study through their HIV seroconverted participants.

CASCADE was part of EuroCoord, the collaboration that encompassed all EU-funded cohort studies in the field of HIV and that ended in 2015. For the time being, scientific productivity within CASCADE is continuing based on the last available joint dataset.

Papers published by CASCADE in 2017

EuroSIDA

The EuroSIDA study is a prospective, observational cohort study of more than 16,500 individuals followed in 103 hospitals in 32 European countries, plus Israel and Argentina. The main objective of the study is to assess the outcomes of HIV-positive individuals across Europe, with an important focus on assessing regional differences across 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 for EuroSIDA.

EuroSIDA was part of EuroCoord, the collaboration that encompassed all EU-funded cohort studies in the field of HIV and that ended in 2015. EuroSIDA has since undergone reorganisation and secured alternative funding to continue this longstanding, highly successful collaboration.

Papers published by EuroSIDA in 2017

RESPOND

In addition to its activities described above, EuroSIDA is also a founding partner of the newly-formed *International Cohort Consortium of Infectious Disease* (RESPOND). RESPOND is a non-interventional, non-randomised, open-label, multi-cohort observational study. The aim of RESPOND is to build a flexible and dynamic cohort consortium for the study of infectious diseases, including HIV and people at risk for HIV.

EuroSIDA will be contributing patient data to RESPOND, together with other cohorts participating in the consortium. In 2018, SHM will contribute pseudonymised data from a number of ATHENA patients for designated RESPOND projects, alongside those data from ATHENA cohort patients already included in EuroSida.

OUR COLLABORATIONS IN 2017

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 living 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.

EPPICC was part of EuroCoord, the collaboration that encompassed all EU-funded cohort studies in the field of HIV. Within EuroCoord, EPPICC was part of the HIV in children collaboration, *Paediatric European Network for Treatment of AIDS* (PENTA). With EuroCoord having ended in 2015, EPPICC has successfully secured alternative funding to continue its research.

Papers published by EPPICC in 2017

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 cART in therapy-naive individuals. In 2017, Prof. Peter Reiss and Dr Ard van Sighem represented SHM in the ART-CC steering group.

Papers published by ART-CC in 2017

D:A:D

The *Data Collection on Adverse Events of Anti-HIV Drugs* (D:A:D) was a prospective multi-cohort study that focused on the potential association between antiretroviral drugs and cardiovascular disease, liver and renal disease, and non-AIDS-defining malignancies.

Funding for the D:A:D study ceased as of 1 February 2016. For the time being, scientific productivity continues based on the last available joint dataset.

Papers published by D:A:D in 2017

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

OUR COLLABORATIONS IN 2017

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 2017, SHM continued its leading role in an ECDC project to better estimate HIV incidence and the undiagnosed population living with HIV in Europe and within individual European countries. In addition, SHM is partner in a collaborative multi-year project led by Dr Annabelle Gourlay and Prof. Kholoud Porter from University College London to improve the monitoring of the HIV continuum of care in Europe.

HIV-CAUSAL

The HIV-CAUSAL collaboration, led by Prof. Miguel Hernan at Harvard University's T.H. Chan School of Public Health, is a multinational collaboration of prospective studies of HIV-positive individuals from six European countries, Brazil, Canada and the United States. Originally HIV-CAUSAL was an acronym for *HIV Cohorts Analyzed Using Structural Approaches to Longitudinal data*. The collaboration aims to answer three main questions: when to start antiretroviral therapy, what antiretroviral regimen to use initially, and when to switch to another regimen. These questions are unlikely to be answered by a single study and therefore require a collaborative approach.

The HIV-CAUSAL collaboration pools data collected for clinical purposes within healthcare systems with few barriers to access. The data are analysed using methods specifically designed for causal inference from complex longitudinal data.

The HIV-CAUSAL collaboration is designed to inform evidence-based guidelines and the planning of clinical trials. In addition, the collaboration facilitates understanding and training in causal modelling across leading HIV observational research groups in the United States and Europe.

Papers published by HIV-CAUSAL in 2017

Imperial College London and Oxford University

SHM has had a longstanding collaboration since 2002 with the Department of Infectious Disease Epidemiology (DIDE), which is part of the Faculty of Medicine, Imperial College London. The collaboration focuses on using mathematical modelling and viral phylogenetics to improve our understanding of the HIV epidemic and the potential impact of different interventions, including 'treatment as prevention' and pre-exposure prophylaxis (PrEP). Until recently, Prof. Christophe Fraser coordinated the collaboration with SHM as part of the faculty at Imperial College London, and currently continues to do so from his new position at the Big Data Institute of Oxford University's Li Ka Shing Centre for Health Information and Discovery.

OUR COLLABORATIONS IN 2017

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

SHM also closely collaborates with Imperial College's DIDE (Dr Mikaela Smit and Prof. Tim Hallett) in modelling the future burden of non-communicable comorbidity and the expected impact of various interventions in the ageing population with HIV in care in the Netherlands.

Papers published by BEEHIVE in 2017

RDI

The *HIV Resistance 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 resistance measurements are not available.

The developed models power the RDI's HIV Treatment Response Prediction System (HIV-TRePS), a free online tool enabling informed, individualised treatment decision-making.

Scientific output in 2017

Scientific output

IN 2017

In 2017, Stichting HIV Monitoring (SHM) received 6 new requests to make use of SHM's cohort data, 3 of which have been approved to date. During the year, 62 articles were published in international peer-reviewed journals. In addition, 53 abstracts were accepted for presentation at 15 meetings and conferences (27 posters and 26 oral presentations). An overview of research projects, publications and presentations can be found on our website.

62
peer-reviewed articles

53
presentations at 15 meetings

Completed research projects

I14096 Primary and recurrent venous thromboembolism in HIV-1 (PREDICT study)
Borjas-Howard J, Rijnders BJA, Rokx C, Tichelaar YIGV, Verbon A, Meijer K.

I14144 GIS-hiv: Geographical Information System to determine high prevalence areas of targeted screening and early case-finding
Op de Coul ELM, Joore IK, van Sighem AI, Bom BCJ, Hillebregt M, Prins JM, Geerlings SE, van Bergen JEAM.

I14157 Overlap between HIV and HCV networks among MSM with HIV/HCV coinfection
Vanhommerig J, Schinkel J, Bezemer D, van der Laar T, van Sighem A, Smit C, Prins M.

I15022 Community viral load as a tool for HIV surveillance in the Netherlands
Op de Coul E, Bolijn R, Heijne J, van Sighem A, Kretzschmar M.

I15142 Use of regular outpatient medication in HIV/HCV co-infected patients in the Netherlands
Smolders E, Burger D, Arends J, van der Valk M, Brinkman K, Rijnders B, Dofferhof T.

Ongoing research projects

I04034 The data collection on adverse events of anti-HIV drugs (D:A:D)

Reiss P.

Date of approval: 2000

Background: Since its start in 2000 until its formal closure in February 2016, the study, which was conceived in 1999, has successfully followed close to 24,000 patients from 11 cohorts in Europe, Australia and the United States.

Methods: The study has been highly successful in meeting 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.

Results: The results from the study are regularly presented at major international conferences (including at CROI 2017), published in high-ranking peer-reviewed journals, and also continue to inform and influence changes in national and international HIV treatment guidelines.
All presentations and publications, including the most recent, can be found on www.cphiv.dk/DAD.

Conclusions: In spite of the study having been highly productive and having generated influential and important findings, it had to be formally stopped on 1 February 2016, given that the Study Group and the D:A:D Oversight Committee were unsuccessful in securing continued funding.
The final data merger was executed in the summer of 2016 on data and validated clinical events accrued up to 1 February 2016. For the time being, scientific productivity continues based on the last available joint dataset.

I05513 HIV Resistance Response Database Initiative (RDI)

Revell A, Larder B, Wang D, Coe D.

Date of approval: 1 October 2005

The main activities of the RDI during 2017 using ATHENA data were as follows:

1. Retrospective evaluation of HIV-TRePS in HIV patients from an unfamiliar setting

Objectives: (1) To evaluate the predictive accuracy of the RDI's latest models that do not require a genotype for their predictions with an independent set of data from an unfamiliar clinical setting (one with no data in the training set used to develop the models). (2) To assess the potential clinical utility of the models for patients from the unfamiliar setting through *in silico* modelling of alternative regimens for patients who failed the new regimen introduced in the clinic.

Read full methods and results here.

ONGOING RESEARCH PROJECTS

Conclusions: In this very small study, the current models used in the HIV-TRePS system for cases without genotypes predicted virological responses to a new antiretroviral regimen introduced in the YRG clinic (Chennai, India) with accuracy that is reduced from that seen during model cross-validation and testing with an independent global test set. Nevertheless, the accuracy was somewhat higher than that observed in numerous studies of genotyping and rules-based interpretation as a predictor of treatment outcomes.

The HIV-TRePS models, using a respond/fail cut-off derived during cross validation, tended to over-predict responses for YRG cases. This may have been due to the longer follow-up times in the YRG data than is typically the case with data provided to RDI, although this remains conjecture.

2. Modelling HIV treatment outcomes with genotypes for HIV-TRePS

Objectives: (1) To develop random forest (RF) models that utilise a genotype to predict virological response to antiretroviral therapy following a switch after virological failure, with the maximum possible accuracy and including as many antiretroviral drugs as possible, as a potential treatment support tool within HIV-TRePS. (2) To compare two different screening strategies to eliminate possibly non-adherent patients from the treatment change episodes (TCEs) used to train and test the models. (3) To evaluate the performance of the models with substantial independent test sets. (4) To compare the performance of the models with each other and with that of genotyping with rules-based interpretation.

Read full methods and results here.

Discussion: The H2 models (trained and tested using data screened with the new adherence filter) were slightly more accurate than the H1 models trained using the old adherence filter. The differences were not statistically significant.

Both sets of models were highly significantly more accurate than genotyping. The in silico analysis using the H2 models was also highly successful with the models identifying alternative regimens that were predicted to give a response in around 90% of cases that failed their new regimen in the clinic.

The new H2 filter removed 60 TCEs from the pool of 1,000 test TCEs, whereas the old filter only removed just 3 cases. The H2 models performed very similarly to the H1 models for the H1 test set, consistent with them being slightly more accurate, but only for those cases that were adherent. In any test with unfiltered cases (as in real life) the models can only be accurate (and the H2 model possibly more accurate) for adherent cases. The results overall for a sample population overall may not be improved noticeably.

Interestingly the H1 models performed slightly better with the H2 test set than with the H1 test set. This is to be expected. The models will tend to

ONGOING RESEARCH PROJECTS

'ignore' the 'noise' created by non-adherent patients during extensive learning (in fact the H2 models were easier to train than the H1 models), but if the test set includes the 60 presumed non-adherent cases this is still likely to have a negative effect on the accuracy of those models.

3. The development of computational models for the prediction of absolute plasma HIV-1 RNA levels over time after a change of cART following virological failure

Background: The objective of this study was to develop computational models that predict the absolute plasma viral load over time after a change to antiretroviral drug treatment in the context of virological failure. This contrasts with the RDI's customary approach of modelling an estimate of the probability of the follow-up viral load being <50 copies HIV RNA/ml. The clinical goal is a decision support system that can provide more useful information about treatment response for clinicians in different settings using different definitions of virological failure and response.

Read full methods and results here.

Discussion: These experimental models achieved reasonably good estimates of the change in viral load from baseline with an r2 of 0.48 during cross validation. Results with the independent test set were a little disappointing with an r2 of 0.4 overall and a scatterplot showing two clusters of predictions, with one set appearing to be correlated but with actual virological responses being much less than the models' predictions. Further research is ongoing to try to define these sub-groups mathematically.

