Annual Report 2013

HIV Monitoring

Contributing to the quality of HIV care

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

Our mission

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

www.hiv-monitoring.nl

Annual report 2013, approved by the Board of Governors of the Stichting HIV Monitoring on 22 April 2014.

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Foreword

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

Apart from monitoring HIV-specific outcomes, such as degrees of viral load suppression, immune recovery, emergence of HIV drug resistance and overall survival, SHM also invests much time and effort in monitoring non-AIDS co-morbidities, which continue to gain in importance as patients with HIV in care survive into older age. The efforts to expand and improve the data collection for viral hepatitis B and C co-infections in those with HIV that were started some time ago have been successfully continued. In turn, these methods have paved the way to explore their application in monitoring patients with hepatitis B and C mono-infection.

In 2013, further steps were undertaken to improve the data collection process. Considerable progress has been made in digitalising the transfer of laboratory data from hospital computer systems through Lab-Link, which is now being used by nine HIV treatment centres and is being tested by several others. In addition, quality control improvements were expanded in 2013, with a marked increase in the number of checks carried out on patient files, improved detection of missing and inconsistent data and ongoing training and personal coaching of data collectors and data quality staff.

Over the past year, SHM has continued to make an important contribution to various European and other more global HIV observational cohort collaborations, in terms of both data and science. Such a contribution makes it possible to tackle scientific questions that cannot be answered by any individual cohort on its own, and outcomes of this research regularly result in modifications to HIV treatment guidelines.

Lastly, I would like to thank all the people living with HIV in 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, 22 April 2014

Message from the Governing Board Chair

Stichting HIV Monitoring (SHM) contributes significantly to the quality of care of HIV-infected people throughout the Netherlands. Through life-long treatment, HIV has become a chronic disease in an expanding group of people who are surviving longer with the infection. Currently, approximately 17,000 HIV-infected people are in care in the Netherlands, and around 1100 persons with new diagnoses enter into care annually. Optimal and timely identification and treatment of the HIV-infected individual benefit not only the individual, but also reduce infectiousness and should thus also slow down the epidemic. On the other hand, suboptimal treatment can have serious implications, notably the emergence of HIV drug resistance. This may affect subsequent treatment options, both for patients already on treatment and, in the event of transmission of drug-resistant viral variants, for newly infected patients. Through continuous monitoring of HIV and its treatment, these threats to individually infected patients and to public health can be uncovered in time, and healthcare and prevention measures can be established before the need becomes critical.

HIV patient care in the Netherlands is currently concentrated in 8 academic and 19 non-academic treatment centres. To safeguard optimal care for persons living with HIV, a new certification process for these HIV treatment centres, the development of which started in 2012, has now been defined and will be implemented in 2014. SHM has been closely involved in defining the most appropriate quality of care indicators, and will be involved in making these indicators available to support certification.

In addition, SHM continues to make important scientific contributions to HIV research both nationally and internationally. Research conducted by SHM yields important information and a sound basis for the treatment and management guidelines that are gratefully used by medical professionals, patients, and policy makers.

Finally, I would like to thank all the SHM employees for their dedication and hard work and all the healthcare professionals and patients for their continued support and collaboration.

Dr Frank Kroon

Chairman of the Governing Board

Amsterdam, 22 April 2014

Progress report

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

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

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

The progress report includes an overview of the 27 treatment centres, as well as overviews of SHM's organisation, data collection, database and data quality management. It also includes reports on registration and monitoring and on the Amsterdam Cohort Studies, which receives its funding through SHM. An overview of SHM's national and international collaborations and ways in which SHM disseminated information during 2013 are also reported.

HIV treatment centres

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

In 2013, the following health institutes were involved as centres or subcentres for adult HIV care (in alphabetical order by town):

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

** The HIV Focus Centrum in Amsterdam was established as a new HIV treatment centre, formally linked to the AMC, at the end of 2013*

Centres for the treatment and monitoring of paediatric HIV and AIDS were:

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

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

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

SHM organisation

Stichting HIV Monitoring (SHM) is overseen by a Governing Board that includes members who represent academic and general hospitals, health insurers, the Netherlands HIV Association (HVN), the Dutch Association of HIV-Treating Physicians (NVHB) and the Academic Medical Centre (AMC), Amsterdam. The board members determine SHM's budget and establish the content of the annual report.

In addition, SHM has an Advisory Board that reviews SHM's activities from a strategic perspective and advises the Governing Board and the Director.

The SHM Working Group, consisting of members and reviewers, advises the Director on executive matters regarding use of data stored in the national HIV database. Therefore, the Working Group is also responsible for reviewing research proposals submitted to SHM.

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

SHM's data collectors are employed in the patient data and quality control unit, which had an average of 13.11 FTEs in 2013. This unit is also responsible for administering patient registrations (new registrations and discontinued registrations) and for assigning an anonymous identification code to each patient.

The data monitors, assistant data monitors and data managers are also part of the patient data and quality control unit. During 2013, the average number of FTEs for the data quality staff was 7.95. Data management activities, which are another responsibility of this unit, are partly outsourced to the Clinical Research Unit (CRU), Department of Clinical Epidemiology and Biostatistics at the Academic Medical Centre of the University of Amsterdam. At least twice a year, in February/March and in June/July, a data freeze takes place to produce a dataset for data processing and analysis. The patient data and quality control unit is managed by the SHM patient data and quality control manager, Sima Zaheri (0.8 FTEs). During 2013, the average number of FTEs for staff in the patient data and quality control unit was 21.06.

The data processing and analysis unit is staffed by researchers in the field of epidemiology, statistics, mathematical modelling of HIV and modelling of transmission networks. Together, these researchers implement the HIV registration programme, the results of which are presented in the annual SHM Monitoring Report published near the time of World Aids Day, as well as in separate articles in peer-reviewed international scientific journals. This unit supports and collaborates nationally with researchers in the HIV

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

In 2013, the unit had one assistant researcher involved in a PhD programme. This programme focussed on mathematical modelling of the impact of various interventions to control the HIV epidemic in the Netherlands. This unit also supports two other PhD programmes: one that compares the effect of combination antiretroviral therapy (cART) on HIV-infected individuals treated in Curaçao with that on HIV-patients from the Netherlands Antilles treated in the Netherlands, and a second that focuses on the optimisation of quality of care for HIV-infected patients in care in HIV treatment centres in the Netherlands.

In 2013 an average of 5.55 FTEs was assigned to the data processing and analysis unit. Since 1 February 2013, this unit has been led by Peter Reiss (0.91 FTE), Director of SHM.

The primary activities of SHM are supported by the office staff, which includes the secretariat, financial and personnel administration, internal controlling and communications. The office staff are supervised by SHM's controller, Daniëlle de Boer (0.7 FTE). In 2013, the average number of FTEs was 3.71 for this group; this number has remained constant over the past years.

As of 31 December 2013, SHM had an average total of 32.73 FTEs. In addition, SHM covers the costs for a total of 7.19 FTEs for data collectors and data entry staff who work at HIV treatment centres, but who are not on the SHM staff. The average sick leave during 2013 was 2.59%, which was 1.68% less than in 2012.

A list of members of SHM's Governing Board, Advisory Board, Working Group and personnel can be found in Appendix 1: Composition of SHM.

Data collection, database & data quality management

In 2013, Stichting HIV Monitoring (SHM) continued to improve its data production processes in line with its quality management system. The key priorities for 2013 were:

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

The following results were achieved in 2013:

Standardisation, automation and steps for improvements

Improvement and standardisation of manual data collection

In 2013, all data collection protocols were evaluated and improved. This review has resulted in the collection of more data, including more detailed data, regarding HIV transmission, adverse events, Centers for Disease Control (CDC) events, antiretroviral medication, co-medication and patient participation in studies.
The protocol for data collection on viral hepatitis infections drawn up in 2012 in close consultation with the Hepatitis Working Group (a collaboration between the Dutch Association of HIV-Treating Physicians [NVHB] and the SHM) has been optimised.
In 2012, a help-desk system was set up to support the data collectors in extracting data from the information sources in the HIV treatment centres and in coding and entry of data into the national SHM database in accordance with SHM protocols. This system was implemented in mid-2013. During 2013, the help desk received 222 queries from data collectors, 162 of which could be answered directly by the responsible data quality staff.

Centralised data collection

The efficiency and quality of data collection and the entry of complex data appears to correlate with the expertise of the data collectors. The process of data collection and entry has therefore been further improved through the centralised collection of complex data by specially trained staff from the SHM office on a flexible basis. For example, from 1 January 2013, within a 6-month period, all prospective and retrospective hepatitis-related data from the entire group of patients with chronic hepatitis C

infection (N = 1,468) in all HIV treatment centres were collected and entered into the national SHM database by trained SHM data collectors.

Improvements in data entry software

In 2013, we launched a project to digitalise new and discontinued registrations. As part of this project, the AMC's Clinical Research Unit (CRU) developed a new registration system that consists of several applications. These applications are based on Java and Microsoft.Net technology and are well integrated with each other and with existing SHM applications, such as Oracle Clinical, the data warehouse and the reporting system. This new registration system was tested in an acceptance environment at the end of 2013. In 2014, after completion of the test phase, the system will be implemented in all HIV treatment centres.
Since the Windows 7 operating system is now in use in almost all HIV treatment centres, the SHM database, Oracle Clinical, required upgrading. In 2013, the CRU carried out preparations to move from Oracle Clinical RDC classic version 4.5.3 to version 4.6.6. The new version was tested by SHM in a test environment and approved; it is expected to be implemented in 2014.

Patient reports, graphs and standard data queries

In 2013, patient and custom reports, graphs and standard data queries that were built in Microsoft Report Builder in 2011 were further developed and improved. Additional data overviews were constructed to enable the data collectors and data quality staff to work more effectively and efficiently. In addition, management reports were built to support the SHM coordinators.

Standardisation of Lab-Link

The move to standardise Lab-Link, the automated link that allows laboratory data from various hospital computer systems to be entered directly and anonymously into the SHM database, was continued in 2013. The standard protocol that was developed in collaboration with the AMC's CRU and General ICT Service (ADICT) for sending laboratory results as HL7 messages (an international standard for electronic data exchange between healthcare information systems) has been discussed with the Erasmus MC Rotterdam, the Kennemer Gasthuis Haarlem, the Slotervaartziekenhuis Amsterdam and the Maastricht UMC+, with the aim of setting up Lab-Link. The standard protocol for Lab-Link has been tested and implemented in the Erasmus MC Rotterdam, and in 2013 it entered the test phase in the Kennemer Gasthuis Haarlem, the Slotervaartziekenhuis Amsterdam, and the Maastricht UMC+. Throughout 2013, the AMC continued to send reports directly from the lab system via an internal connection. In total, nine treatment centres now use Lab-Link, representing laboratory data from 48% of the patients in the SHM database; this is a 20% increase from 2012.

Harmonisation of Lab-Link

A Lab-Link 'mapping tool' has been developed by the CRU in Microsoft Access. This tool receives and standardises laboratory results from different treatment centres with different terminology. In 2013, 856 combinations of laboratory terms and accompanying samples were harmonised.

'Digitalisation' innovation programme

In 2013, an innovation programme was launched to maximise data collection digitalisation, while minimising manual input. Not only is this more efficient, it also improves the quality of the data. SHM's vision for the future involves further digitalisation, which will take place in steps. To this end, several innovation providers were approached in 2013, and a feasibility study by the company, Furore, was commissioned. This study tested the following options:

- Accelerated implementation of Lab-Link in all treatment centres.
- Broadening the use of Lab-Link to other sections of the hospital computer system that would benefit from digital data delivery, such as medication details.
- Simplification of data extraction from electronic patient records by the data collector.

The feasibility study will be completed in 2014, after which implementation of the recommendations will be planned and carried out in stages.

Centre-specific reports

Standard reports are available on the SHM website to provide treatment teams in the treatment centres with a twice-yearly overview of developments, trends and issues within their own patient populations. These centre-specific reports were updated and presented to the HIV treatment centres on two occasions in 2013.

Improvements to data warehouse and data processing

SHM's data warehouse is located on a structured query language (SQL) server in the AMC, and extracts data from all SHM source systems. The data warehouse is updated daily with data that were manually entered into the national SHM database on the previous day and with data sent by treatment centres via Lab-Link. By distinguishing between the production, acceptance and test environments, SHM can efficiently produce data views for data analyses and reports, while maintaining quality. In 2013, the data warehouse contained 285 tables and 288 views that were available daily for data analysis and presentation of data to treatment centres in table and report form. A data freeze takes place twice a year, and, subsequently, the raw data tables from the data warehouse are processed to yield tables suitable for data analysis. The data are cleaned, clustered, and coded according to the standard protocols of various national and international collaborations and the Anatomical Therapeutic Chemical (ATC) classification.

In 2013, these data processing steps resulted in data sets for centre-specific reports, the Co-morbidity and Aging with HIV study, the Mosaic study and ZiZo (*Zichtbare Zorg*, Visible Care). In addition, data processing was carried out, and data sets were generated for

two international collaborations, the D:A:D (Data Collection of Adverse Events of Anti-HIV Drugs) study and COHERE (Collaboration of Observational HIV Epidemiological Research in Europe).

Volume of data collection

Table 1 gives an overview of the data collection. The total volume of manual data collection increased by 5% in 2013 compared with 2012. This reflects an increase in the manual collection of detailed data on viral hepatitis C infection in HIV patients. The volume of automated data collection via Lab-Link dropped by 5% in 2013; this resulted from a one-off peak in 2012 caused by HIV treatments centres sending laboratory results retrospectively as HL7 messages. However, in 2013, the volume of data received via Lab-Link represented only the number of laboratory results collected in 2013. The volume of manual data collection on pregnancies doubled in 2013 compared with 2012; this was due to steps taken to retrospectively reduce the data collection backlog of pregnancies in the OLVG, Amsterdam, which had not been possible until 2013. After a pilot phase and in consultation with paediatric HIV-treating physicians, the collection of data on HIV-exposed, but not infected, children was discontinued in 2013.

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

In 2013, the average long-term backlog in data collection remained at 0%, while the average short-term backlog decreased by 1%. This is an excellent result, given that, in 2013, the data collectors not only focused on collecting and entering follow-up data, but they also focused strongly on resolving discrepancies and improving the quality of existing data. Furthermore, new items were introduced, such as data on hepatitis C. This decrease in the backlog of data collection was also partly due to the ongoing training of data collectors in efficiently organising data collection logistics, where individual patient reports and standard data queries are used to monitor backlogs and establish priorities.

Quality control (QC)

The automated quality checks to support the manual quality checks by data quality staff and the efficiency improvements introduced in 2012 were expanded in 2013. For each data collection item, new validation rules were defined in 2013 to select inconsistencies and missing data to be checked by the data collectors. *Table 3* presents an overview of the automated quality checks in 2013. In total, 162 validation rules were defined (121 more than in 2012), and 21,529 records were selected to be sent to the data collectors for checking. The data collectors were given instructions and training, and the outcomes of the checks were implemented in the national SHM database.

Automated procedures for checking the Lab-Link data were also implemented in 2013. A distinction was made between one-time and structural checks on Lab-Link data in a test, acceptance and production environment. The one-time checks for acceptance of the new Lab-Link connections have been performed on data in both test and acceptance environments. In 2013, the the structural checks on Lab-Link data were performed twice in the production environment. The Lab-Link data were checked for accuracy, completeness, frequency with which data was sent and patient anonymisation.

Table 4 shows the manual quality checks performed by the SHM data quality staff in 2013. These manual checks focus on collected data that are essential for SHM's output, on a random selection of new items for which data were collected in 2013, on complex data that can be used as training material for personal coaching of data collectors and on consistency within the data.

In 2013, data from 260 patients were randomly selected and checked. Data related to cause of death and co-morbidity, defined as 'endpoints', continued to be checked in 100% of cases. Additional data were also collected and classified for data analysis.

As part of the personal coaching programme for the 41 data collectors, an average of seven patient files from each data collector were selected. The outcomes of the quality controls were discussed with the responsible data collector and item-specific training was provided.

In the course of 2013, data from 2,729 patients were checked manually by SHM data quality staff. In addition, 1,110 patient files were selected, and the data collected from these files were checked for reported cardiovascular diseases or other co-morbidities. Data on additional diagnostics were also collected. The causes of death for 247 deceased patients were verified and classified. On average, each HIV treatment centre was visited 20 times by the SHM data quality staff member responsible for that centre.

The number of patients whose files were quality-controlled increased by 175% in 2013 compared with 2012. This was due partly to an increased effort to complete retrospective data on co-morbidities and cause of death with more extensive and detailed checks, and partly to the introduction of efficient data checking to detect missing data on co-morbidities. This investment has resulted in more complete and higher quality data on cause of death and comorbidities in the entire population of HIV-infected persons registered in the SHM database, thereby increasing the possibilities for data analysis and, thus, research into these endpoints.

Training

In 2013, the 12 SHM data collectors involved in collecting data on viral hepatitis were given follow-up training. This training took place bimonthly and was interactive, allowing discussion of content-related developments and practical issues.

In addition to the personal coaching of data collectors, a review day was organised in May 2013, for all data collectors. This review day focused on the entry of liver diagnostics data. The outcomes of the analyses were explained and presented to the group, and SHM's data quality staff provided information on data processing, new online reports and changes to SHM's data structure. There was also a facts quiz with real voting buzzers. The results of the quiz were discussed and the data collectors were trained in procedures and activities related to collecting new data items and to maintaining data quality. Finally, the SHM's help-desk system was launched.

In 2013, the quality control staff were given training on the clinical aspects of hepatitis B and C infection and on how to recognise data related to these infections in the electronic patient record. A number of data quality staff members were also given a tailored three-day course in SQL. Finally, a Microsoft Report Builder training was organised.

In December 2013, some of the data quality staff were trained to recognise various infectious diseases.