The use of a truly random partition of TCEs gave much improved performance in testing, as might be expected given their lack of independence.

Examination of the characteristics of the original training and test sets shows that the proportional representation of TCEs from South Africa and Sub-Saharan Africa generally in the test set was approximately twice that in the training set (15% vs 8%). This is the result of patients treated in high-income countries having on average more treatment changes in their history, more follow-up viral loads per treatment change and, therefore, more TCEs in the qualifying pool than those from lower income countries. In this study the mean number of TCEs from sub-Saharan Africa was 1.8, with a median of 1 compared with a mean of 3.02 and a median of 3 from other settings. Since partitioning is conducted by patient (not TCE) to ensure an independent test set (without the same patient having TCEs in the training set), a greater proportion of the TCEs from low-income countries are partitioned to the test set than are from high income countries. This is borne out by inspection of the patient and TCE dispositions. The countries with proportionally more TCEs in the test set than the training set were Argentina, India, Mexico, Romania, South Africa, and other sub-Saharan African countries. Those countries with proportionally fewer in the test set were Canada, Germany, Netherlands, Spain, UK, USA, and patients from international cohorts and clinical trials.

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Patients from low-income countries tend to have more advanced infection when treatment is started or switched than those from higher income countries, which makes a response to treatment less likely. In this study, for example, patients from sub-Saharan Africa had mean and median baseline CD4 counts of 250 and 205 cells/ml at the point of treatment change compared with 313 and 269 for other settings. This could be part of the explanation for the disappointing and dichotomous test results we found with the original models.

Models such as these could be used to produce predicted follow-up viral loads at different time points after the initiation of a regimen via interpolation, which would be used to produce a curve of predicted viral load over time. This would facilitate clinicians to select the most effective combinations of drugs no matter what definition of virological failure is used.

For the full progress report (including methods and results for each section), please follow this link.

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, Vlugt J, van Sighem A, van der Sande M.

Date of approval: 2008

Ongoing.

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, Pettersson A, Schutten M, Bierman W.

Date of approval: 1 May 2010

Ongoing.

I12045 A HIV-1 genome wide association study to identify viral determinants of HIV-1 plasma concentration (BEEHIVE)
Cornelissen M, Gall A, Vink M, Zorgdrager F, Binters S, Edwards S, Jurriaans S, Ong SH, Bakker M, Gras L, de Wolf F, Reiss P, Kellam P, Berkhout B, Fraser C, van der Kuyl AC.

Date of approval: 12 September 2012

Background: The Bridging the Epidemiology and Evolution of HIV in Europe (BEEHIVE) started in April 2014 and runs until April 2019. The objectives of the study are to use the whole viral genomes to find determinants of disease severity, molecular epidemiology, and dual HIV-1 infections, and to study minority variants. All participants were selected from 7 countries (Belgium, France, Finland, Germany, the Netherlands, Switzerland and the

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United Kingdom), were seroconverters or participants presenting with evidence of recent infection, and were diagnosed with HIV between 1985 and 2013.

Results: Inclusion of samples is complete (n=41 from Rotterdam, n=41 from Nijmegen, n=39 from the OLVG and n=24 from Zwolle); total nucleic acids were isolated from the samples with the method described in Cornelissen *et al*. 2017. As the PI of the BEEHIVE study, Prof. C Fraser, recently moved from Imperial College London to the Big Data Institute in Oxford, the sequence platform was changed to the Oxford Nanopore MinION platform. The final 450 samples will be sequenced on the latter platform. In 2017, 2,892 HIV genomes were sequenced using the Illumina MiSeq or HiSeq platform. To analyse these data, a new software tool, phyloscanner, which analyses pathogen diversity from multiple infected hosts, has been developed. Phyloscanner is a set of methods implemented as a software package; it can be used to detect contamination, multiple infections, recombination and transmission events. The description of the software package and the results will be published in *Molecular Biology and Evolution* in 2018 (Wymant *et al*.).

In 2017, we also finished a minor project on evolution of HIV-1 Tat protein, the essential regulator of viral gene expression, in the BEEHIV dataset. We documented considerable variation in the length of the C-terminal domain of Tat in Dutch HIV-1 sequences, ranging from 77 to 124 amino acids over time. Subsequently, we set up functional assays to analyse whether this polymorphism correlates with changes in Tat activity. A revised manuscript describing our findings has recently been resubmitted to *Retrovirology*.

Conclusions: In 2017, the objectives of the BEEHIVE study were almost fulfilled.

I13032 Combined and comparative analysis of virulence trends across multiple cohorts

Herbeck J, Müller V, de Wolf F, Bezemer D.

Date of approval: 25 May 2013

Ongoing.

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, Zuure F, Alvarez-del Arco D, Prins J, Brinkman K, Leyten E, van Sighem AI, Burns F, Prins M (Dutch clinic data publication).

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

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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, improve diagnosis and prognosis of migrant populations living with HIV by providing evidence to support policy development at 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 identification of barriers for migrants living in the Netherlands.

Methods: Data were collected via two surveys: The first targets HIV-infected migrants; recruitment took place at the HIV clinic (i.e., clinical survey). The second survey targets migrants in general, irrespective of their HIV status, and was disseminated via the Internet (i.e., community survey). All participants self-completed a questionnaire. In addition to the questionnaire, in the clinic survey, data about clinical indicators of HIV disease was collected (data source: SHM).

The clinical survey is a multi-site study that took place in nine European countries. In the Netherlands, recruitment took place in 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 also collected data from native HIV-positive patients to compare the results with those found among the migrant patients. The community survey was disseminated through non-governmental and community based organisations in nine European countries, including the Netherlands.

Results:

Clinical survey

Enrolment took place in three hospitals in the Netherlands. In total, 40 migrants and 42 controls (HIV-positive patients born in the Netherlands that met the remaining aMASE inclusion criteria) were recruited and completed the aMASE questionnaire at the HIV outpatient clinic of the AMC in Amsterdam. Recruitment was stopped in the AMC in August 2014. Recruitment continued in the OLVG hospital in Amsterdam and in total 52 migrants and 72 controls were included. Finally, from March 2015 onwards, 32 migrants and 24 controls were enrolled in the Medisch Centrum Haaglanden. In total 124 migrant and 138 controls patient were included in the three hospitals. Across Europe, a total of 2,117 patients were included.

Community survey

In 2013, the questionnaire for the community survey was developed together with the European partners. Dissemination of the community survey started in May 2014. Recruitment for the

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community survey involved various approaches, working closely with NGOs and the community. Throughout Europe, 1,782 participants were recruited, 134 of which in the Netherlands.

Conclusions: Data on likely country of HIV acquisition and European data of the community survey have been published. The manuscript of the European clinic survey has been submitted for publication. The manuscript of the Dutch clinic survey is currently being prepared for submission, and abstracts have been sent for presentation at various conferences.

Likely country of HIV acquisition
Results from the European clinical survey show an estimated proportion of overall post-migration HIV acquisition of 63% (95% CI: 57%-67%); 72% among men having sex with men (MSM), 58% and 51% in heterosexual men and women, respectively. The probability of post-migration HIV acquisition was 71% for migrants from Latin America & the Caribbean and 45% for people from sub-Saharan Africa. Factors associated with post-migration HIV acquisition among heterosexual women and MSM were age at migration, length of stay in host country and HIV diagnosis year. Among heterosexual men, length of stay in host country and HIV diagnosis year were associated with post-migration HIV acquisition.

HIV testing and access to primary care
Preliminary results from the European clinical survey show there were high rates (82.0%) of previous negative testing among migrant gay/bisexual men, but less than half of women and heterosexual men (46.7% and 43.4% respectively) reported ever having had a negative test. Previous negative testing was associated with migration related factors among three gender-related groups: women (post-migration antenatal care); heterosexual men (permanent residency) and gay/bisexual men (identifying as gay rather than bisexual). Access to primary care was found to be high in all groups and was most strongly associated with current country of residence.

The preliminary results of the Dutch data of the clinical survey show heterosexual men/women (non-migrant and migrant) were less likely to ever have had an HIV-negative test before their diagnosis and were more likely to be diagnosed late than non-migrant MSM. Migrants were more likely to have experienced difficulties accessing healthcare in the Netherlands than non-migrant MSM. Migrant MSM and migrant women were more likely to have ever been discriminated against in the Netherlands because of their HIV-status than non-migrant MSM. Migrant MSM, non-migrant heterosexual men, migrant heterosexual men and migrant women were less likely to have heard of PEP than non-migrant MSM.

Results from the European community survey show that between 60-90% of migrants within this sample had previously tested for HIV. HIV testing was strongly associated with sexual behaviour (all groups); experience of forced sex, region of birth or post-migration antenatal care (women); and region of birth, access to primary

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care and health status (heterosexual men). Between 60-73% of migrants had access to primary care. For women and heterosexual men, access to primary care was associated with current region of residence, region of birth and immigration status; among gay/bisexual men it was associated with current residence, number of years in current region of residence and HIV status.

The final European and Dutch results of the clinic survey are expected to be published in 2018.

I13120 SPREAD Program 3.0 – Surveillance of transmission of HIV-1 drug resistance
Hofstra LM, van Sighem AI, van Litsenburg M, Bierman W, Brinkman K, van der Ende ME, Hoepelman AIM, van Kasteren M, Op de Coul E, Richter C, Boucher CAB, Wensing AMJ.

Date of approval: 19 May 2014

Ongoing.

I14065 Incidence of hepatocellular carcinoma in HIV/HBV co-infected 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

Ongoing.

I14067 Predictive value of cardiovascular risk equations in the HIV-infected population receiving care in the Dutch HIV treatment centers
Van Zoest R, Wit F, Vaartjes I, van der Valk M, Arends J, Law M, Friss-Moller N, Sabin C, Reiss P.

Date of approval: 2 June 2014

Background: Cardiovascular disease (CVD) is more prevalent among people living with HIV (PLHIV) than in HIV-negative individuals. The patho-physiological mechanism is thought to be multifactorial. The current Dutch cardiovascular risk management guidelines recommend risk assessment based on the SCORE risk equation adjusted for national data (SCORE-NL risk equation). However, it is unknown whether the SCORE-NL risk equation also accurately identifies PLHIV at increased risk of CVD. The aim of our study is (1) to assess whether the SCORE-NL risk equation correctly estimates the CVD risk of PLHIV in the Netherlands, and (2) to compare the predictive value of various CVD risk equations in PLHIV.

Methods: We have discussed several methodological issues within our research group, and developed an updated analysis plan. In December 2017 we received an updated SHM data set.

The population that will be used for the current analysis was selected using our predefined inclusion criteria. The baseline date (to) has been defined for all study participants, and all variables have been labelled. We have checked and cleaned the data.

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The risk equations evaluated within this project have been coded in STATA syntax: SCORE-NL equation, D:A:D risk equation 2015 (reduced and full), Framingham risk equation, and Pooled Cohort Risk Equation. In addition, the CVD endpoints have been defined and coded.

We have identified the proportion of missing values per variable. Since the number of missing values is very high for some of the variables (family history of CVD, smoking status, total/HDL cholesterol), we have discussed possible ways of dealing with missing data with a team of experts on imputation/missing data working at the Julius Center Utrecht, and we are planning to impute the missing data using multiple imputation by chained equation.

Results: No results available, analysis ongoing.

Conclusions: No conclusion available, analysis ongoing.

I14087 Clinical experience with rilpivirine (KLIRI study)
Roelofsen E, Burger DM, Touw DJ, Gelinck LBS, Wilms EB, van Sighem AI.

Date of approval: 28 October 2014

Ongoing.

I14145 Evaluation of an evidence-based, Internet-supported self-help program for people living with HIV suffering from mild to moderate depressive symptoms
Garnefski N, Kraaij V, Spinhoven P, van Luenen S.

Date of approval: 23 September 2014

Medical data: The medical data (time since HIV diagnosis, medication use, CD4 cell count, and viral load) were obtained from SHM in 2017. These data will be used to describe the sample and for the moderation analysis (i.e., is time since HIV diagnosis a moderator of intervention effect?).

Background: Many people with HIV suffer from depressive symptoms, but some do not receive adequate treatment for it. We developed an online self-help intervention for people with HIV and depressive symptoms, based on previous research. We investigated the effectiveness of the intervention on depressive symptoms in people with HIV. In addition, the effect of the intervention on anxiety symptoms was examined.

Methods: The effectiveness of the intervention was investigated by comparing the intervention group with a control group in a randomised controlled trial, including a pre-test and three post-tests. Participants were 188 people with HIV and mild to moderate depressive symptoms. The self-help intervention consisted of cognitive behavioural and stress-management techniques. In addition, participants received minimal telephone coaching during eight weeks. The control condition consisted of weekly attention only from a coach and access to the intervention after the second post-test.

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Results: Depressive symptoms decreased in both groups, but in the intervention group the reduction was significantly larger than in the control group (d=-0.56, 95% CI [-0.85, -0.27]). This effect was found in the short term and in the long term. In the intervention group significantly more participants reached the criteria for clinically significant change in depressive symptoms at the first post-test than in the control group. Furthermore, anxiety symptoms significantly decreased in the intervention group, compared to the control group (d=-0.75, 95% CI [-1.05, -0.45]).

Conclusions: The online self-help intervention was effective in reducing depressive symptoms in people with HIV, compared to a control condition that received attention only. The intervention including coaching will be implemented in the Netherlands to improve psychological care for people with HIV.

I15004 The impact of combinations of strategies for HIV prevention among men who have sex with men

Reitsema M, van Hoek AJ, Mangen MJ, van Benthem B, op de Coul E, Wallinga J, van Sighem A, Schim van der Loeff M, Xiridou M.

Date of approval: 28 January 2015

Background: In the Netherlands, men who have sex with men (MSM) account for most new HIV diagnoses. Despite the availability of successful treatment, there is still ongoing transmission. Research thus far has focused mainly on assessing the impact of individual measures, such as early initiation of combination antiretroviral therapy (cART) or pre-exposure prophylaxis (PrEP). However, the impact of combined strategies is unknown. In this project we will assess the impact of several public health interventions, if implemented individually or in combinations. The impact of these interventions on HIV transmission will be investigated, as well as their cost-effectiveness.

Methods: We developed an individual-based model that describes the formation of sexual relationships between MSM and the transmission of HIV. Parameters relating to sexual behaviour were estimated from data from the Amsterdam Cohort Study and the Network Study among MSM in Amsterdam. Parameters relating to HIV progression were estimated from data from Stichting HIV Monitoring (SHM). Frequency of HIV/STI testing was estimated from data in the national database of STI clinics in the Netherlands. The model was calibrated to data on HIV diagnoses from SHM and gonorrhoea positivity rates from STI clinics. In the model, we assumed that from 2015 onwards, all HIV treatment centres in the Netherlands follow the new guidelines for immediate initiation of cART after diagnosis.

Subsequently, we developed an economic model. Direct healthcare costs were calculated using a bottom-up approach and included costs of medical consultations, costs for laboratory tests, and cART medication. Effects of the interventions were

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expressed in quality-adjusted life-years (QALY) gained. The incremental cost-effectiveness ratio (ICER) was calculated, showing the additional costs per QALY gained with the intervention, compared to the current situation. Costs were expressed in 2016 Euros. According to Dutch guidelines, costs were discounted by 4% and effects by 1.5%.
The analyses were carried out from a healthcare payer perspective, considering only healthcare costs relating to HIV testing and HIV care.

Results: Impact of immediate cART initiation:
After ten years with immediate initiation of cART, the projected HIV incidence can be reduced by 34% (interquartile range (IQR), 12% – 50%), from 0.45 infections per 100 person years (PY) without immediate cART to 0.29 infections per 100 PY with immediate cART. MSM with more than 20 partners in the preceding 6 months had a much higher incidence (1.41 infections/100 PY) than men with 3-20 (0.33 infections/100 PY) or 0-2 partners (0.19 infections/100 PY). In 2025, HIV incidence would be higher among MSM who had gonorrhoea in the preceding 12 months (2.56 infections/100 PY) than among MSM who did not (0.21 infections/100PY); in both groups of MSM, HIV incidence in 2025 would be significantly lower with immediate treatment than without immediate treatment.

Costs of HIV testing and HIV care: Costs of HIV testing were estimated at €47 for each negative test and €171 for each positive test (including extra consultation time, visits to testing location, and administration time). Annual costs for each HIV-positive individual in care were calculated at €403 for monitoring and €10,600 for cART medication. Hospitalisation of HIV/AIDS patients with opportunistic infections was estimated at €7,100 per year.

Impact of increased HIV/STI testing: We investigated the impact of a hypothetical increase in HIV/STI testing. Based on data from the national database of STI clinics, we calculated that, in 2015, approximately 20% of MSM tested regularly for HIV/STI every six months. In the hypothetical scenario, we assumed that this percentage increases to 30% in 2018. We calculated the incidence of HIV with 20%, and with 30%, six-monthly testing. The annual number of new HIV infections decreases by 7.9% (95% CI, 5.5- 10%) after two years and by 14.2% (95% CI, 11.9-16.2%) after ten years with increased testing.
By increasing the percentage of six-monthly testers from 20% to 30%, a total of 494 new HIV infections and 37 AIDS cases can be averted over the ten years 2018-2027, resulting in 733 QALYs gained. However, increased HIV testing can result in €8.9 million additional costs due to extra tests, €0.4 million additional costs for HIV/AIDS care (due to earlier initiated and prolonged treatment, partly compensated by savings due to averted HIV/AIDS cases), summing to a total of €9.3 million additional costs and an ICER of €12,700 per QALY gained. Sensitivity analyses indicate that the ICER is most sensitive to the distribution of locations of HIV tests and the discount rates, but our findings are robust to

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variations in the other epidemiologic and economic parameters.

Impact of PrEP: In our model, criteria for PrEP eligibility follow the recent Dutch guidelines on PrEP use: MSM are eligible for PrEP if they are not infected with HIV and they meet one or more of the following criteria: (1) they had a steady HIV-positive partner with a detectable viral load; (2) they were diagnosed with anogenital gonorrhoea in the preceding six months; (3) they had condomless anal intercourse (CAI) with a casual partner in the preceding six months. Eligibility is evaluated when MSM visit healthcare providers for HIV/STI testing. The introduction of PrEP can result in a major reduction in HIV incidence. In the total MSM population, the incidence of HIV infection in 2027 is projected to be 0.300 (IQR, 0.0.186-0.432) infections/100 PY. The incidence in 2027 could be reduced to 0.082 (IQR, 0.047-0.127) infections/100 PY. Among PrEP users, HIV incidence declines from 2.065 infections/100 PY before the start of the programme (2017) to 0.175 infections/100 PY after ten years. With risk compensation (PrEP users have lower probability of using condoms when they are on PrEP than when not on PrEP), there are more MSM eligible for PrEP and the number of PrEP users increases from 5,835 without risk compensation to 6,290 with risk compensation. The incidence rate among PrEP users was higher with risk compensation; however, due to the expanded programme, the HIV incidence in the total MSM population declined further. Assuming a baseline cost of PrEP medication of €125 per three months, the introduction of PrEP can lead to cost savings of €22.5 (IQR, €3-37.5) million and 1,099 (IQR, 646-1,485) QALYs gained over the ten-year period 2018-2027. The majority (96%) of parameter sets result in ICERs below €20,000 per QALY gained. The cost-effectiveness of PrEP is strongly influenced by the price of PrEP medication: if the price is raised to €300 per three months, the ICER is below the threshold of €20,000 per QALY gained only with 48% of the parameter sets; with €1,200 per three months, none of the tested parameter sets result in an ICER below €20,000 per QALY gained.

Conclusions: Our first analyses indicate that immediate cART initiation can result in considerable reductions in HIV transmission. This effect can be enhanced with increased testing and even more with a PrEP programme targeted at high-risk MSM. A small increase in HIV testing can be cost-effective and also a targeted PrEP programme can be cost-effective and even cost-saving, if the costs of PrEP antiretrovirals and PrEP controls are not very high. These results imply that the choice to switch to immediate cART initiation was most likely very sensible. Public health campaigns aiming to increase HIV testing and to implement PrEP among high-risk MSM could lead to reductions in HIV incidence.

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I15021 Global resistance following virologic failure with tenofovir+NNRTI containing antiretroviral regimens: a retrospective multi-centre multi-cohort study and meta-analysis

Rokx C, Gupta R, Rijnders B, Shafer B, Gregson J, Tang M, Hamers R, Raizes E, Crawford K, Marconi V, Hill A, Hosseinipour M, Clumeck N, Kanki P, Lockman S, Rinke de Wit T, Hoffman S, de Oliveira T, Wallis C, Morris L, Hunt G, Dunn D, Blanco JL, Gunthard H, Kumarasamy D, Kaleebu P, Pillay D, Charpentier C, Descamps D, van Damme A, Theys K, Camacho R, Calvez V, Gras L.

Date of approval: 20 February 2015

Background: Tenofovir disoproxil fumarate (TDF) genotypic resistance defined by K65R/N and/or K70E/Q/G occurs in 20% to 60% of individuals with virological failure (VF) on a WHO-recommended TDF-containing first-line regimen. However, the full spectrum of reverse transcriptase (RT) mutations selected in individuals with VF on such a regimen is not known.

Methods: To identify TDF regimen-associated mutations (TRAMs), we compared the proportion of each RT mutation in 2,873 individuals with VF on a WHO-recommended first-line TDF-containing regimen to its proportion in a cohort of 50,803 antiretroviral-naive individuals. To identify TRAMs specifically associated with TDF-selection pressure, we compared the proportion of each TRAM to its proportion in a cohort of 5,805 individuals with VF on a first-line thymidine analogue-containing regimen.

Results: We identified 83 TRAMs including 33 NRTI-associated, 40 NNRTI-associated, and 10 uncommon mutations of uncertain provenance. Of the 33 NRTI-associated TRAMs, 12 - A62V, K65R/N, S68G/N/D, K70E/Q/T, L74I, V75L, and Y115F - were more common among individuals receiving a first-line TDF-containing compared to a first-line thymidine analogue-containing regimen.

Conclusions: These 12 TDF-selected TRAMs will be important for monitoring TDF-associated transmitted drug-resistance and for determining the extent of reduced TDF susceptibility in individuals with VF on a TDF-containing regimen.

I15040 Monitoring recent HIV infections in the Netherlands: implementation of Recent Infection Testing Algorithm (RITA) into routine HIV surveillance

Op de Coul E, van Aar F, van Dam A, van de Laar T, de Bree G, van Benthem B, van Sighem AI, for the RHI in Amsterdam study group and the HIV Transmission Elimination Amsterdam (H-TEAM) initiative.

Date of approval: 2015

Background: Surveillance of recent HIV infections (RHI) has the goal to inform local and national HIV intervention programs. RHI surveillance has been implemented in Dutch STI clinics since 2014, but data for other HIV test sites are lacking.