Table 1: Data collection 2004–2013

	2013	2012	2011
Manual data collection			
HIV-infected adults			
Baseline	65,447	74,184	155,783
Follow-up	2,565,426	3,776,800	2,198,375
End of follow-up	4,457	4,161	4,872
Laboratory results	7,325,242	7,001,369	5,891,432
Subtotal (data points)	9,960,572	10,856,514	8,250,462
HIV and viral hepatitis co-infected adults			
Baseline	15,765	4,376	
Follow-up	49	21	
Laboratory results	2,066,095	619,330	18,656
Liver diagnostics	19,652	3,398	
Subtotal (data points)	2,101,561	627,125	18,656
HIV-infected children			
Baseline	1,521	994	2,090
Follow-up	44,768	48,776	67,897
End of follow-up	215	268	623
Laboratory results	199,208	184,863	385,037
Subtotal (data points)	245,712	234,901	455,647
HIV-exposed children			
Baseline		104	1,105
Follow-up		521	4,860
End of follow-up		170	1,148
Laboratory results		1,484	15,037
Subtotal (data points)		2,279	22,150
Pregnancies			
Baseline	528	430	407
Follow-up and end of pregnancies	12,142	9,967	9,180
Laboratory results	21,065	5,590	9,528
Subtotal (data points)	33,735	15,987	19,115
Total manual data collection (data points)	**12,341,580**	**11,736,806**	**8,766,030**
% increase in manually collected data	**5%**	**33%**	**11%**
	604,774	**2,970,776**	**866,519**
Automated data collection			
Number of lab results per year	2,170,555	3,758,558	3,612,404
Estimated data points	**10,852,775**	**18,792,790**	**14,449,616**
(%) Lab-Link from total lab results	53	70	61
% increase in Lab-Link data	**-5%**	**4%**	**734%**

2010	2009	2008	2007	2006	2005	2004
87,005	121,962	95,818	18,199	23,010	27,177	46,488
2,051,617	1,822,878	1,715,076	1,672,864	1,650,518	1,427,391	1,068,278
4,617	4,213	4,404	5,117	5,120	4,251	3,443
5,601,697	5,356,569	5,135,508	5,090,289	5,272,109	4,139,877	3,798,835
7,744,936	7,305,622	6,950,806	6,786,469	6,950,757	5,598,696	4,917,044
16,440	19,492	21,559				
16,440	19,492	21,559				
449	1,608	441	527	1,243	2,983	756
26,570	47,785	40,901	68,464	138,798	137,542	30,589
162	360	168	248	654	1299	229
86,869	218,464	166,969	366,370	412,443	606,533	187,900
114,050	268,217	208,479	435,609	553,138	748,357	219,474
808	128	755	674			
3,774	1,331	5,095	4,214			
791	205	641	532			
8,429	2384	11,271	1,591			
13,802	4,048	17,762	7,011			
188	116	206	164	428	673	
4,331	3,007	7,018	5,409	11,738	16,947	
5,764	4,888	11,689	9,073	27,759	35,820	
10,283	8,011	18,913	14,646	39,925	53,440	
7,899,511	**7,605,390**	**7,217,519**	**7,243,735**	**7,543,820**	**6,400,493**	**5,136,518**
4%	**5%**	**0%**	**-4%**	**18%**	**25%**	
294,121	**387,871**	**-26,216**	**-300,085**	**1,143,327**	**1,263,975**	
433,254	389,015	222,668	119,668	95,685		
1,733,016	**1,556,060**	**890,672**	**478,672**	**382,740**		
9	9	11	6	5		
11%	**75%**	**86%**	**25%**			

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

		>365 days		<365 days	
HIV treatment centre	**Location**	**2013**	**2012**	**2013**	**2012**
MCA	Alkmaar	0%	0%	2%	4%
Flevoziekenhuis	Almere	0%	0%	21%	20%
AMC-UVA	Amsterdam	0%	0%	5%	8%
OLVG	Amsterdam	0%	0%	6%	5%
St Lucas Andreas Ziekenhuis	Amsterdam	1%	0%	11%	5%
Slotervaartziekenhuis	Amsterdam	2%	0%	7%	13%
MC Jan van Goyen	Amsterdam	0%	0%	11%	3%
VUMC	Amsterdam	1%	0%	15%	18%
Rijnstate	Arnhem	0%	0%	1%	15%
HagaZiekenhuis – Leyweg	Den Haag	1%	1%	2%	3%
MCH – Westeinde	Den Haag	1%	0%	22%	23%
Catharina Ziekenhuis	Eindhoven	0%	0%	17%	22%
MST	Enschede	0%	0%	2%	8%
UMCG	Groningen	0%	0%	31%	31%
Kennemer Gasthuis	Haarlem	1%	1%	10%	10%
MC Leeuwarden	Leeuwarden	0%	0%	10%	10%
LUMC	Leiden	0%	0%	2%	12%
MC Zuiderzee	Lelystad	0%	2%	12%	5%
Maastricht UMC+	Maastricht	0%	0%	13%	10%
Radboud UMC	Nijmegen	0%	0%	2%	1%
Erasmus MC	Rotterdam	1%	0%	13%	10%
Maasstad Ziekenhuis	Rotterdam	0%	0%	8%	4%
St Elisabeth Ziekenhuis	Tilburg	2%	2%	2%	1%
UMCU	Utrecht	0%	0%	3%	3%
Admiraal De Ruyter Ziekenhuis	Vlissingen	0%	1%	3%	7%
Isala Klinieken – Sophia	Zwolle	0%	2%	10%	7%
Mean		**0%**	**0%**	**9%**	**10%**

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

Selection criteria for quality checks	2013		2012	
	Number of validation rules	Number of records	Number of validation rules	Number of records
Consistency checks				
Missing and/or inconsistent baseline data	26	1,698	25	2,759
Missing and/or inconsistent demographic data	12	247	7	431
Missing and/or inconsistent adverse events data	8	178	6	522
Missing and/or inconsistent antiretroviral medication data	16	3,626	15	20,697
Missing and/or inconsistent CDC event data	5	126	6	161
Missing and/or inconsistent data on viral hepatitis infection	7	291		
Missing and/or inconsistent co-medication data	4	202	4	337
Missing and/or inconsistent laboratory data	26	2,986		
Missing and/or inconsistent end of follow-up data	10	610	10	1,297
Cross comparisons based on HICDEP*	48	11,565		
Total number of quality checks	**162**	**21,529**	**41**	**23,014**

***HICDEP*:** HIV Cohorts Data Exchange Protocol*

Table 4: Number of patient files checked by data monitors per data selection criterion

Selection criteria for quality checks	2013	2012	2011
Random selection			
Random selection of adverse event data	0	0	0
Random selection of antiretroviral medication data	3	0	1
Random selection of baseline data	0	56	81
Random selection of CDC event data	0	0	0
Random selection of co-medication data	0	0	0
Random selection of data on pregnancies	88		
Random selection of data on viral hepatitis C infection	169		
Random selection of all patient data		0	0
Random selection of data from last year of follow-up		0	0
Subtotal random selection	**260**	**56**	**82**
Consistency checks			
Inconsistencies in adverse event data	0	32	237
Inconsistencies in antiretroviral medication data	0	2	2
Inconsistencies in baseline data	0	0	11
Priority analysis of baseline data	0	0	0
Inconsistencies in CDC event data	0	0	1
Inconsistencies in co-medication data	0	0	0
Inconsistencies in laboratory data	0	0	1
Subtotal consistency checks	**0**	**32**	**252**
Detection of missed co-morbidities, defined as endpoints			
Cardiovascular disease	184		
Diabetes mellitus	280		
Chronic liver disease	219		
Renal disease	84		
Non-AIDS-defining malignancies	36		
Subtotal of detected missed co-morbidities	**803**		
Comorbidity and cause of death checks			
Total cardiovascular disease:	652	186	223
Myocardial infarction	*(106)*	*(51)*	*(38)*
Invasive cardiovascular procedures	*(131)*	*(49)*	*(49)*
Diabetes mellitus	*(312)*	*(54)*	*(76)*
Stroke	*(103)*	*(32)*	*(60)*
Chronic liver disease	41	12	23
End-stage renal disease	85	16	34
Non-AIDS-defining malignancies	332	294	137
Cause of death in 100% of cases	247	227	185
Subtotal co-morbidity and cause of death checks	**1,357**	**735**	**602**
Subtotal personal coaching of data collectors	309	168	154
Total number of quality checks	**2,729**	**991**	**1,090**
increase (%) per year	**175%**	**-9%**	**-41%**

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

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

General

As of 31 December 2013, a cumulative total of 22,231 persons with HIV infection were registered through the Dutch HIV treatment centres by Stichting HIV Monitoring (SHM) (*Table 5*). Compared to 2012, this represents an increase of 1,214 individuals newly registered in the SHM database (*Table 6*). Of the 22,231 persons, 17,695 (80%) were men, and 4,535 (20%) were women; for one individual, gender had not been registered. A total of 239 persons were registered with an HIV treatment centre specialising in children and adolescents. An AIDS-defining event was recorded in 5,732 (26%) persons, and death was recorded for 2,225 (10%) persons.

Further clinical data was collected for 21,858 registered persons. The remaining 373 (1.7%) persons indicated that they opposed the collection of such data.

In 2013, data was collected from 17,450 (78%) persons in total. Of the 4,781 (22%) persons with no data collected in 2013, 2,097 had died before 2013, 976 had moved abroad and 1,708 had disappeared from care for an unknown reason or had objected to the collection of such data. Taking into account those persons who had objections to data collection and those who died in 2013, as of 31 December, there remained 17,274 HIV-infected persons in care for whom data were collected in 2013.

Adults

Of the 21,858 persons registered in 2013, 21,480 (98%) were adults at the time of registration, comprising 17,260 (80%) men and 4,220 (20%) women. The most common route of HIV transmission was homosexual contact in men (72%) and heterosexual contact in women (88%). The median age at diagnosis was 37.1 years (interquartile range [IQR] 30.3-44.8) for men and 31.3 years (IQR 25.9-38.5) for women. At the end of 2013, 4% of the group had been aware of their positive HIV status for less than a year, 20% had known for 1 to 5 years, 26% had known for 5 to 10 years and 39% had known for more than 10 years, while for 0.5% the HIV diagnosis date had either not, or not yet, been registered. The remaining 10% of the 21,480 adults had died. The median follow-up duration was 7.7 years (IQR 3.6-13.4): 7.5 years for men and 8.6 years for women. The total follow-up in the adult group was 194,044 person-years.

Of the 1,199 HIV-infected adults newly registered in 2013, 1,028 (86%) were men, and 171 (14%) were women. In total, 39 (3.2%) persons objected to further registration of clinical data. Of the 1,160 HIV-positive patients for whom further clinical data were registered, the main transmission route remained homosexual contact in men (78%) and heterosexual contact

in women (85%). The median age at diagnosis was 38.1 years (IQR 29.4-48.3) in men and 35.4 years (IQR 27.3-46.5) in women.

Children

Of the 21,858 persons registered as of 31 December 2013, 378 (2%) were children or adolescents. This group consisted of 180 (48%) boys and 198 (52%) girls. The median age at diagnosis was 3.0 years (IQR 0.7-9.6) for boys and 4.0 years (IQR 0.6-15.5) for girls. In the majority of cases, the route of infection was vertical mother-to-child transmission (69%); in 20% of cases, the route of infection was recorded as sexual transmission. In total, 33% of the infected children were born in the Netherlands, and 56% were born in sub-Saharan Africa. The median duration of follow-up was 9.3 years (IQR 4.1-12.8): 8.8 years for boys and 9.4 for girls. The total follow-up for the group of children and adolescents was 3,452 person-years.

In 2013, 15 children and adolescents (7 boys and 8 girls; 12 children aged between 0-7 years and 3 adolescents aged 14-17 years) were newly registered. Thirteen of the 15 children and adolescents came from sub-Saharan Africa, and 10 children came to the Netherlands in 2013 as the result of adoption.

Pregnant women

In 2013, the total number of registered pregnancies increased from 2,458 in 2012 to 2,659. These pregnancies occurred in 1,565 women. In 56% of the cases, HIV was diagnosed before the start of the pregnancy, and, in 44% of cases, HIV was diagnosed during the pregnancy. The transmission route of HIV in the pregnant women was mainly through heterosexual contact (94%); in 1% of the pregnant women, transmission had occurred through injecting drug use. The median age during the first pregnancy was 29 years (IQR 25-34). In 37% of the women, combination antiretroviral therapy (cART) was started before the first pregnancy was diagnosed, and in 50% cART was started during the pregnancy. In 28% of cases, gestation lasted less than 16 weeks; in those women who were still pregnant after the initial 16 weeks, the median gestation period was 39 weeks (IQR 37-40). Of the pregnancies, 74% resulted in the birth of a child, 31% of which involved C-section. Despite the introduction of a national HIV screening programme for pregnant women in 2004, 8 children have since been infected with HIV through vertical transmission in the Netherlands. In the case of 4 of these children, the mothers were not diagnosed as HIV-positive until after the birth of the child. In 2 cases, the mothers had tested HIV-negative during the pregnancy screening and must have become infected with HIV later on in the pregnancy. One child's mother was known to be HIV-positive during pregnancy, but for unknown reasons the mother was not treated for HIV. In the case of the last child, it is not known whether the mother underwent pregnancy screening. All these children were registered in 2013.

Table 5: Cumulative numbers and percentages of HIV-infected patients registered and monitored by SHM in one of the HIV treatment centres in the Netherlands and on Curaçao on 31 December 2013

		Total		Alive or not registered as deceased		Deceased		Objection[a]		Data in 2013[b]		No data in 2013			
												Deceased before 2013[c]		Other[d]	
HIV treatment centre	**Location**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Adults															
MCA	Alkmaar	305	1.4	279	91.5	26	8.5	1	0.3	257	84.3	22	7.2	26	8.5
Flevoziekenhuis	Almere	156	0.7	151	96.8	5	3.2	2	1.3	144	92.3	4	2.6	8	5.1
AMC-UvA	Amsterdam	2,731	12.4	2,435	89.2	296	10.8	8	0.3	2,146	78.6	283	10.4	302	11.1
HIV Focus Centrum	Amsterdam	98	0.4	98	100	0	0	0	0	98	100	0	0	0	0
MC Jan van Goyen	Amsterdam	616	2.8	579	94.0	37	6.0	4	0.6	536	87.0	33	5.4	47	7.6
OLVG	Amsterdam	3,159	14.4	2,828	89.5	331	10.5	127	4.0	2,440	77.2	313	9.9	406	12.9
Slotervaartziekenhuis	Amsterdam	827	3.8	691	83.6	136	16.4	8	1.0	583	70.5	136	16.4	108	13.1
St Lucas Andreas Ziekenhuis	Amsterdam	375	1.7	333	88.8	42	11.2	0	0	311	82.9	38	10.1	26	6.9
VUMC	Amsterdam	561	2.6	486	86.6	75	13.4	10	1.8	406	72.4	70	12.5	85	15.2
Rijnstate	Arnhem	697	3.2	631	90.5	66	9.5	2	0.3	568	81.5	62	8.9	67	9.6
Haga Ziekenhuis - Leyweg	Den Haag	677	3.1	600	88.6	77	11.4	28	4.1	472	69.7	70	10.3	135	19.9
MCH - Westeinde	Den Haag	941	4.3	864	91.8	77	8.2	29	3.1	719	76.4	74	7.9	148	15.7
Catharina Ziekenhuis	Eindhoven	555	2.5	522	94.1	33	5.9	2	0.4	461	83.1	30	5.4	64	11.5
MST	Enschede	534	2.4	434	81.3	100	18.7	1	0.2	328	61.4	98	18.4	108	20.2
UMCG	Groningen	818	3.7	746	91.2	72	8.8	12	1.5	659	80.6	65	7.9	94	11.5
Kennemer Gasthuis	Haarlem	443	2.0	396	89.4	47	10.6	2	0.5	351	79.2	45	10.2	47	10.6
MC Leeuwarden	Leeuwarden	266	1.2	244	91.7	22	8.3	0	0	219	82.3	22	8.3	25	9.4
LUMC	Leiden	655	3.0	601	91.8	54	8.2	29	4.4	517	78.9	51	7.8	87	13.3
MC Zuiderzee	Lelystad	56	0.3	56	100	0	0	1	1.8	54	96.4	0	0	2	3.6
MUMC+	Maastricht	800	3.6	681	85.1	119	14.9	3	0.4	587	73.4	112	14.0	101	12.6
Radboud UMC	Nijmegen	669	3.0	603	90.1	66	9.9	15	2.2	546	81.6	63	9.4	60	9.0
Erasmus MC	Rotterdam	2,292	10.4	2,045	89.2	247	10.8	9	0.4	1,761	76.8	232	10.1	299	13.0
Maasstad Ziekenhuis	Rotterdam	626	2.8	582	93.0	44	7.0	5	0.8	548	87.5	38	6.1	40	6.4
St Elisabeth Ziekenhuis	Tilburg	1,009	4.6	951	94.3	58	5.7	8	0.8	837	83.0	56	5.6	116	11.5
UMCU	Utrecht	1,542	7.0	1,388	90.0	154	10.0	47	3.0	1,224	79.4	143	9.3	175	11.3
Admiraal De Ruyter Ziekenhuis	Vlissingen	162	0.7	150	92.6	12	7.4	4	2.5	123	75.9	12	7.4	27	16.7
Isala Klinieken - Sophia	Zwolle	422	1.9	396	93.8	26	6.2	15	3.6	348	82.5	22	5.2	52	12.3
Total adults		**21,992**		**19,770**	**90.0**	**2,222**	**10.1**	**372**	**1.7**	**17,243**	**78.4**	**2,094**	**9.5**	**2,655**	**12.1**