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This study aims to gain more insight into the HIV epidemic in Amsterdam and the contribution of different test sites to detecting RHI.

Methods: Samples were collected from newly-diagnosed HIV patients (2013-2015) in care in Amsterdam, and tested with an avidity assay. Cut-off values for the Avidity Index (AI) were AI≤0.80 for recent infection (<6 months), and AI>0.80 (≥6 months) for established infection. AI data were merged with clinical data collected as part of the ATHENA national HIV cohort. To minimise the number of falsely classified RHI, patients with AI<0.80 were reclassified as established infection in the case of an AIDS diagnosis, CD4 count <200 cells/µl and/or a viral load <400 copies/ml.

Results: In total, 451 samples were collected, comprising 65% of newly-diagnosed patients in care in Amsterdam. Their median age was 40 years, 72% were MSM, 53% were of Dutch origin, and 36.6% were diagnosed at an STI clinic.

Overall, 77/451 (17.1%) infections were classified as RHI. Nine established infections (based on AIDS diagnosis, low CD4 count or low viral load) had an AI<0.80.

Proportions of RHI in 2013, 2014 and 2015 were 17.5%, 18.5%, and 13.8% (non-significant trend, p>0.1). RHI was higher among MSM (20.2%) compared to heterosexuals (9.4%) and people with unknown or other risks (5.3%)(p<0.05). People diagnosed at the STI clinic more often had an RHI (26.1%) than those diagnosed at the GP (16.9%), hospital (5.7%) or other test site (10.5%) (p<0.001). RHI among MSM diagnosed at STI clinics increased over time (22.7%, 31.2% and 33.3%), while RHI among MSM diagnosed at GPs declined (20.7%, 17.6%, 7.1%)(p>0.1).

Conclusions: Our findings indicate ongoing HIV transmission in Amsterdam, with MSM being disproportionately affected by new infections. STI clinics capture more RHI compared to other test sites, possibly as a result of intensified HIV (repeated) testing among MSM. MSM remain a priority for prevention efforts, but increased awareness of, and testing for, HIV by GPs seems warranted.

I15043 Cost-effectiveness of the Adherence Improving self-Management Strategy (AIMS) in HIV care: A model-based economic evaluation
De Bruin M, Prins J, Oberjé E, Hiligsmann M, Evers S, van Sighem AI.

Date of approval: 17 June 2015

Ongoing.

I15065 Comparison of the occurrence of severe HBV-related liver disease and (liver-related) mortality between patients with hepatitis B mono-infection and patients coinfected with hepatitis B and HIV in the Netherlands. (HARMONIC)
Arends JE, Richter C, Lieveld FI, Reiss P, Smit C, Spanier M, van Erpecum KJ, Hoepelman IM.

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Date of approval: 28 July 2015

Background: HIV/hepatitis B virus (HBV) co-infected subjects are thought to have faster progression to end-stage liver disease (ESLD) than HBV mono-infected subjects. We assessed whether this remains in the current cART era.

Methods: Data from subjects with follow-up completion post-2003 were compared between HIV/HBV co-infected subjects in the Dutch HIV Monitoring database and HBV mono-infected subjects from two centres. The primary outcome of composite ESLD included portal hypertension, decompensated cirrhosis, hepatocellular carcinoma, liver transplantation, and liver-related mortality. Outcomes were analysed using time-dependent Cox regression models adjusted for follow-up time and relevant covariates. Subset-analyses were done in subjects with follow-up pre-2003.

Results: Incidence of ESLD, all-cause and liver-related mortality was 7% vs. 15%, 13% vs. 6%, and 2% vs. 3% respectively, in 1336 co-infected versus 742 mono-infected subjects. After adjustment, co-infected subjects had no increased probability for ESLD compared to mono-infected subjects (HR 0.5 (95% CI 0.3–0.9), contrary to co-infected subjects monitored pre-2003 in the sub-analyses (HR 8.6 (1.2–64.2). While the probabilities for all-cause (HR 10.8 (6.4–18.0) and liver-mortality (HR 5.9 (2.1–16.8)) were increased in co-infected subjects, these rates decreased compared to pre-2003. In the current combined cohort, treatment with tenofovir or entecavir was inversely associated with all outcomes. Other predictors for ESLD were older age, being of sub-Saharan African descent, advanced fibrosis, elevated alanine aminotransferases, and higher HBV DNA levels.

Conclusions: HIV/HBV co-infected patients no longer seem to be at increased risk for progression to ESLD compared to HBV mono-infected patients, likely due to widespread use of highly effective cART with dual HBV and HIV activity.

I15066 Cost-effectiveness of HIV treatment and care in the Netherlands

Popping S, Verbon A, Nichols BE, Boucher C, van de Vijver D, Geerlings S, Reiss P, van Sighem AI, Kroon FP, Brinkman K.

Date of approval: 24 June 2015

Background: Cost-effectiveness analyses are used to provide the most health benefits at the lowest costs for HIV care. Quality adjusted life years (QALYs) are key in assessing health benefits in a cost-effectiveness analysis. Unfortunately, QALYs available in literature are outdated and obtained at a time when antiretroviral drugs were more toxic and CD4 treatment thresholds were low.

The first part of this study aims to measure QALY scores using the validated EuroQol-5-dimension questionnaire (EQ-5D-5L) among HIV-positive

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individuals. The measured QALY scores will then be combined with cost and clinical data to assess the cost effectiveness of HIV care. The second part of the study aims to assess the additional cost of late presenters in HIV care.

In Europe, as many as 50% of HIV-positive individuals present late to care. Late presentation is associated with high morbidity from AIDS-defining malignancies and opportunistic infections which may substantially increase the cost of care.

Methods: To measure the QALY scores, an observational study was initiated at the Erasmus Medical Center outpatient clinic. Consecutive HIV-positive adult individuals are eligible to fill out the EQ-5D-5L questionnaire during their doctors' appointment. The compliance and feasibility of the EQ-5D-5L was measured during the first two months of the study. The collected QALY scores are combined with clinical data, using the SHM cohort, and cost. QALY difference between patient groups, ART treatment, treatment initiation and duration will be analysed. In addition cost-effectiveness analysis of HIV care will be performed.

For the second part of the study, we used SHM data from individuals who first initiated ART between 1 July 2012 and 1 July 2013 to investigate the cost of late presenters. Costs of ART, hospitalisation, outpatient visits, comedication and HIV laboratory tests were calculated. Factors independently associated with high non-ART costs, were determined by multivariable logistic regression, including parameters with $p<0.1$ from the univariable analysis.

Results: The EQ-5D-5L had a high compliance of 90% that was measured during the first period of the study. Preliminary results show limited problems with mobility, self-care, or daily-activities for HIV infected individuals. However, almost a third of the HIV infected individuals experience pain/discomfort or anxiety/depression problems. The mean QALY-score of HIV infected individuals was comparable to the Dutch population. We are currently compiling a combined dataset with clinical data, QALYs and cost. Further analyses will be following in a timely manner. Late presenters are considered to be more costly. Higher costs are mainly ascribed to the non-ART costs, due to hospitalisation and, to a lesser extent, comedication.

Conclusions: The EQ-5D is an adequate tool to measure QALY scores during outpatient consultations for HIV-infected individuals. Obtained QALY scores are similar to the Dutch population. Moreover, late presentation drives the non-ART costs.

I15090 Fibrosis progression after acute HCV infection in HIV-infected individuals

Van der Valk M, Kooij KW, Newsum AM, Smit C, Reiss P, Prins M, van der Meer J, MOSAIC study group, SHM hepatitis working group.

Date of approval: 27 July 2015

ONGOING RESEARCH PROJECTS

Background: HIV co-infection may accelerate the progression to liver fibrosis and cirrhosis in chronic HCV. Recently, a study among HCV mono-infected patients demonstrated an unexpectedly high rate of fibrosis progression, relatively soon after HCV seroconversion, as measured by the change in FIB-4 score over time. Data on the rate of liver fibrosis progression and its determinants soon after HCV seroconversion in those with underlying HIV infection are lacking. We will retrospectively study liver fibrosis progression, assessed by FIB-4 scores, in HIV-infected individuals within the Netherlands who acquired acute HCV.

Methods: Any HIV-positive individual with an acute HCV infection at or after 1 January 1999, identified in the SHM database, are included. In addition, cases identified in the MOSAIC study are included. Only men who have sex with men (MSM) are included. HCV infection prior to HIV infection is an exclusion criterion. Furthermore, patients need to have sufficient follow up: inclusion criteria are ≥1 FIB-4 value available within 2 years before and ≥ 1 value one year after the estimated HCV infection date. Descriptive analyses and multivariate modelling to assess determinants of FIB-4 progression or regression are ongoing.

Results: Of 312 MSM included, median age at acute HCV infection was 43 years (IQR=36-48) and 198 (63.5%) were on combination antiretroviral therapy. Following acute HCV infection, median follow up was 4.0 years (IQR=2.2-6.4) and median FIB-4 values per MSM was 9 (IQR=5-15). Following acute HCV infection, 41 MSM (13.1%) spontaneously cleared HCV and 224 (71.8%) were treated for HCV at least once, of whom 161 (71.9%) achieved SVR after their first treatment.

FIB-4 course over time appeared mostly stable over time with peaks observed in some patients shortly after acute HCV infection. Prior to acute HCV infection, 307 MSM (98.4%) had FIB-4 <3.25, of whom 47 (15.3%) progressed to FIB-4 ≥3.25 a median of 0.3 years (IQR=0.2- 0.8) after acute HCV infection. However, 40/47 had reverted to FIB-4 <3.25 by the end of follow up.
In multivariable analysis, higher CD4 cell count (per $\log_{10}$ mm^3; aHR=0.14, 95% CI=0.04-0.50) and undetectable HIV RNA (<50 vs ≥50 copies/ml; aHR=0.24, 95% CI=0.11-0.51) were associated with a lower rate of transitioning to FIB-4 ≥3.25.
Older age was associated with a lower rate of reverting from FIB-4 ≥3.25 to FIB-4 <3.25 (per year; aHR=0.95, 95% CI=0.92-0.98).

Conclusions (preliminary): Most MSM with acute HCV infection who developed a FIB-4 ≥3.25 did so during the first year following HCV infection. A FIB-4 ≥3.25 was uncommon by the end of follow up. Well-controlled HIV infection appeared to attenuate FIB-4 progression.

For the full progress report (including all definitions), please follow this link.

ONGOING RESEARCH PROJECTS

I15148 Model based on clinical parameters to predict the natural history of severe liver fibrosis in HIV/HCV co-infected patients

Arends JE, van der Meer AJ, Smit C, Hansen B.

Date of approval: 15 December 2015

Ongoing.

I16011 Type of cART regimen and the risk for immune reconstitution and inflammatory syndrome in HIV-1 infected patients. Is integrase inhibitor use an independent risk factor?

Wijting IEA, Wit FWNM, Rokx C, Leyten EMS, Lowe SH, Brinkman K, Bierman WFW, van Kasteren MEE, Postma AM, Bloemen VCM, Bouchtoubi G, Hoepelman AIM, van der Ende ME, Reiss P, Rijnders BJA.

Date of approval: 2 March 2016

Background: Use of integrase inhibitor-containing cART is associated with a fast HIV-RNA decline and increase of CD4 cells. These factors are also associated with development of IRIS: a pathological inflammatory response against antigens of opportunistic infections (OI). Whether use of integrase inhibitors (INI) increase the risk of IRIS is unknown, as phase 3 studies only include few late presenters.

Methods: Observational study in the ATHENA cohort. Patients who initiated cART after 03-2009 and who had CD4 T-cells <200 cells/mm^3 were selected if they met one of the following criteria: 1) OI prior or after initiation of cART, 2) use of corticosteroids < 12 months after start cART, or 3) died < 12 months after start cART. Manual chart review was performed to further investigate whether they developed IRIS. IRIS was defined according to the predefined definition of French *et al*. ($IRIS_{FRENCH}$) or as diagnosed by the treating physician ($IRIS_{CLINICAL}$). The two primary endpoints of this study were the incidence of $IRIS_{FRENCH}$ and $IRIS_{FRENCH+CLINICAL}$.

Results: A total of 672 patients met the criteria. As we had collected data of 356 patients in 2016, the charts of the remaining 416 patients were reviewed in 2017. Baseline characteristics of patients who initiated an INI-containing cART-regimen (n=155) did not differ from those who initiated a non-INI-containing cART-regimen (n=517). Cox regression showed that use of INI was independently associated with $IRIS_{FRENCH}$ and $IRIS_{FRENCH+CLINICAL}$(HR 1·91, 95% CI 1·17-3·10, p<0·01 and HR 1·80, 95% CI 1·25-2·60, p<0·01). Only raltegravir, but not elvitegravir and dolutegravir, was associated with IRIS: HR 3·18 (95% CI 2·03-4·98, p<0·01).

Conclusions: We found that use of raltegravir is associated with development of IRIS in cART-naive HIV-infected late-presenters. This might be a biased result, as raltegravir was prescribed to specific patient populations. These results have to be confirmed in a large randomised controlled trial before conclusions can be drawn from these findings.

ONGOING RESEARCH PROJECTS

I16038 Immune reconstitution inflammatory syndrome associated with toxoplasmic encephalitis in HIV-infected patients

van Bilsen WPH, van den Berg CHSB, Rijnders BJA, Brinkman K, Mulder JW, Gelinck LBS, Hoepelman AIM, Wit FWNM, van de Beek D, Prins JM.

Date of approval: 20 June 2016

Objectives: To investigate the incidence and risk factors of immune reconstitution inflammatory syndrome (IRIS) associated with toxoplasmic encephalitis (TE) in patients starting combination antiretroviral therapy (cART).

Design: A historical multicentre cohort study.

Methods: We included all HIV-infected patients diagnosed with TE in six Dutch hospitals between 1996 and 2016. Diagnosis of TE-IRIS was made using predefined IRIS criteria. We distinguished paradoxical TE-IRIS (worsening of underlying treated infection) from unmasking TE-IRIS (unmasking of subclinical infection after start of cART). We compared CD4 cell count, plasma viral load and timing of cART initiation between patients with and without paradoxical TE-IRIS.

Results: A total of 211 toxoplasmic encephalitis cases were included. Among 143 cases at risk for paradoxical TE-IRIS, we identified five cases of paradoxical TE-IRIS (3.5%). In six other cases, we could not differentiate paradoxical TE-IRIS from recurrence of disease due to inadequate secondary Toxoplasma prophylaxis. There was no difference in time between start of toxoplasmic encephalitis treatment and cART initiation for patients who did or did not develop paradoxical TE-IRIS (p=0.50). Within the group of 2,228 patients who started cART while having a CD4 cell count below 200 x 10^6 cells/l and receiving adequate primary prophylaxis, we identified eight cases of unmasking TE-IRIS (0.36%). Unmasking TE-IRIS could not be differentiated from a newly occurring toxoplasmic encephalitis in six other patients, as they were not receiving adequate primary prophylaxis against Toxoplasma.

Conclusion: Unmasking TE-IRIS was rare in this cohort, whereas paradoxical TE-IRIS did occur more often. We found no relationship between the timing of cART initiation and the occurrence of paradoxical TE-IRIS.

I16060 Evaluation of dolutegravir use of the treatment of HIV in the Netherlands: focus on switchers and adverse events

Burger D, van Crevel R, Brouwer A, Bollen P, Arends JE, Hakkers CS, Hoepelman IM, Brinkman K, van den Berk GEL, Boender TS, Wit F.

Date of approval: 30 August 2016

Ongoing.

ONGOING RESEARCH PROJECTS

I16072 Comparison of the occurrence of HBV-related liver disease and (liver-related) mortality between patients with hepatitis B mono-infection and patients coinfected with hepatitis B and HIV in the Netherlands
Arends JE, Richter C, Lieveld FI, Reiss P, Smit C, Spanier M, van Erpecum KJ, Hoepelman IM.

Date of approval: 15 August 2016

Ongoing.

I16091 Longitudinal virological outcomes and factors associated with virological failure in HIV infected young adults in the Netherlands 1996-2016
Weijsenfeld AM, Wit FWNM, Pajkrt D.

Ongoing.

I17093 The impact of mutations on the effectiveness of abacavir/lamivudine/dolutegravir regimens prescribed in treatment-experienced patients (The M184V/I – DTG study)
Olearo F, Kouyos R, Bonnet F, Yerly S, Wandeler G, Stoeckle M, Baettig V, Cavassini M, Gayet-Ageron A, Scherrer A, Schmid P, Bucher HC, Günthard H, Böni J, D'Armino A, Zazzi M, Bellecave P, Cazanave C, Daffau P, Rijnders B, Reiss P, Wit F, Calmy A.

Date of approval: April 2017

The project team has met during EACS in Milan. Data exchange criteria have been drafted and currently we are in the process of collecting (and collating) datasets from all participating cohorts. ATHENA has already forwarded all required data for this project.

I17095 Evaluation of diagnosis, referral and treatment of acute HIV-1 infection at the Amsterdam STI clinic: trends over time
De Bree G, Schim van der Loeff M, Dijkstra M, Prins M, Prins J, van Rooijen M, Hogewoning A, van Sighem AI.

Date of approval: 24 November 2017

Ongoing.

Publications

IN 2017

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Factors associated with time to achieve an undetectable HIV RNA viral load after start of antiretroviral treatment in HIV-1-infected pregnant women
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Medicine (Baltimore). 2017 Feb;96(7):e5891. doi: 10.1097/MD.0000000000005891

Phylogenetic evidence for underreporting of male-to-male sex among human immunodeficiency virus–infected donors in the Netherlands and Flanders
van de Laar TJ, Bezemer D, van Laethem K, Vandewalle G, de Smet A, van Wijngaerden E, Claas EC, van Sighem AI, Vandamme AM, Compernolle V, Zaaijer HL.
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Brinkman K, Boender TS, van der Valk M, van Sighem A, Reiss P, Kroon FP.
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van Bilsen WPH, van den Berg CHSB, Rijnders BJA, Brinkman K, Mulder JW, Gelinck LBS, Hoepelman AIM, Wit FWNM, van de Beek D, Prins JM.
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Smolders EJ, Smit C, TMM De Kanter C, Dofferhoff A, Arends JE, Brinkman K, Rijnders B, Van Der Valk M, Reiss P, Burger DM.
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Op de Coul ELM, Joore IK, van Sighem A, Bom BCJ, Hillebregt M, Prins JM, Geerlings SE, van Bergen JEAM.
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Vanhommerig JW, Bezemer D, Molenkamp R, Van Sighem AI, Smit C, Arends JE, Lauw FN, Brinkman K, Rijnders BJ, Newsum AM, Bruisten SM, Prins M, Van Der Meer JT, Van De Laar TJ, Schinkel J; MOSAIC study and the ATHENA national observational cohort.
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AGE$_h$IV

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Langebeek N, Kooij KW, Wit FW, Stolte IG,

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aMASE

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ART-CC

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Antiretroviral pill count and clinical outcomes in treatment naive patients with HIV
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CASCADE

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COBRA

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High cellular monocyte activation in people living with human immunodeficiency virus on combination antiretroviral therapy and lifestyle-matched controls is associated with greater inflammation in cerebrospinal fluid
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COHERE

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Socio-economic Inequalities and HIV Working Group for Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) in EuroCoord.
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Migrant Health Working Group for the Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) in EuroCoord.
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Cardiovascular disease (CVD) and chronic kidney disease (CKD) event rates in HIV-positive persons at high predicted CVD and CKD risk: A prospective analysis of the D:A:D observational study
Boyd MA, Mocroft A, Ryom L, Monforte AD, Sabin C, El-Sadr WM, Hatleberg CI, De Wit S, Weber R, Fontas E, Phillips A, Bonnet F, Reiss P, Lundgren J, Law M.
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ORAL PRESENTATIONS

Co- and multimorbidity in people aging with HIV
Reiss P.
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Body mass index and the risk of serious non-AIDS events: the D:A:D study
Achhra AC, Sabin C, Ryom L, d'Arminio Monforte A, de Wit S, Phillips A, Pradier C, Lundgren JD, Law M.
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Unrestricted DAA access in the Netherlands: rapid therapy uptake in HIV+HCV+ patients
Boerekamps A, Newsum A, Smit C, Reiss P, Richter C, van der Valk M, Arends J, Brinkman K, Rijnders B.
CROI 2017: Conference on Retroviruses and Opportunistic Infections, Seattle, USA, 13-16 February 2017

Association between cardiovascular disease and contemporarily used protease inhibitors
Ryom L, Lundgren JD, El-Sadr WM, Reiss P, Phillips A, Kirk O, Weber R, Sabin C, Mocroft A.
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Cessation of cigarette smoking and the impact on cancer incidence in the D:A:D study
Shepherd L, Ryom L, Petoumenos K, Hatleberg CI, d'Arminio Monforte A, Bonnet F, Reiss P, Lundgren JD, Mocroft A.
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Cardiovascular prevention policy in HIV: Recommendations from a modelling study
van Zoest R, Smit M, Nichols B, Vaartjes I, Smit C, van der Valk M, Wit F, Hallett TB, Reiss P
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Estimating HIV incidence with the ECDC HIV modelling tool
van Sighem A.
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Estimating HIV incidence and the undiagnosed HIV population in the European Union/ European Economic Area
Sighem A, Pharris A, Quinten C, Noori T, Amato-Gauci A, on behalf of The European Surveillance System HIV/AIDS database.
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A new method to estimate the first step in the HIV care continuum
van Sighem A.
International scientific-practical conference actual problems of HIV: women and HIV, Saint Petersburg, Russia, 5-6 June 2017

Unrestricted DAA access in the Netherlands: rapid uptake of treatment in HIV/HCV+ patients in the Netherlands [Onbeperkte DAA toegang in Nederland: snelle opname van behandeling in HIV/HCV+ patiënten in Nederland]
Smit C.
Expert meeting RIVM-CIB, Utrecht, 23 June 2017

Immunodeficiency at the start of combination antiretroviral therapy in low-, middle- and high-income countries
Anderegg N, Kirk O, for the IeDEA & COHERE collaborations.
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HIV-1 infection and sexual functioning among middle-aged men who have sex with men
Dijkstra M, van Lunsen RHW, Kooij KW, Davidovich U, van Zoest RA, Wit FWMN, Prins M, Reiss P, Schim van der Loeff MF, on behalf of the AGE_hIV cohort study.
IAS 2017, Paris, 23-26 July 2017

Closing the gaps: lessons learned in Amsterdam's success in reaching 90-90-90
Prins M, on behalf of the HIV Transmission Elimination Amsterdam initiative.
IAS 2017, Paris, 23-26 July 2017