Table 5 continued

HIV treatment centre	Location	Total N	Total %	Alive or not registered as deceased N	Alive or not registered as deceased %	Deceased N	Deceased %	Objection[a] N	Objection[a] %	Data in 2013[b] N	Data in 2013[b] %	No data in 2013: Deceased before 2013[c] N	No data in 2013: Deceased before 2013[c] %	No data in 2013: Other[d] N	No data in 2013: Other[d] %
Children/adolescents															
Emma KZ, AMC-UvA	Amsterdam	74	31.0	74	100	0	0	0	0	70	94.6	0	0	4	5.4
Beatrix KZ, UMCG	Groningen	22	9.2	22	100	0	0	0	0	21	95.5	0	0	1	4.5
Erasmus MC – Sophia	Rotterdam	73	30.5	71	97.3	2	2.7	1	1.4	58	79.5	2	2.7	13	17.8
WKZ, UMCU	Utrecht	70	29.3	69	98.6	1	1.4	0	0	58	82.9	1	1.4	11	15.7
Total children/adolescents		**239**		**236**	**98.7**	**3**	**1.3**	**1**	**0.4**	**207**	**86.6**	**3**	**1.3**	**29**	**12.1**
Curaçao															
SEHOS	Willemstad	874	98.2	722	82.6	152	17.4	0	0	444	50.8	152	17.4	278	31.8
SEHOS kinderkliniek	Willemstad	16	1.8	6	37.5	10	62.5	0	0	0	0	10	62.5	6	37.5
Total Curaçao		**890**		**728**	**81.8**	**162**	**18.2**	**0**	**0**	**444**	**49.9**	**162**	**18.2**	**284**	**31.9**

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

[b] *Data in 2013: registered by SHM in 2013, or deceased during or after 2013, or last contact with an HIV treatment centre during or after 2013*

[c] *No data in 2013 – deceased before 2013: patients who are not included in 'data in 2013' and who had died before 2013*

[d] *No data in 2013 – other: patients who are not included in 'data in 2013' because they moved abroad before 2013 or because they had no contact with their HIV treatment centre in 2013 for an unknown reason*

Table 6: HIV-infected patients registered in 2013 and monitored by SHM in HIV treatment centres in the Netherlands and on Curaçao

			Total		Alive	Deceased		Objection[a]	
HIV treatment centre	**Location**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Adult									
MCA	Alkmaar	30	2.5	29	96.7	1	3.3	0	0
Flevoziekenhuis	Almere	10	0.8	9	90	1	10	0	0
AMC-UvA	Amsterdam	85	7.1	84	98.8	1	1.2	0	0
HIV Focus Centrum	Amsterdam	4	0.3	4	100	0	0	0	0
MC Jan van Goyen	Amsterdam	34	2.8	34	100	0	0	1	2.9
OLVG	Amsterdam	162	13.5	159	98.1	3	1.9	11	6.8
Slotervaartziekenhuis	Amsterdam	14	1.2	14	100	0	0	0	0
St Lucas Andreas Ziekenhuis	Amsterdam	36	3.0	36	100	0	0	0	0
VUMC	Amsterdam	27	2.3	27	100	0	0	1	3.7
Rijnstate	Arnhem	41	3.4	41	100	0	0	0	0
Haga Zkh - Leyweg	Den Haag	25	2.1	24	96.0	1	4.0	0	0
MCH - Westeinde	Den Haag	62	5.2	62	100	0	0	7	11.3
Catharina Ziekenhuis	Eindhoven	44	3.7	44	100	0	0	0	0
MST	Enschede	26	2.2	26	100	0	0	0	0
UMCG	Groningen	41	3.4	40	97.6	1	2.4	1	2.4
Kennemer Gasthuis	Haarlem	26	2.2	26	100	0	0	0	0
MC Leeuwarden	Leeuwarden	22	1.8	22	100	0	0	0	0
LUMC	Leiden	34	2.8	34	100	0	0	3	8.8
MC Zuiderzee	Lelystad	8	0.7	8	100	0	0	0	0
MUMC+	Maastricht	52	4.3	51	98.1	1	1.9	0	0
Radboud UMC	Nijmegen	32	2.7	32	100	0	0	1	3.1
Erasmus MC	Rotterdam	117	9.8	114	97.4	3	2.6	1	0.9
Maasstad Ziekenhuis	Rotterdam	48	4.0	48	100	0	0	4	8.3
St Elisabeth Ziekenhuis	Tilburg	76	6.3	75	98.7	1	1.3	3	3.9
UMCU	Utrecht	87	7.3	84	96.6	3	3.4	4	4.6
Admiraal De Ruyter Ziekenhuis	Vlissingen	21	1.8	21	100	0	0	0	0
Isala Klinieken - Sophia	Zwolle	35	2.9	35	100	0	0	2	5.7
Total adults		**1,199**		**1,183**	**98.7**	**16**	**1.3**	**39**	**3.3**
Children/adolescents									
Emma KZ, AMC-UvA	Amsterdam	9	60.0	9	100	0	0	0	0
Beatrix KZ, UMCG	Groningen	0	0	0	0	0	0	0	0
Erasmus MC - Sophia	Rotterdam	4	26.7	4	100	0	0	0	0
Wilhelmina KZ, UMCU	Utrecht	2	13.3	2	100	0	0	0	0
Total children/adolescents		**15**		**15**	**100**	**0**	**0**	**0**	**0**
Curaçao									
SEHOS	Willemstad	61	100	61	100	0	0	0	0

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

Monitoring of treatment

In 2013, 88% of the 21,858 HIV patients were treated with cART, whereas 11% of the patients had not yet started treatment. No data had been registered yet for 0.8% of patients, and 0.8% were being treated with non-cART regimens.

In total, 91% of the first-line cART regimens used in 2013 consisted of tenofovir in combination with emtricitabine as the nucleotide/nucleoside HIV-1 reverse transcriptase inhibitor (NRTI) backbone. Efavirenz was the most widely used supplement to this backbone, followed by ritonavir-boosted darunavir and nevirapine. In 2013, efavirenz was used in 37% of the first-line cART regiments, darunavir/ritonavir in 18% and nevirapine in 17%. The most common initial cART regimen in 2013 was tenofovir + emtricitabine + efavirenz, followed by tenofovir + emtricitabine + darunavir/ritonavir and tenofovir + emtricitabine + nevirapine (*Table 7*).

Table 7: *Most frequently used cART combinations 2011–2013 (cART=combination antiretroviral therapy, TDF=tenofovir, FTC=emtricitabine, EFV=efavirenz, DRV/r=darunavir/ritonavir, NVP=nevirapine, ATV/r=atazanavir/ritonavir, AZT=zidovudine, 3TC=lamivudine, LOP/r=lopinavir/ritonavir, RAL=raltegravir, RPV=rilpivirine, ABC=abacavir)*

	2011		2012		2013		Total	
	N	%	N	%	N	%	N	%
Total number of patients commencing first-line cART regimen	1,229	100	1,230	100	929	100	3,388	100
TDF+FTC+EFV	581	47.3	423	34.4	280	30.1	1,284	37.9
TDF+FTC+DRV/r	178	14.5	182	14.8	184	19.8	544	16.1
TDF+FTC+NVP	119	9.7	170	13.8	86	9.3	375	11.1
TDF+FTC+RPV	0	0	138	11.2	179	19.3	317	9.4
TDF+FTC+ATV/r	134	10.9	113	9.2	68	7.3	315	9.3
AZT+3TC+LOP/r	39	3.2	35	2.8	20	2.2	94	2.8
TDF+FTC+RAL	30	2.4	28	2.3	26	2.8	84	2.5
TDF+FTC+LOP/r	18	1.5	15	1.2	14	1.5	47	1.4
AZT+3TC+NVP	10	0.8	16	1.3	7	0.8	33	1.0
ABC+3TC+NVP	8	0.7	10	0.8	12	1.3	30	0.9
ABC+3TC+DRV/r	9	0.7	7	0.6	7	0.8	23	0.7
TDF+FTC+DRV/r+EFV	4	0.3	12	1.0	7	0.8	23	0.7
TDF+FTC+LOP/r+EFV	19	1.5	3	0.2	0	0.0	22	0.6
ABC+3TC+EFV	7	0.6	7	0.6	4	0.4	18	0.5
TDF+FTC+EFV+RAL	10	0.8	5	0.4	2	0.2	17	0.5
TDF+FTC+DRV/r+RAL	3	0.2	8	0.7	6	0.6	17	0.5
ABC+3TC+LOP/r	9	0.7	5	0.4	1	0.1	15	0.4
Other	51	4.1	53	4.3	26	2.8	130	3.8

To date, in 2013, 53 new cases of AIDS were recorded in patients treated with cART, corresponding to an incidence of 0.50 (95% confidence interval [CI] 0.34-0.59) per 100 person-years. This number is likely to increase slightly once short-term data backlogs have been processed. In 2011, there were 95 AIDS cases and the incidence was 0.77 (95% CI 0.62-0.94) per 100 person-years.

In 2013 there were 117 deaths in patients treated with cART. The incidence was 0.92 (95% CI 0.76-1.10) per 100 person-years, which is comparable to previous years.

Antiretroviral resistance

In 2013, data on the results of genotyping of the HIV reverse transcriptase and protease genes were obtained from four virology laboratories involved in monitoring resistance. At this time, a cumulative total of 11,934 sequences have been collected, 299 of which were collected in 2013 (*Table 8*).

Table 8: Number of HIV-1 reverse transcriptase and protease gene sequences generated by each virology laboratory and registered with SHM as of 31 December 2013

		Number of sequences obtained	
Laboratory	**Before 2013**	**In 2013**	**Total**
AMC-UvA, Amsterdam	4,696	124	4,820
UMCU, Utrecht	[a]3,585	[a]0	3,585
LUMC, Leiden	1,529	102	1,631
Erasmus MC, Rotterdam	776	42	818
VUMC, Amsterdam	479	31	510
Slotervaartziekenhuis, Amsterdam	179	0	179
CLB, Amsterdam	391	0	391
Total	**11,046**	**299**	**11,934**

([a] numbers not available at time of printing)

Since 2003, complete resistance to at least one antiretroviral agent has been detected in 149 (3%) of the 4,980 newly diagnosed patients for whom sequences were available within a year of diagnosis. These included 23 patients with resistance to protease inhibitors, 30 patients with resistance to lamivudine and emtricitabine, 38 patients with resistance to other nucleoside reverse transcriptase inhibitors and 108 patients with resistance to non-nucleoside reverse transcriptase inhibitors. In 2013, sequences were available for 149 patients within one year of diagnosis, and four of these patients were completely resistant to at least one agent.

HBV and HCV co-infections

Infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) can cause liver cirrhosis, liver fibrosis and hepatocellular carcinoma. In combination with HIV, the course of such

diseases is likely to be accelerated. Therefore, HBV and HCV are also monitored regularly in the HIV-infected population over time. Chronic HCV co-infection is defined as the presence of HCV RNA for at least 6 months after infection. On the basis of this definition, in 2013, chronic co-infection with HCV was found in 6% of the monitored HIV-infected patients. Chronic HBV co-infection was detected in 7.5% of patients, and chronic co-infection with both HBV and HCV was found in 0.5% of patients. Of the patients with chronic HBV co-infection, 7.3% had hepatic fibrosis, 7.8% had hepatic cirrhosis, and 0.9% were found to have hepatocellular carcinoma. In patients with chronic HCV co-infection, these figures were 20%, 11.0% and 0.5%, respectively.

Quality of care

On behalf of the Ministry of Health, Welfare and Sport, the Institute for Health Care Quality runs the Visible Care programme (*Zichtbare Zorg*, ZiZo). SHM has continued to support HIV treatment centres by delivering quality indicators for ZiZo.

In addition to the activities for ZiZo, in 2013 SHM continued to develop its Quality of Care programme in collaboration with the Academic Medical Centre (AMC) of the University of Amsterdam, Onze Lieve Vrouw Gasthuis in Amsterdam, and the Leids Universitair Medisch Centrum in Leiden. After the programme was awarded a grant from the Aids Fonds in 2012, the research started in April of that year under the direction of Dr Suzanne Geerlings (AMC) and continued in 2013. The aim of this study is to investigate the determinants (patient, medical professional and hospital-related) that lead to a higher quality of care.

Furthermore, the certification process for HIV treatment centres launched in 2012 by the Harmonisation of Quality in Healthcare (*Harmonisatie Kwaliteitsbeoordeling in de Zorgsector,* HKZ) continued in 2013 in collaboration with the Dutch Association of HIV-Treating Physicians (*Nederlandse Vereniging van HIV Behandelaren,* NVHB). This process involved the development of standard criteria that centres should fulfil for either certification or recertification as HIV treatment centres. In addition, procedures were defined for the actual certification process (including independent audits of HIV treatment centres). SHM will play a key role in the process by supplying centres with a number of predefined quality indicators. Certification is planned to start in the course of 2014.

Sample collection and storage

Since the start of the AIDS Therapy Evaluation in the Netherlands (ATHENA) project in 1996, an estimated total of 426,435 plasma samples from patients in follow-up have been stored in microbiology laboratories at the HIV treatment centres or in laboratories associated with the centres. This sample collection is exceptionally valuable for clinical epidemiologic research into resistance development over time and into the response of HIV-1 subtypes, other than the most common subtype B, to antiviral therapy. The outcome of such research carries implications both for the quality of care of individual patients and for public health.

Registration of HIV-infected individuals in Curaçao

The registration and monitoring of HIV-infected persons being followed in the St. Elisabeth Hospital in Willemstad, Curaçao, continued during the past year. Results from the monitoring in Curaçao were presented in the Monitoring Report 2013. In total, 890 patients were registered, of whom 61 were newly registered in 2013.

Key outcomes and recommendations[1]

The HIV epidemic in the Netherlands

As of June 2013, 17,006 persons living with HIV in the Netherlands (16,813 adults, and 193 children and adolescents) were in care in one of the 27 HIV treatment centres. Of these 17,006, 87% (14,817) had started combination antiretroviral therapy (cART), and of these 14,817, 90% (13,369) had suppressed viraemia to below the level of quantification at the time of their last available HIV-RNA measurement. These results are impressive when compared to figures from other parts of the world. However, it is also important to realise that of the total 25,000 individuals that the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates were living with HIV in the Netherlands in 2013, 27% are likely to be unaware of their infection; this means that about 6,750 infected persons have not yet been diagnosed or linked to care and, importantly, still contribute to fuelling the epidemic.

In 2012, an estimated 1100 patients entered care, which is comparable to the annual number reported in the last 3 years. In 2012, the majority (67%) of newly diagnosed infections were in men who have sex with men (MSM), 27% were acquired through heterosexual contact, 1% through injecting drug use (IDU), and 5% through other or unknown modes of transmission. Although the rate of newly diagnosed cases stabilised in the key affected population of MSM, and even steadily declined amongst MSM 35 to 44 years of age, it continued to increase in MSM both 25 years and younger and 55 years and older, as well as in heterosexuals 45 years and older.

The rates of testing for HIV appear to be increasing in certain settings, and the proportion of patients who are identified and start cART earlier in their infection (including during primary HIV infection) has increased, particularly amongst MSM, but less pronounced in women and heterosexual men. However, 43% of newly diagnosed patients in 2012 presented late for care, that is, with AIDS or a CD4 count less than 350 cells/mm^3, and 26% presented with advanced HIV disease, that is, with a CD4 count less than 200 cells/mm^3 or AIDS. Generally, the likelihood of presenting late for care or with advanced HIV disease was greater for men with heterosexually acquired infection, for those originating from South and South-East Asia and sub-Saharan Africa, and for patients 45 years or older. This is also reflected in the fact that the median CD4 count at initiation of cART in 2012 was not higher than 320 cells/mm^3, although, fortunately, this count continues to rise gradually each year.

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

1 *This section of the Annual Report is based on the 'Monitoring Report 2013 – Human Immunodeficiency Virus (HIV) Infection in the Netherlands' published by SHM on 1 December 2013.*

Combination antiretroviral therapy in adults and quality of care

Guidelines for use of first-line cART are adhered to extremely well in the Netherlands. Most patients who first initiated cART in 2012 did so with a once-daily regimen, with tenofovir/emtricitabine as the backbone; this was combined in approximately two thirds of patients with a non-nucleoside reverse transcriptase inhibitor (NNRTI) and in one third of patients with a ritonavir-boosted protease inhibitor (PI). Use of the integrase inhibitor raltegravir, which requires twice-daily dosing, as part of an initial regimen was rare.

Virological response to first-line cART has gradually improved during the era of cART and between 2010 and 2012, 85% of patients who first initiated cART achieved viral suppression to below the level of HIV-RNA quantification within 9 months. Patients originating from areas other than the Netherlands or Western Europe or North America may have been less likely to achieve such a favourable early response, particularly when initiating cART at CD4 counts over 500 cells/mm^3. Of the nearly 10,000 patients who first initiated cART from 1999 onwards, 94% had suppressed viraemia with sustained treatment to less than 50 copies/ml at 12 years.

Overall, 8% of the same patients who first initiated cART from 1999 onwards have experienced virological failure (defined as time to the first of two consecutive plasma HIV RNA levels >200 copies/ml after 24 weeks on therapy) to first-line cART. Importantly, the annual proportion of patients experiencing virological failure has declined over time to less than 5%, but, as expected, remains associated with a substantial risk of emergence of drug resistance.

Patients with heterosexually acquired infection originating from sub-Saharan Africa and the Caribbean or South America, and patients younger than 30 years were identified as being at increased risk of virological failure on both first- and second-line regimens. This suggests that measures aimed at supporting adherence specifically in these groups may be warranted.

Fortunately, international collaborative cohort analyses of the prevalence and incidence of patients experiencing triple-class virological failure (defined as failure of at least two NRTIs, one NNRTI and one ritonavir-boosted PI), to which SHM contributes data, have demonstrated an important improvement in the prognosis of such patients over time, both in terms of their likelihood of achieving resuppression of viraemia and a reduced progression to AIDS and death. These trends are likely mainly driven by the availability of newer drugs with better tolerability, ease of use and limited cross-resistance, indicating the continued public health benefit of introducing new drugs.