Estimating HIV incidence and the undiagnosed HIV population in the European Union / European economic area
van Sighem A, Pharris A, Quinten C, Noori T, Amato-Gauci A, and the ECDC HIV/AIDS Surveillance and Dublin Declaration Networks.
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The effectiveness of a guided Internet-based self-help intervention for people with HIV and depressive symptoms: A randomized controlled trial
Van Luenen S, Garnefski N, Spinhoven P, Kraaij V.
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The cascade of care: how to make predictions for the early steps?
Van Sighem A.
Current Situation and Prevention Strategies of HIV Epidemiology in our Country, Istanbul, Turkey, 14 October 2017

The hepatitis C continuum of care among HIV infected individuals in EuroSIDA
Amele S, on behalf of EuroSIDA.
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PRESENTATIONS IN 2017

HIV and ageing: using cohort data to separate the myths from reality
Van Zoest R, Schouten J.
16th European AIDS Conference, Milan, Italy, 25-27 October 2017

Use of integrase inhibitors is an independent risk factor for immune reconstitution inflammatory syndrome (IRIS) in HIV-1 late presenters: An ATHENA Cohort Study
Wijting I.
16th European AIDS Conference, Milan, Italy, 25-27 October 2017

Greater insight into the HIV epidemic using the ECDC Modelling Tool [Presentation in Dutch]
Van Sighem A.
RIVM, Utrecht, the Netherlands, 9 November 2017

Living positive with HIV: A randomized controlled trial of a guided Internet-based self-help intervention for people with HIV and depressive symptoms
Van Luenen S, Kraaij V, Spinhoven P, Garnefski N.
AIDSImpact, Cape Town, South Africa, 13-15 November 2017

Many introductions but little transmission of HIV 1 non B subtypes in the Netherlands
Bezemer D, Hall M, van Sighem A, Reiss P, Fraser C, Ratmann O.
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Geospatial analysis and mapping of new HIV diagnoses, late presentations and GP testing practices in Amsterdam
Böhnke L, Vu T, van Bergen J, van Sighem A, Groot Bruinderink M, Op de Coul E, Kroone M, Reiss P, Heidenrijk M, de Bree GJ.
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The HIV epidemic in the Netherlands: an update
Reiss P.
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Cost-effectiveness of increased HIV testing among men who have sex with men in the Netherlands
Reitsema M, Steffers L, Wallinga J, van Benthem B, Visser M, de Munnik S, van Sighem, Schim van der Loeff M, Xiridou M, Mangen MJM.
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Estimating HIV incidence and the undiagnosed HIV population in the European Union/ European Economic Area
van Sighem A, Pharris A, Quinten C, Noori T, Amato-Gauci AJ and the ECDC HIV/AIDS Surveillance and Dublin Declaration Networks.
11th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment, Amsterdam, the Netherlands, 21 November 2017

POSTER PRESENTATIONS

Regional differences across Europe in advanced fibrosis and cirrhosis among HIV/HCV co-infected persons between 2010-2015
Amele S, on behalf of EuroSIDA.
HepHIV 2017 Conference, St Julians, Malta, 31 January - 2 February 2017

Variation in ART-coverage and virological suppression among HIV key populations
Laut K, on behalf of EuroSIDA.
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Vascular health and cerebral blood flow in perinatally HIV-infected children
Blokhuis C, Cohen S, Scherpbier HJ, Mutsaerts HJM, Meijers JC, Kootstra NA, Reiss P, Wit F, Teunissen CE, Pajkrt D.
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Longitudinal analysis shows no evidence for accelerated brain ageing in treated HIV
Cole JH, Caan MW, Underwood J, van Zoest R, De Francesco D, Winston A, Sabin C, Sharp DJ, Reiss P.
CROI 2017: Conference on Retroviruses and Opportunistic Infections, Seattle, USA, 13-16 February 2017

Central nervous system penetration of antiretroviral therapy in HIV-infected children
Hof MV, Blokhuis C, Cohen S, Scherpbier HJ, Wit F, Pistorius M, Kootstra NA, Teunissen CE, Mathot R, Pajkrt D.
CROI 2017: Conference on Retroviruses and Opportunistic Infections, Seattle, USA, 13-16 February 2017

Stopping secondary TE prophylaxis in suppressed patients with CD4 100-200 is not safe
Miro JM.
CROI 2017: Conference on Retroviruses and Opportunistic Infections, Seattle, USA, 13-16 February 2017

First and recurrent venous thrombosis in HIV patients of the Dutch ATHENA cohort
Rokx C, Borjas Howard J, Smit C, Wit F, Pieterman ED, Meijer K, Bierman W, Tichelaar V, Rijnders B.
CROI 2017: Conference on Retroviruses and Opportunistic Infections, Seattle, USA, 13-16 February 2017

PRESENTATIONS IN 2017

Darunavir/r use and incident chronic kidney disease in HIV-positive persons
Ryom L, Lundgren JD, Reiss P, Kirk O, Law M, Ross M, Morlat P, Fux CA, Mocroft A.
CROI 2017: Conference on Retroviruses and Opportunistic Infections, Seattle, USA, 13-16 February 2017

Earlier diagnosis and treatment reduces HIV transmission in MSM in the Netherlands
van Sighem A, Bezemer D, Op de Coul E, Branger J, de Boer M, Reiss P.
CROI 2017: Conference on Retroviruses and Opportunistic Infections, Seattle, USA, 13-16 February 2017

Integrase inhibitors are an independent risk factor for IRIS: an ATHENA cohort study
Wijting I, Rokx C, Wit F, Postma A, Hoepelman A, van der Ende I, Reiss P, Rijnders B.
CROI 2017: Conference on Retroviruses and Opportunistic Infections, Seattle, USA, 13-16 February 2017

Durability of first-line combination antiretroviral therapy (cART) for HIV in the Netherlands
Boender TS.
21st International Workshop on HIV Observational Databases, Lisbon, Portugal, 30 March-1 April 2017

HIV-1 status is independently associated with decreased erectile function among middle-aged men who have sex with men
Dijkstra M.
21st International Workshop on HIV Observational Databases, Lisbon, Portugal, 30 March-1 April 2017

Initiation of cART: a nationwide overview of variation between HIV treatment centres
Smit C.
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People living with HIV and HIV-negative individuals with similar lifestyles show greater age advancement compared to healthy blood donors
De Francesco D, Oehlke S, Bürkle A, Wit FW, Franceschi C, Kootstra NA, Libert C, Grune T, Weber D, Jansen EHJM, Reiss P, Sabin CA, for the Co-morBidity in Relation to Aids (COBRA) Collaboration.
IAS 2017, Paris, 23-26 July 2017

Initiation of cART: a nationwide overview of variation between HIV treatment centres in the Netherlands
Boender TS, Smit C, Brinkman K, Prins JM, Kroon FP, Geerlings SE, Reiss P.
IAS 2017, Paris, 23-26 July 2017

PRESENTATIONS IN 2017

Cardiovascular disease (CVD) and chronic kidney disease (CKD) event rates in HIV-positive persons at high predicted CVD and CKD risk: results from the D:A:D study
Boyd MA, Mocroft A, Ryom L, d'Arminio Monforte A, Sabin C, El-Sadr W, Hatleberg CI, De Wit S, Weber R, Fontas E, Phillips A, Dabis F, Reiss P, Lundgren J, Law M, D:A:D Study Group.
IAS 2017, Paris, 23-26 July 2017

International trends in new HIV diagnoses among men who have sex with men in North America, Western Europe and Australia 2000-2014
Chapin-Bardales J, Sullivan PS, Guy RJ, Kaldor J, McGregor S, Sasse A, Archibald C, Rank C, Casabona Barbarà J, Folch-Toda C, Vives Martin N, Cowan SA, Cazein F, Velter A, an der Heiden M, Gunsenheimer-Bartmeyer B, Marcus U, Op de Coul ELM, Van Sighem A, Aldir I, Cortes Martins H, Berglund T, Velicko I, Gebhardt M, Schmidt AJ, Delpech V, Hughes G, Nardone A, Hall HI, Johnson AS.
IAS 2017, Paris, 23-26 July 2017

The application of artificial intelligence to predict response to different HIV therapies, without a genotype: new models for therapy optimisation in resource-limited settings
Revell A, Hamers R, Morrow C, Wood R, Reiss P, van Sighem A, Johnson M, Ruiz L, Alvarez-Uria G, Sierra-Madero J, Montaner J, Lane HC, Larder B, RDI Data and Study Group.
IAS 2017, Paris, 23-26 July 2017

From HIV infection to HIV suppression: improvements in the time to reach successive stages in the HIV care continuum in the Netherlands
van Sighem A, Op de Coul E, Boender TS, van Benthem B, Bouwhuis J, Brinkman K, Reiss P, on behalf of the ATHENA national HIV cohort.
IAS 2017, Paris, 23-26 July 2017

Abacavir usage patterns and hypersensitivity reactions (HSR) in the EuroSIDA cohort
Roen A, Laut K, Pelchen Matthews A, Borodulina E, Caldeira L, Clarke A, Clotet B, d'Arminio Monforte A, Fätkenheuer G, Gatell Artigas JM, Karpov I, Kuznetsova A, Kyselyova G, Mozer-Lisewska I, Mulcahy F, Ragone L, Scherrer A, Uzdavin V.
16th European AIDS Conference, Milan, Italy, 25-27 October 2017

Estimating the country-specific burden of late presentation to HIV care across Europe between 2010-2014
Laut K on behalf of the Late Presentation Working Group in the COHERE and EuroSIDA studies.
16th European AIDS Conference, Milan, Italy, 25-27 October 2017

PRESENTATIONS IN 2017

Occurrence of hypersensitivity reaction and hepatotoxicity in patients receiving integrase inhibitors: Results from the EuroSIDA study
Shepherd L, Peters L, Begovac J, Benfield T, Curtis L, De Wit S, Horban A, Jablonowska E, Johnson M, Khromova I, Losso MH, Lundgren J, Nielsen LN, Raben D, Ridolfo AL, Schmied B, Stephan C, Thalme A, Vannappagari V, Yust I, Kirk O.
16th European AIDS Conference, Milan, Italy, 25-27 October 2017

Discontinuation of dolutegravir- and elvitegravir-containing cART in the Netherlands; incidence rates and risk factors
Bollen PDJ, Hakkers CS, Boender TS, van Crevel R, Brouwer A, Hoepelman AIM, Reiss P, Wit FWNM, Arends JE, Burger DM, on behalf of the ATHENA national observational HIV cohort.
16th European AIDS Conference, Milan, Italy, 25-27 October 2017

Differences in access to HIV testing, treatment and healthcare among nonmigrants and migrants living with HIV in the Netherlands: a cross-sectional study
Bil JP, Zuure FR, Alvarez-del Arco D, Prins J, Brinkman K, Leyten E, van Sighem A, Burns F, Prins M.
AIDSImpact, Cape Town, South Africa, 13-15 November 2017

Differences in access to HIV testing, treatment and healthcare among nonmigrants and migrants living with HIV in the Netherlands: a cross-sectional study
Bil JP, Zuure FR, Alvarez-del Arco D, Prins J, Brinkman K, Leyten E, van Sighem A, Burns F, Prins M.
11th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment, Amsterdam, the Netherlands, 21 November 2017

The impact of immediate initiation of combination antiretroviral therapy on the HIV epidemic among MSM
Reitsema M, Wallinga J, van Benthem B, van Sighem A, Schim van der Loeff M, Xiridou M.
11th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment, Amsterdam, the Netherlands, 21 November 2017

The impact of increased HIV/STI testing on the spread of HIV and gonorrhoea among men who have sex with men
Reitsema M, Wallinga J, van Benthem B, van Sighem A, Schim van der Loeff M, Visser M, Xiridou M.
EPIDEMICS, Sitges, Spain, 29 November – 1 December 2017

Financial report

Income

In 2017, Stichting HIV Monitoring's (SHM) total income was €3,805,785. The majority of this income came from the structural institute grant for HIV monitoring in the Netherlands that SHM receives each year from the Centre for Infectious Disease Control Netherlands of the National Institute for Public Health and Environment (*Centrum Infectieziektenbestrijding, Rijksinstituut voor Volksgezondheid en Milieu*, RIVM-CIb), 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 and contributions.