The proportion of patients achieving greater immunological recovery on cART continues to improve year after year. Nonetheless, a substantial number of patients fail to achieve restoration of CD4 cells to levels above which the risk of both traditionally HIV-associated and non-AIDS-related morbidity may no longer be accentuated by the infection. This

particularly holds true for those who commence treatment at a more advanced level of immunodeficiency. In 2012, 15% of patients in care had a last available CD4 measurement below 350 cells/mm^3. Patients who start cART at a CD4 count of more than 350 cells/mm^3 and have sustained fully suppressed viraemia after 8 years, including patients more than 50 years old at the time of treatment initiation, are likely to achieve long-term CD4 counts similar to those in the general population. Similar trends were observed in the patients' ability to achieve a CD4/CD8 ratio greater than 1, which may be a marker of reduced residual immune activation whilst on suppressive cART. Future analyses (potentially in collaboration with other cohorts) are needed to address whether CD4/CD8 ratios independent of CD4 counts are associated with an increased risk of morbidity, including from non-AIDS events.

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

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

The monitoring by SHM of patients with HIV in care plays an important role in facilitating the assessment of the quality of care provided by the treatment centres. It also supports the formal certification process for HIV treatment centres in the Netherlands, which is currently being prepared by the Harmonisation of Quality in Healthcare (*Harmonisatie Kwaliteitsbeoordeling in de Zorgsector,* HKZ) in collaboration with the Dutch Association of HIV-treating Physicians (NVHB). SHM helps the treatment centres with collating and making available the key information required to support certification, which is planned to become operational in 2014.

Morbidity and mortality

Mortality rates remain low in HIV-infected patients in care in the Netherlands. There has been a sustained decline in death from AIDS, with a shift towards death from other causes. Non-AIDS co-morbidities, including non-AIDS defining malignancies (NADM), cardiovascular disease (CVD) and chronic liver disease, comprise a sizable fraction of those other causes. Nonetheless, the proportion of patients dying of AIDS (nearly 25%) remained substantial between 2007 and 2012. Once more, this seems to be largely driven by late presentation and entry into care, and it stresses the importance of identifying and linking individuals to care earlier in the course of the infection. Of note, a recent analysis by the Collaboration of Observational HIV Epidemiological Research Europe (COHERE), to which SHM is an important

contributor, showed that the incidence of AIDS-defining illnesses was higher in individuals with a current CD4 count of 500 to 749 cells/mm^3 compared to those with a CD4 count of 750 to 999 cells/mm^3; in addition, the incidence did not decrease further at higher CD4 counts, even in patients suppressed on cART. These findings suggest that immune reconstitution may not be complete until the CD4 count increases to more than 750 cells/mm^3.

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

As expected, older age was also found to be an important risk factor for these co-morbidities, which are traditionally associated with aging. In this context, it is important to note that the average age at which individuals with newly diagnosed HIV enter care in the Netherlands has gradually increased over time; 20% were more than 50 years of age in 2012. At the same time, the age distribution of the overall patient population with HIV in care in the Netherlands has also changed, with 37% currently older than 50 years. Of particular concern is the increasing proportion of patients with multiple co-morbidities. Nearly 20% of those now in care who are more than 65 years of age have two or more of the following, reliably documented co-morbidities: hypertension, myocardial infarction, stroke, diabetes mellitus, chronic kidney disease, and non-AIDS defining malignancies. Data from the AGE$_h$IV Cohort Study, in which SHM collaborates with the Academic Medical Centre, the Amsterdam Institute for Global Health and Development and the Public Health Service of Amsterdam (GGD Amsterdam), show that both the presence of multiple co-morbidities and individual cases of hypertension, CVD, peripheral artery disease and chronic kidney disease are significantly more prevalent amongst those with HIV than in an uninfected control population of a similar age distribution. Besides older age, smoking and a positive family history (for hypertension, myocardial infarction, diabetes mellitus, or hyper-cholesterolaemia), duration of time spent with a CD4 count less than 200 cells/mm^3, increasing levels of markers of inflammation and innate immune activation, central obesity and longer prior exposure to ritonavir at total doses of ≥ 800 mg were independently associated with the prevalence of co-morbidity.

Whilst the overall incidence of non-AIDS-defining malignancies in the population with HIV in care has remained stable over time since the introduction of cART, the absolute number and proportion of deaths due to these malignancies has increased. Future analyses will focus on individual malignancies, of which those addressing anal cancer will be particularly pertinent and informative. In addition, collaborative analyses conducted on

much larger datasets as part of the D:A:D study will provide the statistical power to address the possible contribution of prolonged exposure to particular antiretrovirals.

Awareness of the role of modifiable, often lifestyle-related risk factors, like smoking, and their management by both physicians and HIV-infected patients, particularly those who are older or otherwise at high a priori risk of certain co-morbidities, offers important hope of a lower co-morbidity burden and healthy aging. This applies not only to conditions such as cardiovascular disease and diabetes mellitus, but also to measures to prevent cancer, chronic kidney disease and bone loss.

Hepatitis B and C co-infections

Screening for hepatitis B (HBV) and C (HCV) co-infection has, with time, increasingly become part of the standard of care in the Netherlands. As a result, the presence or absence of HBV or HCV infection is now documented for nearly all HIV-infected patients in care in the Netherlands. Approximately 12% of patients had evidence of ever having been exposed to HCV, 5% were documented as having chronic infection and 1% had acute infection. Eight percent of patients were shown to have chronic HBV infection.

HCV genotype 1 infection was the most common genotype in patients with either chronic or acute HCV infection, and most patients with HCV infection were male and from the Netherlands or other European countries. Acute HCV infection is seen mainly in MSM, with the incidence steadily increasing over time from 0.47 cases per 1,000 person-years in 2003 to 4.5 cases per 1,000 person-years in 2011, indicating the need for continued preventive efforts in these men.

An estimated 28% of HIV-infected patients overall and 22% of MSM either had not been exposed to HBV or had not been successfully vaccinated and may remain at risk of acquiring HBV. Thus, it is important that efforts are undertaken to increase successful vaccination rates amongst this subgroup of patients.

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

The uptake of treatment for HCV has markedly increased in recent years, with 62% of patients having received treatment by 2012. However, currently available treatment still remains associated with considerable toxicity and suboptimal efficacy. Amongst patients treated with a combination of pegylated interferon alpha (peg-IFN alpha) and ribavirin

(RBV), only 39% overall could be considered cured. Thus, a substantial number of patients in care co-infected with HIV and HCV either remain untreated or have not yet been successfully treated for HCV. The direct-acting antivirals boceprevir or telaprevir became available in the Netherlands early in 2012. When added to peg-IFN alpha and RBV for HCV genotype 1 infection, they have shown improved response rates, but their use remains limited because of high cost and association with clinically significant toxicities and drug-drug interactions with cART.

The availability of combinations of direct-acting pan-genotypic antivirals against HCV that are much better tolerated and more efficacious is eagerly awaited. It is hoped that these combinations, which will potentially allow the use of interferon-free regimens, will contribute to further reducing the burden of severe chronic liver disease, hepatocellular carcinoma and liver-related mortality amongst persons living with HIV.

HIV in pregnant women and in children

Universal screening for HIV in pregnant women and the increasingly effective use of cART during pregnancy, fortunately, has made perinatal transmission of HIV extremely rare in the Netherlands.

Nonetheless, the observation that approximately 20 to 30% of HIV-infected pregnant women do not have fully suppressed viraemia around the time of delivery indicates the need for continued vigilance.

Treatment outcomes for children living with HIV in the Netherlands and receiving care in one of the four designated paediatric treatment centres are generally favourable. These outcomes include long-term immunological responses to cART, particularly in children who started treatment soon after birth.

More and more of these children, however, are transitioning into adult care, and as many as a third do not have fully suppressed viraemia at the time of transition. Optimisation of long-term care for this particularly vulnerable and difficult to manage group of young individuals is needed.

Amsterdam Cohort Studies

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

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

In the beginning of 2013, the ACS was evaluated by an international scientific advisory committee (SAC) led by Prof. A. Hofman (chair) of the Erasmus MC in Rotterdam. The SAC issued an extremely positive assessment of the ACS and recommended that the RIVM continues its financial contribution to the ACS. The RIVM has agreed with this recommendation. Based on the research plans and the current HIV epidemic in the Netherlands, the ACS project leaders have proposed enlarging the group of HIV-negative MSM and reducing the follow-up of the DU group over the coming years. This idea has been approved by the SAC, and the changes will be initiated as of January 2014.

The ACS is unique because it allows the follow-up of two populations at risk for HIV infection, namely, the HIV-negative populations of homosexual men and drug users. These populations are followed by the GGD Amsterdam. HIV-infected persons in the ACS also continue to be followed, primarily through HIV care and the monitoring of HIV by SHM. In addition to the provision of care, research samples are collected and stored for specific immunological and virological studies. This includes material from persons who were initially HIV-negative and were infected during the ACS follow-up or who are still at risk of HIV infection, as well as those who were already infected when they started participating in the ACS.

As of 31 December 2013*, 2,564 MSM and 1,661 injecting DU were included in the ACS. Since the start of the ACS, MSM have visited the GGD Amsterdam 53,667 times (52,686 of which involved physical visits) and DU 27,407 times. In 2013, 664 MSM, 120 of whom were HIV-positive, were followed by the GGD Amsterdam. Since January 2013, 53 of these participants were newly recruited and one participant died. A total of 252 DU (28 HIV-positive) were followed by the

GGD Amsterdam in 2013; there were no new inclusions in this group in 2013, and 14 participants died. The preliminary HIV incidence in 2013 was 0.24 per 100 person-years among MSM, and there were no HIV seroconverters among DU. These figures may still change as data are not yet complete.

*Note: Total numbers for 2013 were still being collected and were not yet complete at time of printing.

Collaborations

National collaborations

AMC-UvA

SHM collaborates with the Academic Medical Centre (AMC) of the University of Amsterdam (UvA) on various projects. The Co-morbidity and Aging with HIV (AGE_hIV) cohort study, led by Prof. Peter Reiss (Department of Global Health, AMC, Amsterdam; Director SHM from 1 February 2013) and supported, amongst others, by a grant from the Netherlands Organisation for Health Research and Development (Zon-Mw), aims to assess the incidence and prevalence of a broad range of co-morbidities and known risk factors for these co-morbidities in HIV-infected patients. SHM collaborates with the AMC in this study by providing the data collection infrastructure for monitoring the incidence and prevalence of a number of these co-morbidities. The results obtained from this research may be used to inform and adapt national and international guidelines for prevention and management of co-morbidities in ageing HIV-infected individuals.

In a separate project, Bridging the Epidemiology and Evolution of HIV in Europe (BEEHIVE), the AMC and SHM collaborate with Imperial College, London and the British Sanger Institute on a study of viral whole genome association. The aim of this study is to identify viral virulence factors, which could ultimately shed new light on the pathogenesis of the HIV-1 virus.

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

CIb-RIVM

The Centre of Disease Control (CIb, headed by Prof. Jaap van Dissel) of the National Institute for Public Health and the Environment (RIVM) receives and coordinates data on the registration of new HIV infections within the framework of the national HIV registration and surveillance programme.

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

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

GGD Amsterdam

SHM contributes to the MSM Observational Study of Acute Infection with Hepatitis C (MOSAIC) coordinated by the Public Health Service of Amsterdam (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 HCV infection. The aims of the study are to look at the contribution of this group to the transmission of HIV; to explore the driving factors of the HCV epidemic and HIV's role in it; and to examine the impact of acute HCV infection, reinfection and treatment on disease progression. SHM and GGD Amsterdam also work together on the Amsterdam Cohort Studies (ACS, reviewed earlier in the report), in collaboration with the AMC-UvA.

International collaborations

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

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

ART-CC

The Antiretroviral Therapy Cohort Collaboration (ART-CC), coordinated by Prof. Jonathan, Sterne, University of Bristol, is a long-standing international collaboration that includes 19 cohort studies in Europe and North America. ART-CC was initiated to carry out prognostic studies to assess the effect of combination antiretroviral therapy (cART) in therapy-naive patients. In 2013, Prof. Peter Reiss and Dr Ard van Sighem were the principal investigators for this collaboration on behalf of SHM. ART-CC has financial support from the Medical Research Council of the United Kingdom.

An overview of papers published by ART-CC in 2013 can be found under 'Research projects and publications in 2013'.

CASCADE

Concerted Action on SeroConversion to AIDS and Death in Europe (CASCADE) was established in 1997 as a collaboration between 25 cohorts from 15 European countries, Australia, Canada and Africa. CASCADE's main aim is to monitor newly infected individuals and those already enrolled in studies for the entire course of HIV infection. By pooling data, issues can be addressed that cannot be reliably addressed from single studies alone. The Amsterdam Cohort Studies (ACS) participates in this study.

An overview of papers published by CASCADE in 2013 can be found under 'Research projects and publications in 2013'.

COHERE

The Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) is a unique collaboration of 33 cohorts in Europe that helps to answer scientific questions requiring a large sample size of patients that the contributing cohorts cannot answer individually and that do not overlap with existing collaborations between participating COHERE cohorts. COHERE'S mission is conduct epidemiological research on the prognosis and outcome of HIV-infected populations throughout Europe, including pregnant mothers, children and adults. Two Regional Coordinating Centres have been established, one in Bordeaux and one in Copenhagen.

SHM also participates in the Pursuing Later Treatment Options (PLATO II) scientific project of COHERE, which focuses on triple-class virological failure.

An overview of papers published by COHERE in 2013 can be found under 'Research projects and publications in 2013'.

D:A:D study

The Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) is a prospective multi-cohort study that focuses on the early recognition of adverse events, amongst which are cardiovascular problems and liver and renal diseases that could result from HIV treatment with antiretroviral agents. Jens Lundgren (Department of Infectious Diseases, Hvidovre Hospital, Copenhagen) coordinates the study, and Prof. Peter Reiss is the principal investigator for SHM/AIDS Therapy Evaluation in the Netherlands (ATHENA).

An overview of papers published by the D:A:D study in 2013 can be found under 'Research projects and publications in 2013'.

DIDE

The Department of Infectious Disease Epidemiology (DIDE) is part of the Faculty of Medicine, Imperial College in London. Prof. Christophe Fraser, Dr Tim Hallett and Prof. Sir Roy Anderson coordinate the collaboration with SHM. DIDE and SHM have collaborated since 2002,

focusing on DIDE's statistical and mathematical support of SHM for analysis of observational cohort data and execution of the HIV registration programme. An important goal of the DIDE research programme is to gain more insight into the interplay of variables that determine the typical progress of infection in a host or in a particular population. Techniques that can provide answers to such questions include the study of the qualities of nonlinear differential equations, organisation and management of large-scale field studies into the transmission and control of an infection in populations, and analysis of large data sets.

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

In a separate project, Bridging the Epidemiology and Evolution of HIV in Europe (BEEHIVE), the DIDE and SHM collaborate with the AMC-UvA and the Sanger Institute, UK, on a viral whole genome association study. The aim of this study is to identify viral virulence factors, which could ultimately shed new light on the pathogenesis of the HIV-1 virus.

ECDC

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

In 2013, SHM continued its leading role in a collaborative project to better estimate the prevalence of HIV in Europe and within individual European countries. This project was commissioned by the ECDC in Stockholm. SHM collaborates in this project together with Prof. Christophe Fraser from the DIDE at Imperial College in London, Prof. Andrew Phillips from the Department of Population Health at University College London, Dr Daniela De Angelis from the Medical Research Council Biostatistics Unit at Cambridge University and Prof. Matthias Egger from the Institute of Social and Preventive Medicine at the University of Bern.

EPPICC

The European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC) conducts epidemiological research on the prognosis and outcome of HIV infections in pregnant women and children, as well as in children exposed to HIV *in utero*, across Europe. EPPICC currently consists of 13 studies, including the European Collaborative Study (ECS). As the

number of children infected with HIV in Europe is relatively small, a single network running paediatric trials and cohorts is essential to efficiently answer research questions in this population.

An overview of papers published by EPPICC in 2013 can be found under 'Research projects and publications in 2013'.

EuroCoord

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

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

EuroSIDA

The EuroSIDA study is a prospective, observational cohort study of more than 16,500 patients followed in 103 hospitals in 32 European countries, plus Israel and Argentina. The main objective of the study is to assess the impact of antiretroviral drugs on the outcomes in the general population of HIV-infected patients in Europe. The primary hospital in the Netherlands providing information for this study is the AMC in Amsterdam. At the request of the principal investigator of EuroSIDA, Prof. Peter Reiss, SHM collects data from the AMC in Amsterdam for EuroSIDA.

An overview of papers published by EuroSIDA in 2013 can be found under 'Research projects and publications in 2013'.

HIV-CAUSAL

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

An overview of papers published by HIV-CAUSAL in 2013 can be found under 'Research projects and publications in 2013'.

HIV in Europe

HIV in Europe is a pan-European initiative begun in Brussels in 2007. It provides a European platform for exchange of information and activities to improve early diagnosis and earlier care of HIV across Europe. The initiative is directed by an independent group of experts with representation from civil society, policy makers, health professionals and European public-health institutions. It has put the issue of earlier diagnosis of HIV on the political agenda and involved the various constituencies. Moreover, it has been able to initiate specific projects to enhance optimal testing and care. Its overall objective is to ensure that HIV-positive patients enter care earlier in the course of their infection than they do at present and to study the decrease in the proportion of HIV-positive persons presenting late for care.

RDI

The HIV Resistance Response Database Initiative (RDI) is made up of a small research team based in the United Kingdom, an International Scientific Advisory Group, and a network of collaborators and supporters. The main activities of the RDI are exploring the relationship between changes in the genetic code of HIV (genotype), as well as other clinical and laboratory factors and response to HIV drug therapy, and developing computational models to help physicians and their patients select the best individualised combination of drugs.

An overview of papers published by RDI in 2013 can be found under 'Research projects and publications in 2013'.

Dissemination

SHM actively disseminates data and information about our activities through a wide variety of communication channels. Our aim is to provide information to HIV-treated individuals, their physicians, researchers, other health care professionals, the media and other interested parties.

SHM website and eNewsletters

In 2011, we introduced a new website on which the first eNewsletters were published. These quarterly eNewsletters are all archived on the website and can be accessed via a direct link. Four new eNewsletters were added in 2013, covering topics that ranged from hepatitis monitoring, online reporting, quality of care, research collaborations and the Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV).

SHM animation

In 2013, the SHM developed an animated clip to provide the general public with a concise overview of SHM's activities. The animation gives a clear presentation of who we are, our activities and the results of these activities. In addition, the clip emphasises the important contributions made by SHM to the treatment and care of people with HIV at both a national and an international level. The animation is presented on the homepage of the SHM website.

Monitoring Report 2013 'HIV Infection in the Netherlands'

In addition to the Annual Report, SHM publishes a yearly Monitoring Report on or near December 1, World AIDS Day. The Monitoring Report presents major developments in the HIV epidemic in the Netherlands and the effects of treatment on the course of HIV infection and the HIV epidemic, with data extending back to 1996.

The 2013 Monitoring Report confirmed that the previously reported positive trends in the Netherlands continued in 2013. In particular, the data confirmed more frequent HIV testing, earlier diagnosis and earlier start of treatment in specialised HIV treatment centres. However, despite these encouraging findings, late diagnosis remains a problem, as does HIV infection in the group of people who are infected but probably unaware of this and, thus, have not yet been diagnosed. This group is thought to be fuelling the epidemic in the Netherlands.

As a result of increasingly effective treatment strategies, the number of older HIV-infected patients continued to increase in 2013, as did the number of accompanying age-related diseases. These age-related diseases, particularly cardiovascular disease and non-AIDS-related tumours, are more common in HIV-infected patients than in the general population. These observations, presented in the 2013 Monitoring Report, further underline the importance of earlier HIV diagnosis, start of treatment and continuity of HIV care in specialised treatment centres.

The 2013 Monitoring Report also presented data on HIV and hepatitis C virus (HCV) co-infection, seen in 1 in 20 HIV-infected patients. These patients carry a greater risk of developing chronic liver disease and liver cancer. The number of patients receiving treatment for HCV has increased markedly in recent years, and the introduction of two new HCV treatment compounds in 2012 appears to have led to improved, but as yet suboptimal, cure rates. However, use of the new treatments remains limited due to significant side effects.

NCHIV 2013

In 2013, SHM's work was also presented at the 7th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV). This annual conference is organised by SHM in collaboration with the Centre for Infectious Disease Control of the National Institute for Public Health and the Environment (CIb-RIVM), the Aids Fonds, the Amsterdam Institute for Global Health and Development (AIGHD), the Academic Medical Centre of the University of Amsterdam (AMC-UvA) (Department of Global Health), and the Dutch Association of HIV-Treating Physicians (NVHB). In 2013, 290 participants attended NCHIV. During the course of the day, 18 presentations were given, including 9 by guest speakers and 9 as abstract presentations on pathogenesis, epidemiology, prevention and treatment of HIV and HIV/HCV co-infection. In addition, 37 posters were accepted for the poster presentations.

Research projects and publications

In addition to its yearly Monitoring Report, SHM also contributes to the knowledge and understanding of the HIV/AIDS epidemic and the effect of antiretroviral treatment on the course of HIV infection through research projects and scientific publications. In 2013, SHM cohort data was included in 51 publications in peer-reviewed international scientific journals and 79 oral and poster presentations at international peer-reviewed conferences, workshops and meetings. A full overview of scientific output is included in a later section of this report.

Financial report

Income

In 2013, Stichting HIV Monitoring's (SHM) total income was €4,267,154. The largest portion of this income came from the structural institute grant that the SHM receives each year from the National Institute for Public Health and Environment (*Rijksinstituut voor Volksgezondheid en Milieu,* RIVM) on behalf of the Ministry of Health, Welfare and Sport (*ministerie van Volksgezondheid Welzijn en Sport,* VWS). In addition, SHM participates in various national and international collaborations involving observational cohort studies, for which it receives additional funding.

Income for regular HIV monitoring activities in the Netherlands

SHM is a VWS-recognised healthcare institute with a structural institute grant (Public Health Grants Ruling, Chapter II Institute Grants).

On 2 November 2012, the Governing Board established that SHM required a structural institute grant of €3,134,335 for HIV monitoring in 2013. On 10 January 2013, the RIVM, VWS, awarded an institute grant of €3,004,371.

In addition, on 16 August 2013, indexation for the wage-sensitive part of the budget was set at 2.64% (€60,865); material costs were not indexed. Consequently, the total budget for 2013 allocated by the VWS to SHM for monitoring HIV in the Netherlands was €3,065,236. On 15 November 2013, the VWS revised the 2012 grant, reducing the 2012 budget by €6,902; SHM absorbed this correction by adjusting the 2013 budget.

As of 1 June 2012, 17,060 of the registered patients (16,852 adults and 208 children) were in active follow-up in HIV treatment centres. This represents an increase of 7.59% compared to the number of patients in 2011. On the RIVM's request, this increase in the number of patients monitored by SHM was not reflected in the structural institute grant awarded by the VWS in 2013.

Income from HIV monitoring-related collaborations

SHM's participation in international and national collaborations is highly important for both individual patients and quality of care. Individual registration and monitoring programmes (such as SHM) are often too small to adequately address certain questions regarding individual comorbidities and prognosis associated with large-scale HIV treatment. Collaborations that combine data from various cohorts make it possible to answer questions that cannot be addressed by individual cohorts, and are also an efficient way of providing reliable insight into the long-term effects of HIV treatment. As such, participation in national and international studies is in line with the SHM's mission and objectives. In 2013, the SHM received €1,139,829 as income from the following collaborations related to HIV monitoring (this income is €4,899 less (-0.1%) than that earned through collaborations in 2012):

1. Amsterdam Cohort Studies (ACS)

SHM has been responsible for governing and administering the Amsterdam Cohort Studies (ACS) since 2005. Since 1984, the ACS has 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 institutes involved in this collaboration make use of data and body samples provided by HIV-1 infected persons and persons at high risk of contracting HIV. Following approval of research proposals that involve collaboration with one or several ACS partners, external parties can also gain access to the data and stored body samples. The RIVM provides the ACS with an annual grant of €500,000. In addition, the collaborating institutes, including the Academic Medical Centre (AMC) of the University of Amsterdam (UvA), the Municipal Health Service of Amsterdam (GGD Amsterdam), SHM, and the University Medical Centre Utrecht (UMCU), make a financial contribution to the coordination, management and financial management costs. The GGD Amsterdam and the AMC-UvA each contribute individually to the storage of patient data and samples. The conditions for the contribution to be paid by the UMCU are still under negotiation.

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

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

In 2013, SHM contributed for the fourteenth time to the data merge and received €350,619 in compensation for this activity from the Hvidovre University in Copenhagen, Denmark, the organisation that coordinates the D:A:D study. D:A:D has been made financially possible by the Oversight Committee for the Evaluation of Metabolic Complications of HAART and various pharmaceutical manufacturers of antiretroviral compounds. The D:A:D funding decreased in 2013 after 3 of the 9 original participating pharmaceutical manufacturers withdrew from the collaboration. As a result, the budget of each participating cohort had to be reduced, which meant that SHM received €77,827 less in 2013 than in 2012. Nevertheless, the number of person-years added by SHM in 2013 was equivalent to that entered in 2012.

For the registration and validation of endpoints collected specifically for the D:A:D study, SHM received an additional fee of €74,516 in 2013.

3. EuroSIDA

SHM participates in the EuroSIDA study within a European context. EuroSIDA is a collaboration between clinical cohorts and individual treatment centres distributed throughout Europe (including Eastern Europe). The Netherlands is involved in this collaboration through the SHM's role in facilitating the provision of data from a small group of patients from the AMC. EuroSIDA carries out research into a broad range of clinical issues relating to HIV, making it possible to compare specific regional differences between centres throughout Europe. For its participation in the EuroSIDA study in 2013, SHM received a payment of €3,095. The knowledge that SHM gains through its participation in EuroSIDA is also valuable in terms of improving the national data collection by SHM in the Netherlands.

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

The ECDC awarded SHM a grant of €104,885 for the project entitled: 'Improving tools to estimate HIV prevalence in EU/EAA countries'. This two-year project (January 2013 through to January 2015), coordinated by SHM, is a collaboration with the University College London, UK, Imperial College, UK, MRC Biostatistics Unit, UK, and the University of Bern, Switzerland. The project aims to develop methods to improve the reliability of estimates of HIV prevalence in different European countries. This participation should also improve the ability to make such estimates in the Netherlands.

5. Aids Fonds grant

SHM has received a grant from the Aids Fonds for a project entitled 'Controlling the HIV epidemic'. In 2013, the contribution was €77,726. SHM has appointed a PhD student for this project, with the aim of developing a mathematical individual-based model to describe the HIV epidemic in various at-risk groups in the Netherlands. This model should provide greater insight into the factors that drive new HIV infections. Furthermore, it will be possible to study the effect of intervention strategies on the prevention of new HIV infections. In this way, this study should improve our understanding of the course of the HIV epidemic in the Netherlands and give insights into how to fight the HIV epidemic in the Netherlands.

6. EuroCoord funding

In 2013, SHM received a sum of €15,361 from EuroCoord. SHM's participation in EuroCoord improves harmonisation between SHM's HIV-related data in the Netherlands and data from other HIV cohorts in Europe. This, in turn, improves the quality of international collaborations since certain research questions can only be studied by combining databases from several HIV cohorts (including that of the Netherlands).

7. HIV-Causal funding

HIV-CAUSAL (HIV Cohorts Analyzed Using Structural Approaches to Longitudinal data) is a multinational collaboration of prospective studies involving HIV-infected persons

from 6 European countries and the USA. SHM provides this study with data and for this service we received a sum of €7,739 in 2013. This collaboration aims to develop innovative statistical and epidemiological techniques for analysing longitudinal observational data sets. By participating in this study, SHM is able to broaden the knowledge within the SHM analysis group, which may also be beneficial for analyses carried out on SHM's own data.

8. **Comorbidity in relation to HIV/AIDS (COBRA)**

In 2013, SHM received a payment of €5,888 from the COBRA study. This project is financed by the European Union's 7th framework programme and SHM is one of the 12 COBRA partners in Europe. SHM's main contribution involves data management and analyses for COBRA. The study focuses primarily on investigating whether the reported comorbidities are more common and possibly occur at a younger age in HIV-infected persons compared to non HIV-infected persons. In addition, in-depth research is being done into the various underlying mechanisms, including those associated with HIV infection as well as those associated with the use of antiretroviral treatment. The knowledge acquired from this project will help the SHM in establishing priorities for collecting national comorbidity data. Furthermore, the results of the COBRA study may contribute to improving the prevention and treatment of comorbidities in HIV-positive persons.

9. **Other income**

In 2013, SHM received €69,991 from other sources of income. Most of this income arose from salary expenses charged by SHM to HIV treatment centres to cover the costs of assistance provided by SHM for the collection and entering of anonymised patient data. SHM staff are also involved in organising the Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV); the associated salary expenses are charged to Stichting NCHIV.

Expenditure

In 2013, the total expenses of Stichting HIV Monitoring were €3,807,417. Three different types of expenses are outlined below for 2013:

1. **Personnel expenses**

Personnel expenses once again represented the largest expenditure for SHM during 2013. As per 31 December 2013, SHM had a total of 42 employees (an average of 33 FTE). This number does not include employees of HIV treatment centres that carry out their own data collection and for which the treatment centres receive a payment from SHM.

2. **Material expenses**

In addition to staff expenses in 2013, structural expenses were incurred for the depreciation of automation equipment, database licenses, maintenance of the SHM database, data management and other operational costs.

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

In 2013, HIV treatment centres received a payment of € 59.30 per patient, based on the number of patients in active follow-up on 31 December 2012 and on the budget set by the RIVM. In 2013, a number of hospitals requested SHM to provide assistance in data collection. The associated costs were deducted from the payment made by SHM to the hospitals in question for patient data collection and entry. Fifteen treatment centres have transferred the role of data collection to SHM. In addition, HIV treatment centres received € 11.90 per patient as a contribution towards the costs of collecting and storing patients' plasma. In total, SHM paid the HIV treatment centres € 634,369 for patient data collection and entry and storage of patients' samples.

D:A:D event payments to HIV treatment centres

As part of the D:A:D study, physicians are required to complete Cause of Death (CoDe) forms. SHM paid HIV treatment centres € 23,901 for this work.

ACS payments

In line with the budget, the funding assigned by the RIVM to the ACS is passed on by SHM to the GGD Amsterdam and the AMC. The AMC pays a fee to the Sanquin Blood Supply Foundation (*Stichting Sanquin Bloedvoorziening*) for the processing and storage of white blood cells. The SHM does not charge the ACS any management costs.

NCHIV expenses

In 2013, SHM contributed financially to the organisation of the Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment.

Operating result

The operating result (€ 459,737) indicates that the total expenditure in 2013 remained well within SHM's income for 2013. The largest addition to the reserves is the result of the D:A:D study.

The interest income was € 47,846. SHM conducts a very conservative but accurate treasury policy.

Reserves

The total financial reserves of SHM (including continuity reserve, general reserve and earmarked reserves for investment) amounted to € 3,283,906 on 31 December 2013.

1. **Continuity reserve**

The continuity reserves amounted to a positive balance of € 154,378 on 31 December 2013. This amount includes the 2013 result for HIV monitoring in the Netherlands. The continuity reserve is held in reserve to guarantee operational continuity over a certain period of time.

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

3. **Earmarked reserves for HIV-related projects**
   As per 31 December 2013, a total of €2,747,322 has been reserved for HIV-related projects. SHM has committed to participate in these projects for an average of three years.

Continuity risks

SHM applies the principle that 25% of the annual turnover related to monitoring HIV in the Netherlands is to be kept in reserve to ensure continuity of HIV monitoring in the Netherlands. The continuity reserve was approximately 5% of the 2013 budget.

Balance sheet as of 31 December 2013

Assets	31 Dec 13 (€)	31 Dec 12 (€)
Fixed assets		
Tangible fixed assets	28,956	30,616
Total fixed assets	**28,956**	**30,616**
Current assets		
Receivables and accrued assets	313,053	764,570
Liquid assets	4,957,875	3,329,058
Total current assets	**5,270,928**	**4,093,628**
Total assets	**5,299,884**	**4,124,244**

Liabilities	31 Dec 13 (€)	31 Dec 12 (€)
Capital reserves		
Continuity reserve	154,378	36,114
General reserve	382,206	382,206
Earmarked reserves	2,747,322	2,358,003
Total reserves	**3,283,906**	**2,776,323**
Short-term liabilities		
Short-term liabilities and accrued expenses	2,015,978	1,347,921
Total liabilities	**5,299,884**	**4,124,244**

2013 profit and loss account

Profits	2013 (€)	2012 (€)
Total funding	4,198,163	4,203,062
Other operating revenue	68,991	73,089
Total net revenue	**4,267,154**	**4,276,151**
Operating costs		
Personnel expenses	2,109,344	2,064,944
Depreciation of tangible fixed assets	11,857	7,166
Other operating costs	527,708	383,566
Payments HIV treatment centres	634,369	755,741
Payments D:A:D events	23,901	0
Payments Amsterdam Cohort Studies	500,000	559,139
Payments NCHIV	239	8,056
Payments COBRA	0	533
Total operating costs	**3,807,417**	**3,779,144**
Operating result	**459,737**	**497,007**
Financial profits	48,553	61,387
Financial losses	707	745
Year result	**507,583**	**557,649**

Scientific output 2013

In 2013, 11 requests were made to use the Stichting HIV Monitoring's (SHM) cohort data. During the year, 51 articles were published in international peer-reviewed journals. In addition, 79 abstracts were accepted for presentation at 14 meetings and conferences (48 posters and 31 oral presentations). An overview of research projects, publications and presentations can be found on our website, *www.hiv-monitoring.nl*.

Completed research projects

I07252 Study on sexual behaviour among HIV-infected homosexual men

Stolte S, Krol A, Prins M, van Eeden A, Groot M, Visser GB, Heijman T

Date of approval: 11 May 2010

The inclusion of MSM at the Medisch Centrum Jan van Goyen (MC JvG) started in March 2009. By the end of 2009, 19 MSM were willing to participate in the Amsterdam Cohort Studies (ACS) and had completed and returned the questionnaire. By the end of 2011, this number remained the same and all these men are still being followed according to our HOP (HIV study of recent HIV-positive MSM) protocol. This allowed us to combine all data from all HIV-positive participants followed at the JvG, resulting in a total population of 49 at the MC JvG and 79 elsewhere.

In 2010/11, data on sexual risk behaviour were used for a study investigating change in sexual risk behaviour before and after seroconversion during a period before and after cART. Results indicate that sexual risk behaviour decreases after seroconversion, but during the period of cART, this decrease is only temporary; after 4 years, it is almost the same as before seroconversion.

Collection of data from these men has now been incorporated into the ACS protocols and will continue as part of the ACS; therefore, the current project will be closed.

I05548 Incidence of HPV-related anogenital cancers in HIV-infected patients

Richel O, Prins J

Date of approval: 2005

Publication in 2013:

Gradually decreasing anal cancer incidence in the HIV+ population in the Netherlands after a decade of cART.
Richel O, van der Zee RP, Smit C, de Vries HJ, Prins JM
Sex Health 2013 Nov;10(6):586. doi: 10.1071/SHv10n6ab33.

I10043 Evaluatie van het gebruik van therapeutic drug monitoring bij HIV positieve kinderen in Nederland

[Evaluation of the use of therapeutic drug monitoring in HIV-positive children in the Netherlands]

Bastiaans D, Burger D, van Luin M, Hartwig N

Date of approval: 1 November 2010

This project was not deemed feasible and will therefore not be carried out.

Ongoing research projects

I04034 The Data Collection on Adverse Events of Anti-HIV Drugs (DAD)

Reiss P

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

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

An overview of publications during 2013 is included later in this section of the report. For additional information, please see www.cphiv.dk (under the tab D:A:D)

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

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

Date of approval: May 2010

Background: Quantifying the contribution of HIV transmission from different stages of infection is critical for the design of appropriate public health measures. In particular, transmissions from individuals already enrolled in care represent a distinct opportunity for prevention.

Objective: To characterise HIV transmissions among MSM in the context of universal access to care and high ART coverage.

Design: A combined phylogenetic and clinical analysis of HIV-positive individuals with registered date of diagnosis and at least one HIV-1 B partial pol sequence in the ATHENA cohort by March 2013.