STRUCTURAL INSTITUTE GRANT FOR HIV MONITORING IN THE NETHERLANDS

SHM is a ministry of VWS-recognised healthcare institute with a structural institute grant (RIVM-CIb grants framework). This grant, awarded for monitoring HIV in the Netherlands, was set at €3,164,200 for 2017. During the course of 2017, the wage-sensitive part of the institute grant was increased by 2.04%, equivalent to €52,325. As such, in the fiscal year of 2017, the ministry of VWS allocated SHM a total institute grant of €3,216,525 for monitoring HIV in the Netherlands.

On 30 November 2017, the RIVM officially determined the final amount for the 2016 institute grant. Because the deferred grant reserve had exceeded the maximum permitted amount, the 2016 institute grant was reduced by €56,278, of which €11,153 related to 2015 and €45,125 related to 2016.

STRUCTURAL INSTITUTE GRANT FOR THE AMSTERDAM COHORT STUDIES (ACS)

Since 1984, the ACS have been carrying out multidisciplinary research into the epidemiology, psychosocial determinants, natural course and pathogenesis of HIV-1 infection and, more recently, other blood-borne and sexually-transmitted diseases. The collaborating institutes, including the Academic Medical Center of the University of Amsterdam (AMC-UvA), the Public Health Service of Amsterdam (*Geneeskundige en Gezondheidsdienst*, GGD Amsterdam), and SHM, make use of data and body samples provided by HIV-1 positive individuals and people at high risk of acquiring 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.

SHM is responsible for the financial administration of the ACS and submits the application to the RIVM for the annual structural institute grant of €500,000 for the ACS. In addition, the collaborating institutes within the ACS make a contribution to the coordination, management and financial management costs. GGD Amsterdam and the AMC-UvA each contribute individually to the storage of patient data and samples.

INCOME

HIV MONITORING-RELATED COLLABORATIONS: GRANTS AND FINANCIAL CONTRIBUTIONS

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 more reliable insight into the long-term effects of HIV treatment. As such, participation in national and international studies is fully in line with SHM's mission and objectives.

In 2017, SHM received €124,424 as income from HIV monitoring-related collaborations. This income is €448,702 less than that earned through collaborations in 2016. This marked reduction in income from scientific collaborations is due to the fact that, in 2016, SHM contributed to the *Data collection on Adverse Effects of Anti-HIV Drugs* (D:A:D) study for the 17th, and final, time. For this contribution, SHM received a sum of €479,932 in 2016.

During the course of 2017, SHM received financial contributions through participation in the following scientific collaborations:

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

In 2017, ECDC awarded SHM a grant of €24,500 for the project entitled 'Supporting the implementation of the HIV modelling tool'. This project lasted 10 months and ran until the end of 2017. In addition, SHM received €30,041 from University College London as part of the ECDC framework contract. This contract will continue in 2018.

2. Comorbidity and Ageing with HIV (AGE_hIV)

In 2017 SHM received a sum of €33,147 from the AGEhIV study. This study aims to describe the incidence and prevalence of a wide range of comorbidities and known associated risk factors in ageing HIV-positive individuals compared with HIV-negative individuals. SHM plays an important role in this study, which is coordinated by the Amsterdam Institute for Global Health and Development (AIGHD) at the AMC-UvA.

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

As part of this scientific research collaboration, SHM received a sum of €26,280. EPPICC carries out epidemiological research throughout Europe into the prognosis and outcomes of HIV-positive children and pregnant women, as well as children exposed to HIV *in utero*. Due to the relatively small number of children living with HIV in Europe, it is essential to combine data within a

INCOME

single network to efficiently address questions arising within this specific population. Currently, EPPICC comprises 13 studies, including the European Collaborative Study (ECS).

OTHER INCOME

In total, SHM received €21,114 from other sources of income. SHM staff were involved in organising the Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) in 2017 and the associated salary expenses (€21,073) were charged to Stichting NCHIV.

Expenditure

In 2017, SHM's total expenses were €3,948,362. Three main expense categories for 2017 are outlined below:

1. PERSONNEL COSTS

A large portion of SHM's expenses comprises personnel costs. In 2017, personnel costs once again represented the largest expense for SHM at €2,396,557, equivalent to 61% of the total expenditure. As per 31 December 2017, SHM had a total of 45 employees (with an average of 37.5 full-time equivalents [FTEs]). This number does not include employees of HIV treatment centres that carry out their own data collection and data entry and for which the treatment centres receive a payment from SHM.

2. MATERIAL COSTS

In 2017, material costs amounted to €643,364 and comprised license and maintenance costs for the national HIV monitoring database, housing costs, administration and consultancy costs, and other operational costs. Depreciation of the investment in the LISA IT project will commence in February 2018.

3. PAYMENTS

Amsterdam Cohort Studies payment

In line with the budget, SHM transfers the RIVM funding (€500,000) earmarked for the ACS to GGD Amsterdam and the AMC-UvA. SHM is responsible for ACS's financial administration, but did not charge the ACS any management costs for this service.

Payments to HIV treatment centres

SHM employees now carry out data collection and entry for 16 treatment centres. In 2017, SHM paid the remaining HIV treatment centres that carry out their own data collection and entry of data into SHM's database a sum of €53.98 per patient per year, based on the number of patients in active follow up on 31 December 2016. In 2017, a number of these hospitals requested data collection assistance from SHM. 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 a sum as a contribution towards the costs of collecting and storing patients' plasma.

In total, in 2017 SHM paid HIV treatment centres €481,478 for patient data collection and entry and for storage of patients' samples. For the assistance in data collection provided by SHM employees, an amount of €73,037 was deducted from the above-mentioned payments.

Operating result

The operating result (€-140,649) indicates that the total costs in 2017 exceeded SHM's income. The portion of the operating result that relates to HIV monitoring in the Netherlands (€-183,988) will be deducted from the deferred grant reserve. The remainder of the operating result (€43,339) will be added to the general reserve.

RESERVES

SHM's total financial reserves (including the deferred grant revenue, eligible costs reserve and designated reserve earmarked for investment) amounted to €3,994,348 on 31 December 2017.

1. Deferred VWS grant reserve

As of 31 December 2017, the deferred grant reserve amounted to €0. This amount includes the negative 2017 financial result (€-183,988) for HIV monitoring in the Netherlands. The deferred grant revenue is intended to guarantee operational continuity over a certain period of time. To ensure that this amount remains positive, €130,975 from the reserve for other purposes has been added to the deferred grant reserve.

2. General reserve

The general reserve is not earmarked for a specific purpose and, on 31 December 2017, amounted to €2,331,841.

3. Eligible costs reserve

From 2002 through 2007, SHM built an eligible costs reserve of €382,206. This sum arose through financing from the Healthcare Tariffs Board (*Tarieven Gezondheidszorg*) and, later, the Dutch Healthcare Authorities (Nederlandse Zorgautoriteit).

4. Designated reserve

As per 31 December 2017, the reserve designated for the LISA IT project amounted to €1,280,301. Future depreciation of this investment will be charged against this reserve.

CONTINGENCY RESERVE AS OF 31 DECEMBER 2017

To cover the financial obligations and risks, SHM must have a sufficiently large contingency reserve. The governing board has decided that, based on SHM's obligations and risks, the target necessary for the contingency reserve should be €1.5 million.

Risk disclosure

SHM's governing board and director/deputy director are primarily responsible for avoiding and detecting fraud, ensuring that legislation is adhered to, and identifying any risks that may pose a threat to SHM. It is important that the management of SHM, under the auspices of those responsible for governance, devote the necessary attention to these risks. This approach requires the commitment to develop a culture of integrity and ethical conduct, and can be reinforced by active supervision. As such, SHM's governing board maintains a culture of honesty and ethical conduct and has taken management measures to limit SHM's risk as far as possible.

RISK MANAGEMENT

SHM strives to foster a culture of respectful and honest conduct; such a culture forms the foundation for preventing any form of fraudulent conduct. Moreover, SHM has taken certain measures, both soft and hard, to maintain this culture. One of SHM's core values is respectful conduct towards external parties and between employees themselves. As such, employees are supported in displaying appropriate behaviour, not only by management setting the example, but also by means of various current protocols and procedures. For example, SHM has a code of conduct to which all employees have access and that includes protocols and procedures on issues such as integrity, privacy, IT use, and reporting abuse or improper use of SHM property. Furthermore, SHM has a confidential mediator to whom employees can turn with personal concerns and to report incidents, including fraudulent conduct.

This culture and the measures taken to maintain it are an important part of SHM's risk management. Other risk management measures have been taken in response to a number of risks identified by the board. An internal analysis of the most important of these risks has been carried out, and appropriate mitigating measures have been taken for each identified risk to minimise any residual risk.

Balance sheet

AFTER APPROPRIATION OF PROFITS

Assets	31-Dec-17 (€)	31-Dec-16 (€)
Fixed assets		
Intangible fixed assets	1,128,727	422,509
Tangible fixed assets	9,219	9,947
Total fixed assets	**1,137,946**	**432,456**
Current assets		
Accounts receivable	3,735	3,287
Receivables and accrued assets	175,167	185,707
Liquid assets	3,997,933	4,634,489
Total current assets	**4,176,835**	**4,823,483**
Total assets	**5,314,781**	**5,255,939**

Liabilities	31-Dec-17 (€)	31-Dec-16 (€)
Capital reserves		
Deferred grant revenue	0	53,013
General reserve	2,331,841	2,419,477
Eligible costs reserve	382,206	382,206
Earmarked reserve	1,280,301	1,280,301
Total capital reserves	**3,994,348**	**4,134,997**
Short-term liabilities		
Accounts payable	362,359	131,949
Short-term liabilities and accrued expenses	958,074	988,993
Total short-term liabilities	**1,320,433**	**1,120,942**
Total liabilities	**5,314,781**	**5,255,939**

Profit and loss account

Profits	Budget 2017 (€)	2017 (€)	2016 (€)
Structural institute grants	3,664,200	3,660,247	3,664,202
Other grants and financial contributions	62,000	124,424	573,126
Other revenue	20,500	21,114	27,400
Total net revenue	**3,746,700**	**3,805,785**	**4,264,728**
Operating costs			
Personnel costs	2,308,000	2,396,557	2,432,077
Depreciation of fixed assets	122,500	6,120	18,466
Other operating costs	675,000	632,978	643,467
Project-related costs	0	4,266	33,015
Payments	925,000	908,441	955,674
Total operating costs	**4,030,500**	**3,948,362**	**4,082,699**
Year result	**-283,800**	**-142,577**	**182,029**

Financial profit and loss	Budget 2017 (€)	2017 (€)	2016 (€)
Interest and similar revenue	10,000	2,968	8,614
Interest and similar expenses	-1,200	-1,040	-1,161
Total financial profit and loss	**8,800**	**1,928**	**7,453**
Year result	**-275,000**	**-140,649**	**189,482**

Appropriation of year result	2017 (€)	2016 (€)
The year result was distributed as follows:		
Deferred grant revenue	-53,013	-117,677
General reserve	-87,636	307,159
	-140,649	**189,482**

2018

BOARD RESOLUTIONS

As of May 2017, SHM had registered 20,110 individuals. Here, the term *registered* refers to all patients for whom data were collected during the past two years. These included 227 children, 170 pregnant women and 288 individuals who had died. Excluding those who had died, as of May 2017, a total of 19,822 registered individuals were still in care. This represents an increase of 540 compared to May 2016.