Methods: We used phylogenetic methods to identify transmission clusters and date coalescent events between the viral lineages of MSM for whom at least one viral sequence was available. Potential transmitters to all clustering MSM in acute or early HIV infection at time of diagnosis were identified based on available clinical, demographic and molecular genetic data. Time resolved statistical analyses were conducted to relate transmission probabilities to independent transmission risk factors of the potential transmitters, including stage of HIV infection, age, treatment status after treatment initiation and plasma viral load.

Results: 73% of an estimated 14,000 MSM living with HIV are in care at one of the 26 HIV treatment centres in the Netherlands. We could group 2068 MSM with registered date of diagnosis into 596 potential transmission clusters based on their partial pol HIV-1 B sequences. 1026 potential direct transmitters to 804 clustering MSM in acute or early HIV infection at time of diagnosis were identified. A detailed characterisation of these potential transmission pairs is ongoing.

I05513 HIV Resistance Response Database Initiative (RDI)

Revell A, Larder B, Wang D, Coe D

Date of approval: October 2005

During 2013, the main activities of the RDI using ATHENA data were as follows:

Study 1: An update of the HIV-TRePS system: The development of new computational models that do not require a genotype to predict HIV treatment outcomes

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

Methods: Random forest models were trained to predict the probability of virological response to therapy (<50 copies HIV RNA/mL) following virological failure using the following data from 22,567 treatment change episodes including 1,090 from southern Africa: baseline viral load and CD4 count, treatment history, drugs in the new regimen, time to follow-up and follow-up viral load. The models were assessed during cross-validation and with an independent global test set of 1,000 cases including 100 from southern Africa. The models' accuracy (area under the receiver-operating characteristic (ROC) curve [AUC]) was evaluated and compared with genotyping, using rules-based interpretation systems for those cases with available genotypes.

Results: The models achieved AUCs of 0.79-0.84 (mean of 0.82) during cross validation, 0.80 with the global test set and 0.78 with the southern African subset. The AUCs were significantly lower (0.56-0.57) for genotyping.

Conclusions: The models predicted virological response to HIV therapy without a genotype as accurately as previous models that included a genotype. They were accurate for cases from southern African and significantly more accurate than genotyping. These models have the potential to optimise antiretroviral therapy in resource-limited settings where genotyping is not generally available. The models were uploaded in July 2013 and are accessible via the online treatment support tool HIV-TRePS.

Study 2: A comparison of computational models with and without genotyping for the prediction of response to second-line therapy

Background: HIV genotyping is not available in many resource-limited countries. The RDI has developed computational models that predict virological response to antiretroviral therapy as an aid to treatment decision-

making. Here we compared the use of computational models developed with and without HIV genotype to predict virologically effective regimens for patients experiencing first-line virological failure in a range of resource-rich and resource-limited settings, and we also compared the models with genotyping itself.

Methods: Two sets of 10 random forests models predicted the probability of virological response for 99 three-drug regimens in common use for patients on a failing regimen of one non-nucleoside and two nucleoside/nucleotide reverse transcriptase inhibitors in the second-line study. One set used baseline viral load, CD4 count and genotype, plus treatment history and time to follow-up, to make its predictions; the second set did not include genotype. Genotypic sensitivity scores were derived, and the ranking of the alternative regimens was compared to those of the models. The accuracy of the models and genotyping as predictors of the virological responses of second-line regimens was compared.

Results: The rankings of alternative regimens by the two sets of models correlated significantly in 60% of cases for 24-week follow-up and in 69% of cases at 48 weeks' follow-up. Moreover, correlation between the models that included genotyping and genotyping itself was 60% at both time points. The models identified alternative regimens that were predicted to be effective in 97% and 100% of cases. The area under the ROC curve, the primary measure of the accuracy of prediction of treatment response, was 0.72 and 0.74 for the two sets of models and significantly lower (0.55) for genotyping.

Conclusions: Both sets of models performed comparably well and significantly outperformed genotyping as predictors of response. The models identified alternative regimens predicted to be effective in almost all cases. It is encouraging that models that do not require a genotype were able to predict responses to second-line therapies in common use in settings where genotyping is unavailable and/or unaffordable.

Study 3. The development of new computational models that include the HIV genotype in their predictions of virological response to therapy

Background: It is critical that the models used to predict treatment response in the RDI's online HIV Treatment Response Prediction System (HIV-TRePS) are regularly updated to reflect current clinical practice. Here we developed new models that include a genotype in their input variables to predict response.

Methods: 11,417 treatment change episodes (TCEs) were identified that met all the criteria for the study. A committee of 10 random forest (RF) models was trained to predict the probability of virological response (follow-up viral load <50 copies HIV RNA/ml) from the following 105 input variables: baseline viral load, baseline CD4 count, baseline genotype (62 mutations), drugs in the new regimen (20 drugs covered), 20 individual treatment history variables, and time to follow-up. The models were developed with a 10x cross validation scheme. Their accuracy was assessed during cross validation, in terms of the area under the ROC curve (AUC).

Results: The RF models achieved an average AUC of 0.86 (range 0.79-0.88) during cross validation. Overall accuracy was 80% (77-82%) sensitivity 73% (69-77%) and specificity 83% (80-86%). During validation with an independent dataset, the AUC was 0.83. Overall accuracy was 77%, sensitivity was 63% and specificity 83%.

Discussion: The models achieved a consistent, high level of accuracy in predicting treatment response, which was superior to that achieved by the previous models. It was encouraging that a high-level specificity was achieved, minimising the potential for false positive predictions of virological response. The models were tested and then up-loaded into the HIV-TRePS system in November 2013.

Publications in 2013:

Computational models can predict response to HIV therapy without a genotype and may reduce treatment failure in different resource-limited settings.
Revell AD, Wang D, Wood R, Morrow C, Tempelman H, Hamers RL, Alvarez-Uria G, Streinu-Cercel A, Ene L, Wensing AMJ, de Wolf F, Nelson M, Montaner JS, Lane HC, Larder BA.
J Antimicrob Chemother 2013; 68(6):1406-14

An update to the HIV-TRePS system: The development of new computational models that do not require a genotype to predict HIV treatment outcomes.
Revell AD, Wang D, Wood R Morrow C, Tempelman H, Hamers R, Alvarez-Uria G, Streinu-Cercel A, Ene L, Wensing A, Reiss P, van Sighem AI, Nelson M, Emery S, Montaner JS, Lane HC, Larder BA.
J Antimicrob Chemother 2013; doi:10.1093/jac/dkt447

Potential impact of a free online HIV treatment response prediction system for reducing virological failures and drug costs after antiretroviral therapy failure in a resource-limited setting.
Revell AD, Alvarez-Uria G, Wang D, Pozniak A, Montaner J, Lane HC, Larder BA.
BioMed Res Int 2013; doi 10.1155/2013/579741.

Presentations in 2013:

The development of computer models that accurately predict response to HIV therapy without a genotype: a potential tool for therapy optimisation in resource-limited settings.
Revell AD, Wang D, Streinu-Cercel A, Ene L, Dragovic GJ, Hamers R, Morrow C, Wood R, Tempelman H, Wensing AMJ, Reiss P, van Sighem A, Pozniak A, Montaner J, Lane HC, Larder BA on behalf of the RDI study group.
Poster presentation PE22/9 at 14th European AIDS Conference, Brussels, Belgium, 16-19 October 2013

Accurate prediction of response to HIV therapy without a genotype: a potential tool for therapy optimisation in resource-limited settings
Larder BA, Revell AD, Wang D, Hamers R, Tempelman H, Barth R, Wensing AMJ, Morrow C, Wood R, van Sighem A, Reiss P, Nelson M, Emery S, Montaner JM, Lane HC, on behalf of the RDI study group.
Oral presentation at the International Workshop on HIV & Hepatitis Drug Resistance and Curative Strategies, Toronto, Canada, 4-8 June 2013

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

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

Date of approval: 3 August 2013

Interim analyses have been performed for all patients (n=44) reaching week 12 of therapy. These results were published at last year's European AIDS Clinical Society (EACS) conference in Brussels.

Presentation in 2013:

High on-treatment virologic response rates with boceprevir or telaprevir in naive and pre-treated HIV/ HCV co-infected patients
Arends JE, Brinkman K, Richter C, Smit C, Schippers EF, van der Valk M, van de Ende M, de Vries-Sluijs TE, Schinkel J, Reiss P, van der Meer J, Hoepelman AIM
Poster presentation at 14th European AIDS Conference, Brussels, Belgium, 16-19 October 2013

I13032 Combined and comparative analysis of virulence trends across multiple cohorts

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

Date of approval: 25 May 2013

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

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

The HIV Virulence Trends Working Group aims to use large-scale data analysis, together with mathematical modelling, to investigate past virulence trends and to predict future virulence trends. The Working Group is an initiative of scientists from the University of Washington School of Medicine, Seattle, and Eötvös Loránd University, Institute of Biology, Budapest. To accomplish the goal, the group will:

1) bring together a collaborative network of HIV cohorts representing the US, Europe and Africa to create a database of relevant clinical and epidemiological information;
2) assess whether the HIV virulence has changed over the course of the pandemic;
3) investigate whether variation in regional epidemiology explains discrepancies among previous HIV virulence studies; and
4) use mathematical modelling to predict future trends of HIV virulence, considering the effect of potential interventions, e.g., the effect of widely used HIV antiretroviral therapy. The results of this study by the HIV Virulence Trends Working Group will inform public policy on past and future trends of HIV virulence.

A detailed plan for analysis with input from all participating cohorts has been drawn up. A document describing the format of the requested data (HICDEP format where possible) has been distributed. Data from individual cohorts has not yet been sent to the study centre. A meeting at the National Evolutionary Synthesis Centre in Durham, NC, USA, has been scheduled for 28 February and 1 March 2014.

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

De Wolf F, Cornelissen M, Fraser C, Kellam P, Gall A, Gras L, van Sighem A, Boucher C, Schuurman R, Claas E

Date of approval: 16 September 2012

The first phase of the Bridging the Epidemiology and Evolution of HIV in Europe (BEEHIVE) collaboration included 1) testing the logistics of stored serum/plasma samples from patients selected for inclusion in the study of virulence factors associated with severity of infection and 2) testing the efficacy of HIV RNA isolation procedures needed for whole genome sequencing. Procedures have been developed to support these logistics, and the most productive and efficient isolation procedures have been selected. The very first sequencing results were available at the end of 2012 and, at the same time, the study entered a second phase that continued in 2013. During this second phase, 593 samples from 5 associated virology laboratories in the Netherlands were located and transported. Viral RNA was isolated by the laboratory for Experimental Virology at the AMC in Amsterdam and was subsequently sent to the Welcome Trust Sanger Institute where a number of whole genome sequences have successfully been obtained. Sample collection after obtaining patient informed consent will continue in 2014, as will the sequencing of isolated RNA. Construction of a database holding clinical and sequence data has started.

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

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

Date of approval: 3 June 2013

We received the data 4 weeks after approval by the SHM advisory board. In collaboration with Luuk Gras from SHM, our research team prepared all data to fit our desired scientific analyses. This process lasted approximately 4 months. Currently, we are working on our predefined analysis of the data. We will be able to present the first results on the NVP data at the NVHB mid-winter meeting on 24 January, 2014.

Presentations in 2013:

Increased risk of virological failure with lamivudine compared to emtricitabine in tenofovir and nevirapine containing antiretroviral therapy.
Rokx C, Fibriani A, van de Vijver DAMC, Schutten M, Verbon A, Rijnders BJA.
Oral presentation at 14th European AIDS Conference 2013, Brussels, Belgium, 16-19 October 2013

Increased risk of virological failure with lamivudine compared to emtricitabine in tenofovir and nevirapine containing antiretroviral therapy.

Rokx C, Fibriani A, van de Vijver DAMC, Schutten M, Verbon A, Rijnders BJA.
Poster presentation at 7th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment, Amsterdam, 19 November, 2013.

I13051 aMASE: advancing Migrant Access to Health Services in Europe (EuroCoord Work Package 14: Migrants and HIV). Barriers to HIV prevention, testing and treatment service uptake by migrants in the Netherlands

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

Date of approval: 22 July 2013

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

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

The clinical survey is a multi-site study in 10 European countries; in the Netherlands we aim to recruit at 2 sites. In addition to the European study, in the Netherlands we will also collect data from native HIV-positive patients to compare the results with those found among the migrant patients. The community survey will be disseminated in 10 European countries including the Netherlands.

Results in 2013: Recruitment of HIV-positive patients in the clinical survey started in July 2013 in the Academic Medical Centre (AMC) of Amsterdam and will continue until the beginning of 2014, after which we expect to have included approximately 80 patients (migrants and native HIV-patients).
In 2013, the questionnaire for the community survey was developed with all the European partners. Dissemination of the community survey is expected to start at the beginning of 2014.

Expected results for 2014: In 2014, recruitment in other HIV treatment centres in the Netherlands will start (clinical survey) and results of the Dutch data will be presented.

I10042 The use of nevirapine dose escalation in patients who switch from efavirenz to nevirapine
Burger D, Blonk M, Wit F, Smit C, van Luim M, Gelinck L. Sprenger H, Koopmans P

Date of approval: 11 May 2010

Presentations in 2013:
Nevirapine dose escalation or immediate full dose when switching from efavirenz to nevirapine in HIV-infected patients in the ATHENA cohort study.
Blonk M, van Luin M, Smit C, Wit F, Kappelhoff B, Burger D.
14th International Workshop on Clinical Pharmacology of HIV Therapy, Amsterdam, 22-24 April 2013

Nederlandse Ziekenhuisfarmacie dagen 2013, 30-31 May 2013, Nunspeet, The Netherlands

7th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment, Amsterdam, 19 November, 2013
Abstract and presentation at NVHB spring meeting, Utrecht, 5 June 2013

I13059 Clinical, immunological, virological and social outcomes of cART treated HIV-infected children after transition into adult healthcare services (CLIVIA study)
Weijsenfeld A, Mutschelknauss M, Nellen F, Smit C, Pajkert D

Date of approval: 7 October 2013

Ongoing

I13061 Factors associated with time to HIV RNA suppression in women with HIV infection starting antiretroviral treatment during pregnancy
Mudrikova T, van Snippenburg W, Wensing A, Nellen J, Godfried M, Smit C

Date of approval: 11 July 2013

Ongoing

I13153 Factors associated with late diagnosis of HIV in the Netherlands
Op de Coul E, van Sighem A, Brinkman K, van der Ende I, Geerlings S

Date of approval: 17 December 2013

Ongoing

I12001 The rate of mother-to-child-transmission of hepatitis C virus in HIV-1 infected mothers
Van de Ende I, Snijdewind I, Smit C, Schutten M, Hartwig N, de Wolf F

Date of approval: 9 February 2012

Ongoing

I08044 Primo SHM R5x4 HAART
Grijsen M, Welkers M

Ongoing

Publications 2013

HIV-infected mental health patients: characteristics and comparison with HIV-infected patients from the general population and non-infected mental health patients
Schadé A, van Grootheest G, Smit JH.
BMC Psychiatry. 2013 Jan 23;13:35. doi: 10.1186/1471-244X-13-35.

High incidence of intermittent care in HIV-1-infected patients in Curaçao before and after starting cART
Hermanides HS, Holman R, Gras L, Winkel CN, Gerstenbluth I, de Wolf F, Duits AJ.
AIDS Care. 2013 Feb 21. [Epub ahead of print]

Prolonged decrease of CD4+ T lymphocytes in HIV-1 infected patients after radiotherapy for a solid tumor
Sankatsing SU, Hillebregt MM, Gras L, Brinkman K, van der Ende M, de Wolf F, Stalpers LJ, Prins JM.
J Acquir Immune Defic Syndr. 2013 Apr 15;62(5):546-9.
doi: 10.1097/QAI.0b013e318285d934. Epub 2013 Jan 10.

Has the rate of CD4 cell count decline before initiation of antiretroviral therapy changed over the course of the Dutch HIV epidemic among MSM?
Gras L, Geskus RB, Jurriaans S, Bakker M, van Sighem A, Bezemer D, Fraser C, Prins JM, Berkhout B, de Wolf F; for the ATHENA national observational cohort.
PLoS One. 2013 May 27;8(5):e64437. doi: 10.1371/journal.pone.0064437. Print 2013.

Contribution of genetic background, traditional risk factors, and HIV-related factors to coronary artery disease events in HIV-positive persons
Rotger M, Glass TR, Junier T, Lundgren J, Neaton JD, Poloni ES, van 't Wout AB, Lubomirov R, Colombo S, Martinez R, Rauch A, Günthard HF, Neuhaus J, Wentworth D, van Manen D, Gras LA, Schuitemaker H, Albini L, Torti C, Jacobson LP, Li X, Kingsley LA, Carli F, Guaraldi G, Ford ES, Sereti I, Hadigan C, Martinez E, Arnedo M, Egaña-Gorroño L, Gatell JM, Law M, Bendall C, Petoumenos K, Rockstroh J, Wasmuth JC, Kabamba K, Delforge M, De Wit S, Berger F, Mauss S, de Paz Sierra M, Losso M, Belloso WH, Leyes M, Campins A, Mondi A, De Luca A, Bernardino I, Barriuso-Iglesias M, Torrecilla-Rodriguez A, Gonzalez-Garcia J, Arribas JR, Fanti I, Gel S, Puig J, Negredo E, Gutierrez M, Domingo P, Fischer J, Fätkenheuer G, Alonso-Villaverde C, Macken A, Woo J, McGinty T, Mallon P, Mangili A, Skinner S, Wanke CA, Reiss P, Weber R, Bucher HC, Fellay J, Telenti A, Tarr PE; MAGNIFICENT Consortium; INSIGHT; Swiss HIV Cohort Study.
Clin Infect Dis. 2013 Jul;57(1):112-21. doi: 10.1093/cid/cit196. Epub 2013 Mar 26.