In 2018, the number of registered individuals is predicted to increase by 1.6% compared to 2017. This increase is based on the average increase in the number of HIV-positive individuals over time since 2004. Since 2004, this rate has been decreasing and it is expected to become negative for the first time in 2021. As a result, the number of individuals in care is expected to decline from that year onwards.

The gradual increase in the proportion of older individuals in SHM's database and the associated increase in age-related comorbidity makes it increasingly important to adequately collect clinical information about age-related comorbidity and associated risk factors. Furthermore, even when an HIV infection is well suppressed with antiretroviral therapy, HIV-positive individuals remain at increased risk of age-related comorbidity. In addition to collecting information on non-infectious comorbidity (including cardiovascular disease, diabetes mellitus, renal function and malignancies [other than the traditionally registered AIDS-defining malignancies such as Kaposi's sarcoma and non-Hodgkin's lymphoma]), it is also necessary to collect information on chronic liver disease, which is frequently, but not exclusively, associated with hepatitis B virus (HBV) and hepatitis C virus (HCV) co-infection. Moreover, with the advent of the now rapidly expanded arsenal of direct-acting antiviral agents (DAAs) against HCV, registration and monitoring of the use of these agents have become extremely important. Equally, of increasing importance is the registration of the short and longer-term impact of these agents on the incidence of new HCV infections and on that of long-term liver complications.

In 2009, the hepatitis working group, set up by SHM together with the Dutch Association of HIV-Treating Physicians (NVHB), developed a protocol for the standardised collection of an extensive set of relevant data on HBV and HCV co-infection and related morbidity and mortality in people living with HIV. As a result, SHM invested in expanding the data collection capacity, with priority initially assigned to collecting more extensive data on HCV, followed by more extensive collection of HBV data from 2014 onwards; the latter has now been completed. This investment has allowed efficient and effective registration of the use of DAAs in HCV treatment and of the impact of this treatment. In the future, this development will also make it possible to register the effect of interventions to 'cure' HBV, which, similar to HIV, is a persistent viral infection. Research into such interventions is currently making rapid progress.

2018

As of 1 January 2018, SHM's current data entry system, Oracle Clinical, will no longer be supported by the AMC, which hosts and manages the system. SHM therefore had to purchase a new data entry system to replace Oracle Clinical. A key requirement in selecting a new system was that it should be better tailored to SHM's core activities and sit well within SHM's innovation strategy. Following a thorough analysis of existing systems during an intensive preparatory period, a suitable data entry system was selected. This system, which involves a collaboration between LogicNets, ICT automatisering, SHM and the AMC's ADICT (abbreviated to 'LISA'), was implemented at the start of 2018, as planned. The anticipated improvement in efficiency, which should become apparent from 2018 onwards, is based on various aspects of the new system, such as a modern structure that facilitates data import from external sources, the ability to collect information according to a protocol-based structure programmed within the system, the obviation of a number of manual quality control procedures, the integration of data collection protocols, independent functional management of the system by SHM without requiring services of the supplier, and the possibility of expanding the system with additional modules. The total investment in the LISA project from 2015 through to early 2018 is estimated to be €1,291,000.

GRANTS/OTHER FINANCIAL CONTRIBUTIONS IN 2018

The structural institute grant provided to SHM by the ministry of VWS through the RIVM-CIb for HIV monitoring in the Netherlands represents the largest portion of SHM's income in 2018. In 2017, the RIVM awarded SHM a sum of €3,164,200. In addition, on 7 September 2017, the wage-sensitive part of the 2017 grant was indexed by 2.04%, providing an additional sum of €52,325. This brings the total 2017 institute grant for HIV monitoring in the Netherlands to €3,216,525. The 2018 budget will be based on this sum.

The institute grant for the ACS from the RIVM-CIb on behalf of the ministry of VWS is also paid out to SHM on an annual basis. SHM pays this structural institute grant of €500,000 in full to the two organisations that carry out the research, namely the AMC-UvA and GGD Amsterdam. SHM is solely responsible for the financial administration for the ACS.

In addition to these structural institute grants, SHM's income consists of project-related grants and contributions, including both national and international grants.

In 2018, SHM will start a pilot registration of individuals in care with HCV mono-infection in around seven hospitals. This pilot study, estimated to cost €124,900, is expected to be financed by HepNed, the scientific organisation of hepatitis-treating physicians at the Dutch academic medical centres.

2018

Contributions totalling €85,800 have been budgeted for the following projects in which SHM is involved: ECDC, AGE$_h$IV, CIPHER/ EPPICC, H-TEAM, and Curaçao data collection.

STAFFING IN 2018

The budgeted number of SHM staff for 2018 is equivalent to 37.3 FTEs. Compared with 2017, this represents a decrease of 0.2 FTEs.

EXPENSES IN 2018

The budget for 2018 has taken into account the salary increases approved as part of the 2015-2017 collective labour agreement (CAO) for university medical centres in the Netherlands. Consequently, SHM applied an indexation of 1.55% to salaries as of 1 January 2018. SHM also follows the CAO by increasing salaries by one periodic step on the salary scale for employees with good performance and who have not yet reached the maximum on their salary scale. In total, gross salaries in 2018 will amount to €1,930,600.

A total of 13.45% of the gross salaries, equivalent to €259,500, have been budgeted for social security contributions. This rate is based on the forecast for 2017.

In 2017, SHM's pension insurer, Zwitserleven, informed SHM that the pension contract would terminate as of 1 January 2018. In response, SHM sought quotes from various insurance companies for both a defined benefit pension plan (equivalent to that provided by SHM until the end of 2017) and a defined contribution pension plan. Following a thorough selection process, during which staff representatives were consulted, a defined contribution plan was selected. This new contract with Zwitserleven will come into effect on 1 January 2018. The pension costs for 2018 will be €158,900, which is €18,900 more than forecast for 2017.

The budgeted amount for training costs is €24,100, equivalent to 1.25% of salary costs. A large number of employees will receive training during the course of 2018 as part of the LISA project.

The IT depreciation costs have risen markedly in the 2018 budget, from €123,700 in 2017 to €258,200 in 2018. The costs associated with the LISA project are expected to remain within the approved budget of €1,291,000 and will be written off over a 5-year period. This depreciation will be covered by the designated reserves earmarked for this project.

2018

The estimated costs for 2018 for the use and maintenance of automation systems (LogicNets system, data warehouse, website, administration software, office IT equipment) are markedly lower than in 2017 (€266,900 versus €348,000) due to implementation of the new data entry system resulting from the LISA IT project.

Other operating costs for 2018 (housing, consultants, office supplies, and conferences) are lower than forecast for 2017 and represent a total decrease of €24,900 over a budget of €264,600 (-9%). This decrease has been achieved by a change in payroll service provider as of January 2018 (€5,000 saving), lower legal and fiscal advice costs (€15,000 less), and not having to make a contribution to NCHIV in 2018 (€7,000).

A sum of €495,000 has been budgeted as payment to those HIV treatment centres that carry out data collection themselves (the projected payment for 2017 is €498,500).

In 2018, the ACS institute grant of €500,000 that is expected to be paid to SHM will be paid out fully to the two organisations that carry out this study, namely the AMC-UvA and GGD Amsterdam.

FINANCIAL RESULTS

SHM's estimated financial result for 2018 is €-258,200.

This 2018 financial result is distributed across the following SHM activities and projects:

HIV monitoring in the Netherlands	€	-4,124
LISA IT project	€	-258,200
Other projects	€	4,124
Total result for 2018	**€**	**-258,200**

2018

2018 BUDGET

Profits	Budget 2018 (€)
VWS / RIVM grant for HIV monitoring in the Netherlands	3,216,500
VWS / RIVM grant for ACS	500,000
Project-based grants and financial contributions	210,700
Other revenue	500
Total net revenue	**3,927,700**
Operating costs	
Personnel costs	2,404,100
Other personnel costs	48,100
Subtotal personnel costs	*2,452,200*
Depreciation of fixed assets	266,200
IT expenses	266,900
Third party services	60,000
Subtotal third party costs	*326,900*
Housing expenses	109,700
Travel and conference expenses	40,800
Reporting	24,000
Office expenses	30,100
Project-specific expenses	7,000
Subtotal other operating costs	*211,600*
Payments Amsterdam Cohort Studies	500,000
Payments HIV treatment centres	432,500
Subtotal payments	*932,500*
Total operating costs	**4,189,400**
Year result	**-261,700**
Financial profit and loss	
Interest and similar revenue	5,000
Interest and similar expenses	-1,500
Total financial profit and loss	**3,500**
Year result	**-258,200**

Note: The 2018 financial results will be influenced by incidental depreciation and other costs related to the LISA IT project.

Appendix

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 immuno-deficiency virus), and characterised by failure of the immune system to protect against infections and certain cancers.

AIGHD
Amsterdam Institute for Global Health and Development.

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

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.

TERMINOLOGY & DEFINITIONS

CD4 (T4) 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 HIV. 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 (< 200 CD4 cells per mm^3 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).

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.

DAAs
Direct-acting antivirals (DAAs) are new-generation drugs that treat hepatitis C virus infection by targeting specific steps in the hepatitis C virus life cycle. There are different classes of DAAs, defined by their mechanism of action and therapeutic target.

DNA
Deoxyribonucleic acid. A complex protein that carries genetic information. HIV can insert its own genetic material 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 (Geneeskundige en Gezondheidsdienst).

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.

TERMINOLOGY & DEFINITIONS

Hepatitis C virus (HCV)
A viral infection that affects the liver and 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 Vereniging
Dutch HIV association.

Immunological failure
A type of HIV treatment failure. There is no consensus on the definition of immunological failure. However, some experts define immunological 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.

TERMINOLOGY & DEFINITIONS

Non-nucleoside reverse transcriptase inhibitor (NNRTI)
Antiretroviral 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.

Nucleoside reverse transcriptase inhibitor (NRTI)
Antiretroviral HIV drug class. Nucleoside reverse transcriptase inhibitors (NRTIs) block 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.

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

Nucleotide reverse transcriptase inhibitor (NtRTI)
A type of antiretroviral (ARV) HIV drug. Nucleotide reverse transcriptase inhibitors (NtRTIs) interfere with the HIV life cycle in the same way as NRTIs. Both block reverse transcription. NtRTIs 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 that combines the number of persons and their time contribution (e.g., in years) to the study. In the ATHENA cohort, person years generally refer to the cumulative number of years that individuals were followed by SHM.

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

TERMINOLOGY & DEFINITIONS

Pseudonymisation
Pseudonymisation is a privacy-enhancing technique that replaces personal identifiers with coded data. Certain identifiers (such as gender and age) are included in the record, but personal information is removed or replaced by a randomised string of characters. The data collected from people living with HIV are stored in SHM's database in a pseudonymised form. Pseudonymisation takes place within the HIV treatment centre and the key to the code is only available to the HIV treating physician.

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.

RIVM
The Netherlands' National Institute for Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu).

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.

Sustained virologic response (SVR12 or SVR24)
A measure of the response to hepatitis C virus (HCV) treatment. SVR12 or SVR24 indicates an undetectable level of HCV in blood 12 or 24 weeks, respectively, after completion of antiviral therapy for chronic HVC infection.

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 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.

TERMINOLOGY & DEFINITIONS

Virological failure
A type of HIV treatment failure. Virological 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.

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

HIV Monitoring