Long-term response to combination antiretroviral therapy in HIV-infected children in the Netherlands registered from 1996-2012
Cohen S, Smit C, van Rossum AM, Fraaij PL, Wolfs TF, Geelen SP, Schölvinck EH, Warris A, Scherpbier HJ, Pajkrt D; on behalf of the Dutch paediatric HIV study group.
AIDS. 2013 Jul 9. [Epub ahead of print]

Loss to follow-up and mortality rates in HIV-1 positive patients in Curaçao before and after the start of combined antiretroviral therapy
Hermanides HS, Holman R, Gras L, Winkel C, Gerstenbluth I, de Wolf F, Duits A.
AIDS Res Hum Retroviruses. 2013 Aug 8. [Epub ahead of print]

HIV-1 transmission networks amongst men having sex with men and heterosexuals in Kenya
Bezemer D, Faria NR, Hassan AS, Hamers RL, Mutua G, Anzala O, Mandaliya KN, Cane PA, Berkley JA, Rinke de Wit TF, Wallis CL, Graham SM, Price MA, Coutinho R, Sanders EJ.
AIDS Res Hum Retroviruses. 2013 Aug 15. [Epub ahead of print]

The effect of statin therapy on pneumonia in an HIV-infected population in the Netherlands
Janssen NE, van Lelyveld SF, Hoepelman AI, Gras L, Groenwold RH, Oosterheert JJ.
J Infect. 2013 Sep;67(3):238-41. doi: 10.1016/j.jinf.2013.04.011. Epub 2013 Apr 19.

Age biases in a large HIV and sexual behaviour-related internet survey among MSM
Marcus U, Hickson F, Weatherburn P, Schmidt AJ.
BMC Public Health. 2013 Sep 10;13(1):826. [Epub ahead of print]

How effectively can HIV phylogenies be used to measure heritability?
Shirreff G, Alizon S, Cori A, Günthard HF, Laeyendecker O, van Sighem A, Bezemer D and Fraser C.
EMPH (2013) 2013 (1): 209-224. doi: 10.1093/emph/eot019. First published online: September 13, 2013

Changes in first-line cART regimens and short-term clinical outcome between 1996 and 2010 in the Netherlands
Smit M, Smit C, Geerlings S, Gras L, Brinkman K, Hallett TB, de Wolf F; Athena Observational Cohort.
PLoS One. 2013 Sep 30;8(9):e76071. doi: 10.1371/journal.pone.0076071.

The Presence of CXCR4-using HIV-1 prior to start of antiretroviral therapy is an independent predictor of delayed viral suppression
Gijsbers EF, van Sighem A, Harskamp AM, Welkers MR, de Wolf F, Brinkman K, Prins JM, Schuitemaker H, van 't Wout AB, Kootstra NA.
PLoS One. 2013 Oct 1;8(10):e76255.

Gradually decreasing anal cancer incidence in the HIV+ population in the Netherlands after a decade of cART
Richel O, Van der Zee RP, Smit C, De Vries HJ, Prins JM.
Sex Health. 2013 Nov;10(6):586. doi: 10.1071/SHv10n6ab33

A simplified combination antiretroviral therapy regimen enhances adherence, treatment satisfaction and quality of life: results of a randomized clinical trial
Langebeek N, Sprenger H, Gisolf E, Reiss P, Sprangers M, Legrand J, Richter C, Nieuwkerk P.
HIV Med. 2013 Nov 11. doi: 10.1111/hiv.12112. [Epub ahead of print]

Publications related to collaborations

ART-CC

An internationally generalizable risk index for mortality after one year of antiretroviral therapy
Tate JP, Justice AC, Hughes MD, Bonnet F, Reiss P, Mocroft A, Nattermann J, Lampe FC, Bucher HC, Sterling TR, Crane HM, Kitahata MM, May M, Sterne JA.
AIDS. 2013 Feb 20;27(4):563-72. doi: 10.1097/QAD.0b013e32835b8c7f.

Insurability of HIV positive people treated with antiretroviral therapy in Europe: collaborative analysis of HIV cohort studies
Kaulich-Bartz J, Dam W, May MT, Lederberger B, Widmer U, Phillips AN, Grabar S, Mocroft A, Vilaro J, van Sighem A, Moreno S, Dabis F, Monforte AD, Teira R, Ingle SM, Sterne JA; Writing committee for the Antiretroviral Cohort Collaboration.
AIDS. 2013 Feb 25. [Epub ahead of print]

Durability of first ART regimen and risk factors for modification, interruption or death in HIV-positive patients starting ART in Europe and N. America 2002-2009
Abgrall S; The Antiretroviral Therapy Cohort Collaboration (ART-CC).
AIDS. 2013 Mar 13;27(5):803-13. doi: 10.1097/QAD.0b013e32835cb997. Epub 2012 Nov 28.

Cohort profile: Antiretroviral Therapy Cohort Collaboration (ART-CC)
May MT, Ingle SM, Costagliola D, Justice AC, de Wolf F, Cavassini M, D'Arminio Monforte A, Casabona J, Hogg RS, Mocroft A, Lampe FC, Dabis F, Fätkenheuer G, Sterling TR, Del Amo J, Gill MJ, Crane HM, Saag MS, Guest J, Brodt HR, Sterne JA; the Antiretroviral Cohort Collaboration.
IJE 18 April 2013 [Epub ahead of print].

Lower incidence of Pneumocystis jirovecii pneumonia among Africans in the Netherlands; host or environmental factors?
Schoffelen AF, van Lelyveld SF, Barth RE, Gras L, de Wolf F, Netea MG, Hoepelman AI.
AIDS. 2013 Apr 24;27(7):1179-84. Epub 2012 Dec 31.

Higher rates of AIDS during the first year of antiretroviral therapy among migrants: the importance of tuberculosis
Antiretroviral Therapy Cohort Collaboration (ART-CC), Shepherd BS, Jenkins CA, Parrish DD, Glass TR, Cescon A, Masabeu A, Chene G, de Wolf F, Crane HM, Jarrin I, Gill J, del Amo J, Abgrall S, Khaykin P, Lehmann C, Ingle SM, May MT, Sterne JA, Sterling TR.
AIDS. 2013 May 15;27(8):1321-9. doi: 10.1097/QAD.0b013e32835faa95.

Influence of geographical origin and ethnicity on mortality in patients on antiretroviral therapy in Canada, Europe and the United States
Del Amo J, Jarrin I, May M, Dabis F, Crane H, Podzamczer D, Sterling TR, Abgrall S, Lampe F, Justice A, Castagna A, Boesecke C, Staehelin C, De Wolf F, Guest J, Mugavero MJ, Khaykin P, Samji H, Ingle S, Sterne JAC, Gill MJ for the ART-CC
Clin Infect Dis. 2013 Jun;56(12):1800-9. doi: 10.1093/cid/cit111. Epub 2013 Mar 1.

CASCADE

Immunovirologic control 24 months after interruption of antiretroviral therapy initiated close to HIV seroconversion
Lodi S, Meyer L, Kelleher AD, Rosinska M, Ghosn J, Sannes M, Porter K.
Arch Intern Med. 2012 Sep 10;172(16):1252-5. doi: 10.1001/archinternmed.2012.2719.

Risk of tuberculosis following HIV seroconversion in high-income countries
Lodi S, del Amo J, d'Arminio Monforte A, Abgrall S, Sabin C, Morrison C, Furrer H, Muga R, Porter K, Girardi E; CASCADE collaboration in EuroCoord.
Thorax. 2013 Mar;68(3):207-13. doi: 10.1136/thoraxjnl-2012-201740. Epub 2012 Oct 31.

Impact of HIV-1 subtype on CD4 count at HIV seroconversion, rate of decline, and viral load set point in European seroconverter cohorts
Touloumi G, Pantazis N, Pillay D, Paraskevis D, Chaix ML, Bucher HC, Kücherer C, Zangerle R, Kran AM, Porter K; CASCADE collaboration in EuroCoord.
Clin Infect Dis. 2013 Mar;56(6):888-97. doi: 10.1093/cid/cis1000. Epub 2012 Dec 7.

Effect of HCV infection on cause-specific mortality following HIV seroconversion before and after 1997
Van der Helm J, Geskus R, Sabin C, Meyer L, Del Amo J, Chêne G, Dorrucci M, Muga R, Porter K, Prins M; CASCADE collaboration in EuroCoord.
Gastroenterology. 2013 Apr;144(4):751-760.e2. doi: 10.1053/j.gastro.2012.12.026. Epub 2012 Dec 22.

Performance of parametric survival models under non-random interval censoring: a simulation study
Pantazis N, Kenward MG, Touloumi G, on behalf of CASCADE Collaboration in EuroCoord.
Computational Statistics and Data Analysis 2013;63,16-30.

Virologic and immunologic response to cART by HIV-1 subtype in the CASCADE collaboration
Touloumi G, Pantazis N, Chaix ML, Bucher HC, Zangerle R, Kran AM, Thiebaut R, Masquelier B, Kucherer C, Monforte Ad, Meyer L, Porter K, for CASCADE Collaboration in EuroCoord.
PLoS One. 2013 Jul 30;8(7):e71174. doi: 10.1371/journal.pone.0071174. Print 2013.

Natural history of HIV control since seroconversion
Madec Y, Boufassa F, Porter K, Prins M, Sabin C, Monforte AD, Amornkul P, Bartmeyer B, Sannes M, Venet A, Lambotte O, Meyer L, on behalf of the CASCADE Collaboration in EuroCoord.
AIDS. 2013 Aug 1. [Epub ahead of print]

Symptomatic illness and low CD4 cell count at HIV seroconversion as markers of severe primary HIV infection
Lodi S, Fisher M, Phillips A, De Luca A, Ghosn J, Malyuta R, Zangerle R, Moreno S, Vanhems P, Boufassa F, Guiguet M, Porter K, for CASCADE Collaboration in EuroCoord.
PLoS One. 2013 Nov 14;8(11):e78642. doi: 10.1371/journal.pone.0078642. eCollection 2013.

COHERE

Predictors of CD4+ T-cell counts of HIV type 1-infected persons after virologic failure of all 3 original antiretroviral drug classes
The Pursuing Later Treatment Option II (PLATO II) Project Team of the Collaboration of Observational HIV Epidemiological Research Europe (COHERE).
J Infect Dis. 2013 Mar 1;207(5):759-67. doi: 10.1093/infdis/jis752. Epub 2012 Dec 7.

The incidence of AIDS-defining illnesses at a current CD4 count ≥200 cells/μL in the post-combination antiretroviral therapy era
Mocroft A, Furrer HJ, Miro JM, Reiss P, Mussini C, Kirk O, Abgrall S, Ayayi S, Bartmeyer B, Braun D, Castagna A, d'Arminio Monforte A, Gazzard B, Gutierrez F, Hurtado I, Jansen K, Meyer L, Muñoz P, Obel N, Soler-Palacin P, Papadopoulos A, Raffi F, Ramos JT, Rockstroh JK, Salmon D, Torti C, Warszawski J, de Wit S, Zangerle R, Fabre-Colin C, Kjaer J, Chene G, Grarup J, Lundgren JD; for the Opportunistic Infections Working Group on behalf of the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) study in EuroCOORD.
Clin Infect Dis. 2013 Aug 6. [Epub ahead of print]

Risk factors and outcomes for late presentation for HIV-positive persons in Europe: Results from the Collaboration of Observational HIV Epidemiological Research Europe Study (COHERE)
Mocroft A, Lundgren JD, Sabin ML, Monforte AD, Brockmeyer N, Casabona J, Castagna A, Costagliola D, Dabis F, De Wit S, Fätkenheuer G, Furrer H, Johnson AM, Lazanas MK, Leport C, Moreno S, Obel N, Post FA, Reekie J, Reiss P, Sabin C, Skaletz-Rorowski A, Suarez-Lozano I, Torti C, Warszawski J, Zangerle R, Fabre-Colin C, Kjaer J, Chene G, Grarup J, Kirk O; Collaboration of Observational HIV Epidemiological Research Europe (COHERE) study in EuroCoord.
PLoS Med. 2013 Sep;10(9):e1001510. Epub 2013 Sep 3.

D:A:D

Atazanavir is not associated with an increased risk of cardio or cerebrovascular disease events
Monforte AD, Reiss P, Ryom L, El-Sadr W, Dabis F, De Wit S, Worm SW, Law MG, Weber R, Kirk O, Pradier C, Phillips AN, Lundgren JD, Sabin CA.
AIDS. 2013 Jan 28;27(3):407-15.

Antiretroviral drug-related liver mortality among HIV-positive persons in the absence of hepatitis B or C virus coinfection: the data collection on adverse events of anti-HIV drugs study
Kovari H, Sabin CA, Ledergerber B, Ryom L, Worm SW, Smith C, Phillips A, Reiss P, Fontas E, Petoumenos K, De Wit S, Morlat P, Lundgren JD, Weber R.
Clin Infect Dis. 2013 Mar;56(6):870-9. doi: 10.1093/cid/cis919. Epub 2012 Oct 22.

Association between antiretroviral exposure and renal impairment among HIV-positive persons with normal baseline renal function: the D:A:D study
Ryom L, Mocroft A, Kirk O, Worm SW, Kamara DA, Reiss P, Ross M, Fux CA, Morlat P, Moranne O, Smith C, Lundgren JD; D:A:D Study Group.
J Infect Dis. 2013 May 1;207(9):1359-69. doi: 10.1093/infdis/jit043. Epub 2013 Feb 4.

Association between ALT level and the rate of cardio/cerebrovascular events in HIV-positive individuals: The D:A:D study
Sabin CA, Ryom L, Kovari H, Kirk O, de Wit S, Law, Reiss P, Dabis F, Pradier C, El Sadr W, Monforte AD, Kamara D, Phillips AN, Lundgren JD.
J Acquir Immune Defic Syndr. 2013 Aug 1;63(4):456-63

Non-AIDS defining cancers in the D:A:D study - time trends and predictors of survival: a cohort study.
Worm SW, Bower M, Reiss P, Bonnet F, Law M, Fätkenheuer G, D Arminio Monforte A, Abrams DI, Grulich A, Fontas E, Kirk O, Furrer H, De Wit S, Phillips A, Lundgren JD, Sabin CA.
BMC Infect Dis. 2013 Oct 9;13(1):471. [Epub ahead of print]

Predictors of advanced chronic kidney disease and end-stage renal disease in HIV-positive persons.
Ryom L, Mocroft A, Kirk O, Ross M, Reiss P, Fux CA, Morlat P, Moranne O, Smith C, El-Sadr W, Law M, Lundgren JD.
AIDS. 2013 Dec 19. [Epub ahead of print]

EPPICC

Use of combination neonatal prophylaxis for the prevention of mother-to-child transmission of HIV infection in European high-risk infants
Chiappini E, Galli L, Giaquinto C, Ene L, Goetghebuer T, Judd A, Lisi C, Malyuta R, Noguera-Julian A, Ramos JT, Rojo-Conejo P, Rudin C, Tookey P, de Martino M, Thorne C; European Pregnancy and Paediatric HIV Cohort Collaboration study group in EuroCoord.
AIDS. 2013 Mar 27;27(6):991-1000. doi: 10.1097/QAD.0b013e32835cffb1.

Missed opportunities among HIV-positive women to control viral replication during pregnancy and to have a vaginal delivery
Aebi-Popp K, Mulcahy F, Glass TR, Rudin C, Martinez de Tejada B, Bertisch B, Fehr J, Grawe C, Scheibner K, Rickenbach M, Hoesli I, Thorne C; for the European Collaborative Study in EuroCoord and the Swiss Mother & Child HIV Cohort Study.
J Acquir Immune Defic Syndr. 2013 Sep 1;64(1):58-65.

EuroSIDA

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Towards the Amsterdam Cohort Studies 30th year: the unique story of HIV and its risk groups
Prins M
7th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2013, Amsterdam, 19 November 2013

Ongoing HIV-1 subtype B transmission networks amongst MSM in the Netherlands
Bezemer DO, Ratmann O, van Sighem A, Hermanides G, Dutilh BE, Faria NR, van den Hengel R, Gras L, Duits A, Reiss P, de Wolf F, Fraser C, the observational cohort ATHENA
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Predictors and correlates of adherence to combination antiretroviral therapy (cART) for chronic HIV infection: a meta analysis
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Association between age and long-term CD4 cell count trajectory in HIV-1 infected individuals with sustained viral suppression depends on CD4 cell count at start cART
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Greater arterial stiffness in middle-aged HIV-positive men on cART may be explained by an increased prevalence of hypertension, smoking and systemic inflammation
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An updated prediction model of the global risk of cardiovascular disease in HIV-positive persons; The Data collection on Adverse effects of Anti-HIV Drugs (D:A:D) study
Friis-Møller N, Ryom L, Smith C, Weber R, Reiss P, Dabis F, De Wit D, d'Arminio Monforte A, Kirk O, Fontas E, Sabin C, Phillips A, Lundgren JD, Law M, D:A:D Study Group
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Prevalence of detected drug resistance across different regions of Europe: Data from EuroSIDA 1997-2012
Schultze A, Phillips AN, Paredes R, Battegay M, Rockstroh J, Machala L, Tomazic J, Kirk O, Lundgren JD, Cozzi-Lepri A, EuroSIDA in EuroCOORD
14th European AIDS Conference, Brussels, 16-19 October 2013

Long-term response to combination antiretroviral therapy in HIV-infected children in the Netherlands registered from 1996-2012
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Vitamin D level in HIV-infected persons: prognostic value for all-cause death, and association with inflammatory markers, results from the EuroSIDA cohort study
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Reduced bone mineral density (BMD) is largely explained by lower body weight in HIV-positive individuals and more pronounced in younger men having sex with men (MSM), regardless of HIV-status
Kooij KW, Wit FW, Bisschop PH, Schouten J, Stolte I, Prins M, van der Valk M, van Eck-Smit BL, Lips P, Reiss P, on behalf of the AGE$_h$IV Cohort Study Group
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The spectrum of clinical disease in HIV-positive persons and relationship with markers of deteriorating renal function
Mocroft A, Ryom L, Begovac J, D'Arminio Monforte A, Vassilenko A, Gatell J, Florence E, Ormaasen V, Kirk O, Lundgren J, EuroSIDA in EuroCOORD
14th European AIDS Conference, Brussels, 16-19 October 2013

Response to combination antiretroviral treatment in HIV positive individuals in Europe: variation by educational level
Lodi S, COHERE in EuroCoord
14th European AIDS Conference, Brussels, 16-19 October 2013

Mortality in migrants living with HIV in Western Europe: differences by geographical origin and gender
Monge S, on behalf of COHERE in EuroCoord
14th European AIDS Conference, Brussels, 16-19 October 2013

Infection related and unrelated malignancies, HIV and the aging population
Shepherd L, Borges A, Ledergerber B, Domingo P, Rockstroh J, Knysz B, Kirk O, Mocroft A, Lundgren J, EuroSIDA in EuroCOORD
14th European AIDS Conference, Brussels, 16-19 October 2013

Cascade of HIV care in the Netherlands from 2002 to 2013
Engelhard EAN, Smit C, van Sighem AI, Reiss P, Brinkman K, Geerlings SE, on behalf of the Q-HIV and the ATHENA National Observational Cohort Study Groups
14th European AIDS Conference, Brussels, 16-19 October 2013

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14th European AIDS Conference, Brussels, 16-19 October 2013

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[HIV delay study – time to care]
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Pre-exposure prophylaxis versus 'test and treat' amongst men who have sex with men in the Netherlands
Van Sighem A, van den Hengel R, Bezemer D, de Wolf F
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Association between age and long-term CD4 cell count trajectory in HIV-1 infected individuals with sustained viral suppression depends on CD4 cell count at start cART
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Pre-exposure prophylaxis amongst men who have sex with men in the Netherlands
Van Sighem A, van den Hengel R, Bezemer D, de Wolf F
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An individual-based stochastic simulation model of the natural history of HIV infection
Nakagawa F on behalf of the Stochastic Simulation of Outcomes of Peoplse with HIV in Europe (SSOPHIE) project working group in EuroCoord
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Cumulative viral burden is associated with all-cause, AIDS-related and non-AIDS-related mortality following ART initiation among treatment naïve HIV-1-infected patients
Sterne J on behalf of ART-CC
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Association of time-varying adherence to ART on rates of AIDS/death: cross-cohort analysis
Turner N on behalf of ART-CC
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Longitudinal modelling of HCV RNA levels in chronically infected individuals with documented HCV seroconversion intervals
Prins M on behalf of Amsterdam Cohort Studies
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Reduced bone mineral density (BMD) is largely explained by lower body mass index in HIV-positive individuals, and more pronounced in younger MSM, regardless of HIV-status
Kooij K on behalf of The AGE$_h$IV cohort study
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Higher rates of triple class virologic failure in perinatally HIV-infected teenagers compared to heterosexually infected young adults in the PLATO II study
Rojo Conejo P on behalf of COHERE in EuroCoord
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Increased risk of cardiovascular disease with age in men: A comparison of D:A:D with HIV-cardiovascular disease risk equations
Petoumenos K, El-Sadr W, d'Arminio Montforte A, Sabin C, Reiss P, Ryom L, De Wit S, Rickenbach M, Lundgren J, Law M, for D:A:D Study Group
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

Mortality after starting ART in treatment-naïve adults in 3 continents: collaborative analysis of international epidemiologic databases to evaluate AIDS in Southern Africa and ART Cohort Collaboration cohorts
Boulle A, Schomaker M, May M, Egger M, Sterne J and site investigators from IeDEA-SA and ART-CC Collaborations
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Poster presentations

Calendar age predicts CD8+ T-cell senescence in long-term treated HIV-infected patients but not in HIV-uninfected controls
Joerink M, Wit FWNM, Maurer I, Harskamp AM, Schouten J, Prins M, Reiss P, Leeuwen EMM van, Kootstra NA, on behalf of the AGE$_h$IV Study Group
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Risk of non-AIDS-defining events amongst HIV-infected patients not yet on antiretroviral therapy
Van Sighem AI, Zhang S, Kesselring A, Gras L, Prins JM, Hassink E, Kauffmann R, Richter C, de Wolf F, Reiss P
7th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2013, Amsterdam, 19 November 2013

Ethnicity has diminished as a risk factor for chronic kidney disease in the current HIV treatment era
Schoffelen AF, Kesselring AM, van Lelyveld SFL, Reiss P, Barth RE, Hoepelman AIM, on behalf of the ATHENA national observational cohort study
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Long-term changes in CD4/CD8 ratio in cART treated HIV-1 infected patients
Gras L, Brinkman K, Prins JM, Reiss P
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Risk factors associated with HIV resuppression on 2nd line treatment following 1st line combination antiretroviral therapy (cART) virologic failure
Bierhoff M, Gras LAJ, Reiss P, ten Kate RW
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Nevirapine dose escalation or immediate full dose when switching from efavirenz to nevirapine in HIV-infected patients in the ATHENA cohort study
Blonk MI, Van Luin M, Smit C, Wit FWNM, Kappelhoff BS, Burger DM
7th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2013, Amsterdam, 19 November 2013

Cascade of HIV care in the Netherlands from 2002 to 2013
Engelhard EAN, Smit C, Van Sighem AI, Reiss P, Brinkman K, Geerlings SE
7th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) 2013, Amsterdam, 19 November 2013

Estimation of HIV-infected populations in Europe: a pilot study using data for men who have sex with men in the UK
Nakagawa F on behalf of the Stochastic Simulation of Outcomes of People with HIV in Europe (SSOPHIE) project working group in EuroCoord
14th European AIDS Conference, Brussels, 16-19 October 2013

Investigating the causal impact of PI- and NNRTI-containing combination antiretroviral therapy (cART) on the risk of mortality: methodological challenges
Smith C, Ford D, Hernan M, Sabin C, Reiss P, de Wit S, d'Arminio Montforte A, Pradier C, Law M, Weber R, Bruyand M, Fontas E, El Sadr W, Philips A, Ryom L, Lundgren J, D:A:D Study
14th European AIDS Conference, Brussels, 16-19 October 2013

A survey of ATRIPLA use in clinical practice among treatment-naïve HIV-positive patients in Europe
Kirk O, Reiss P, Rakhmanova A, Benhegyi D, Phillips AN, De Wit S, Ristola M, Lundgren JD, Grarup J, Mocroft A, EuroSIDA in EuroCoord
14th European AIDS Conference, Brussels, 16-19 October 2013

Estimation of percentage of HIV-infected people with future limited antiretroviral drug options in a closed observational setting over the period 2007-2011 and beyond
Cozzi-Lepri A, Phillips AN, Paredes R, Jablonowska E, Florence E, Pedersen C, Staub T, Ledergerber B, Kirk O, Mocroft A, Lundgren J, EuroSIDA in EuroCoord
14th European AIDS Conference, Brussels, 16-19 October 2013

Development of thrombocytopenia (TCP) and AIDS (ADEs) and serious Non-AIDS (NADEs) Events in Europe
Borges AH, Lundgren JD, Kirk O, Ridolfo A, Katlama C, Antunes F, Grzeszczuk A, Blaxhult A, Mitsura VM, Mocroft A on behalf of EuroSIDA in EuroCOORD
14th European AIDS Conference, Brussels, 16-19 October 2013

The development of computer models that predict response to HIV therapy accurately without a genotype: A potential tool for therapy optimisation in resource-limited settings
Revell AD, Streinu-Cercel A, Ene L, Dragovic G, Hamers R, Morrow C, Wood R, Tempelman H, Wensing AM, Reiss P, van Sighem A, Pozniak A, Montaner J, Lane HC, Larder BA, RDI Study Group
14th European AIDS Conference, Brussels, 16-19 October 2013

The effect of antiretroviral penetration into the central nervous system on the incidence of AIDS-defining neurological conditions in a prospective observational study
Caniglia E
15th International Workshop on Adverse Drug Reactions and Co-Morbidities in HIV, Brussels, 15-17 October 2013

Ontwikkelingen in de hiv-epidemie in Nederland
[Developments in the HIV epidemic in the Netherlands]
Van Sighem A
Nascholing Sectie Infectieziektebestrijding van de Vereniging voor Infectieziekten (VIZ-sib), IJmuiden, 12-13 September 2013

Higher rates of triple class virologic failure in perinatally HIV-infected teenagers compared to heterosexually infected young adults in the PLATO II study
Gibb DM, on behalf of the PLATO II Project Team of COHERE
7th IAS Conference on HIV Pathogenesis, Treatment and Prevention 2013, Kuala Lumpur, Malaysia, 30 June-3 July 2013

Late HIV diagnosis, late initiation of combination ART and mortality in Europe: variation by educational level
Lodi S, COHERE in EuroCoord
7th IAS Conference on HIV Pathogenesis, Treatment and Prevention 2013, Kuala Lumpur, Malaysia, 30 June-3 July 2013

Use of longitudinal case reporting data for estimation of HIV prevalence
Van Sighem A
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SHM: Monitoring of HIV in the Netherlands
Van Sighem A, Zaheri S, Reiss P
Meeting of experts on HIV surveillance and strategic information, Cairo, Egypt, 24-26 June 2013

Accurate prediction of response to HIV therapy without a genotype a potential tool for therapy optimisation in resource-limited settings
Larder BA, Revell AD, Wang D, Hamers R, Tempelman H, Barth R, Wensing AMJ, Morrow C, Wood R, van Sighem A, Reiss P, Nelson M, Emery S, Montaner JM, Lane HC, on behalf of the RDI study group
International Workshop on HIV & Hepatitis Drug Resistance and Curative Strategies, Toronto, Canada, 4-8 June 2013

Transmission dynamics of the worldwide HIV-1 subtype B epidemic regarded from a Caribbean island
Bezemer D, Hermanides G, Rodrigues Faria N, Van Sighem A, Fraser C, De Wolf F, Duits A
20th International HIV Dynamics & Evolution, Utrecht, 8-11 May 2013

HIV-1 subtype B transmission networks of heterosexually infected patients co-infected with HCV
Bezemer D, Smit C, Van Sighem A, De Wolf F
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Response to anti-HCV treatment in HIV-infected patients chronically infected with hepatitis C
Smit C, Van der Meer J, Van der Ende I, Arends J, Van der Valk M, Brinkman K, Schippers E, De Wolf F, Schutten M, Schinkel J, De Vries-Sluijs D, Hoepelman A, Richter C
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

The effect of antiretroviral penetration in the central nervous system on the incidence of AIDS-defining neurological conditions in a prospective observational study
Caniglia E, on behalf of the HIV-CAUSAL Collaboration
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Immune reconstitution inflammatory syndrome: opportunistic infections and AIDS malignancies in patients initiating combination antiretroviral therapy
Lodi S, on behalf of the HIV-CAUSAL Collaboration
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Differences in high HIV-1 viraemia following acute infection and cumulative burden over 2 years by HIV-1 subtype
Touloumi G, on behalf of the CASCADE Collaboration in EuroCoord
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

The effect of boosted lopinavir versus boosted atazanavir-containing regimens on immunologic, virologic and clinical outcomes in a prospective observational study
Cain L, on behalf of HIV-CAUSAL Collaboration
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Short and long term prognostic value of vitamin D for AIDS, non-AIDS defining events and all-cause mortality
Shepherd L, on behalf of EuroSIDA for EuroCoord
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

An evaluation of 10 elite controller definitions over ART naïve follow-up within a large seroconverter cohort collaboration
Olson A, on behalf of the CASCADE Collaboration in EuroCoord
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Age and CD4 count increase on cART: a look beyond the effect of older age on the average CD4 recovery to acquire additional insight on the phenomenon
Cozzi-Lepri A, on behalf of EuroSIDA in EuroCoord.
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Temporal trends in prognostic markers of HIV disease progression and transmission
Pantazis N, on behalf of CASCADE Collaboration in EuroCoord
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Modeling the course of the HCV epidemic among HIV-positive MSM in the Netherlands
Prins M, on behalf of the MOSAIC Study Group
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Is response to anti-HCV treatment predictive of mortality in HCV/HIV positive patients?
Cozzi-Lepri A, on behalf of COHERE in EuroCoord
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Cardiovascular risk profiles in HIV infection in Europe
Schultze A, on behalf of EuroSIDA in EuroCoord
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Prevalence and impact of transmitted drug resistance on response to antiretroviral therapy in children
Wittkop L, on behalf of the EuroCoord-CHAIN Joint Project
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Risk factors for preterm delivery among HIV-positive pregnant women in a Ukrainian cohort
Bagkeris E, on behalf of the European Collaborative Study in EuroCoord
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Tuberculosis in pediatric ART programs in lower income countries: a global view on diagnostics and screening practices
Davies M-A, on behalf of the International Epidemiologic Database to Evaluate AIDS (IeDEA)
17th International Workshop on HIV Observational Databases, Cavtat, Croatia, 11-13 April 2013

Risk of non-AIDS-defining events amongst HIV-infected patients not yet on antiretroviral therapy
Van Sighem A, Kesselring A, Gras L, Prins J, Hassink E, Kauffmann R, Richter C, Reiss P, De Wolf F
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

Contribution of AIDS and Non-AIDS deaths to lower life expectancy of ART-treated HJIV+ individuals compared with the general population
May M, Mocroft A, Guest J, Crane H, Reiss. P, d'Arminio Monforte, Labarga P, Wasmuth J-C, Ingle S, Hogg R, and ART Cohort Collaboration
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

Effect of HIV-1 subtypes on virological and immunological response to initial cART: A European multicohort study
Wittkop L, on behalf of EuroCoord-CHAIN Subtype Project Team
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

Mortality of treated HIV-1+ individuals according to viral subtype in Europe and Canada: ART Cohort Collaboration
May M, Gill M, Harrigan R, Klein M, Reiss P, Mocroft A, d'Arminio Montforte A, Zangerle R, Cavassini M, Sterne J, and ART Cohort Collaboration
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

Increased risk of ARV drug discontinuation among patients with high hyaluronic acid, a marker of liver fibrosis
Grint D, Peters L, Rockstroh J, Lundgren J, De Wit S, Mitsura V, Kynsz B, Pedersen C, Kirk O, Mocroft A and EuroSIDA
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

Cancer risk and use of protease inhibitor- or NNRTI-based cART; The D:A:D study
Bruyand M, Ryom L, Shepherd L, Reiss P, de Wit S, d'Artimio Monforte A, Rickenbach M, Philips A, Lundgren L, Sabin C, and D:A:D Study Group
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

Improvements in short-term mortality following myocardial infarction: The Data Collection on Adverse events of Anti-HIV Drugs study
Sabin C, Ryom L, Law M, El-Sadr W, Kirk O, Bruyand M, Reiss P, Pradier C, Ledergerber B, Lundgren J and D:A:D Study Group
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

A comparison of estimated glomerular filtration rates using Cockcroft-Gault and the Chronic Kidney Disease Epidemiology Collaboration Estimating Equations
Mocroft A, Ryom L, Reiss P, Ledergerber B, d'Aminio Monforte A, Gatell J, de Wit S, Beniowski M, Lundgren J, Kirk O and EuroSIDA in EuroCOORD
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

Predictors of advanced chronic kidney disease and end-stage renal disease in HIV+ persons: D:A:D
Ryom L, Mocroft A, Kirk O, El-Sadr W, Ross M, Reiss P, De Wit S, Morlat P, Fux C, Lundgren J, and D:A:D Study Group
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

The incidence and risk of AIDS-defining illnesses at current CD4 counts of 500/mm³ or higher
Mocroft A and COHERE in EuroCOORD
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

Mean asymptomatic viral load, steady state viral load and CD4 cell count following acute infection as predictors of HIV disease progression
Olson A, Touloumi G, Geskus R, Meyer L, Prins M, Chêne G, De Luca A, Costagliola D, and Porter K for CASCADE Collaboration in EuroCOORD
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

Trends and factors associated with virological failure among women conceiving on cART in Western Europe
Bailey H, Townsend CL, Cortina Borja M, Thorne C for the European Collaborative Study in EuroCOORD
20th Conference on Retroviruses and Opportunistic Infections, Atlanta, USA, 3-6 March, 2013

Appendix 1: Composition of SHM

SHM Governing Board

Name	Position	Affiliation
Dr F.P. Kroon	Chair	NVHB
Dr J.S.A. Fennema	Secretary	GGD Nederland
Prof. K. Stronks	Interim treasurer (from 1 December 2012)	AMC-UvA
L.J.M. Elsenburg	Member	HIV Vereniging Nederland
Dr R.J.M. Hopstaken	Member	NFU
Drs. P.E. van der Meer	Member	NFZ
Drs. M.I. Verstappen	Member	AGIS

SHM Advisory Board

Name	Affiliation
Prof. J.M.A. Lange (chair)	AMC, Dept. of Global Health; AIGHD, Amsterdam
Prof. Sir R.M. Anderson	Imperial College, Faculty of Medicine, Dept. of Infectious Disease Epidemiology, London, UK
Prof. G. Chene	Université Victor Segalen, Bordeaux, France (from 1 January 2013)
Prof. M. Egger	University of Bern, Switzerland; University of Bristol, UK
Dr S.E. Geerlings	AMC, Dept. of Internal Medicine, Amsterdam
Prof. D.R. Kuritzkes	Brigham and Women's Hospital, Section of Retroviral Therapeutics, Boston, MA, USA
C. Rümke†	HIV Vereniging Nederland, Amsterdam
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Appendix 2: Terminology & definitions

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

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

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

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

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

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

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

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

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

cART
Combination antiretroviral treatment.

CD4 (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 the HIV virus. In the course of the HIV infection the number of CD4 cells may drop from normal levels (+ 500 per mm^3) to dangerously low levels (fewer than 200 CD4 cells per mm^3 of blood).

CDC
US Centers for Disease Control and Prevention.

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

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

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

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

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

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

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

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

GGD
Dutch municipal health service (www.ggd.nl).

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

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

Hepatic
Pertaining to the liver.

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

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

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

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

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

Immune recovery
If treatment is effective and HIV is well-controlled, the immune cells regain their normal function and CD4 cell counts are close to normal. This is defined as immune recovery.

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

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

Mono-infection
When a person has only one infection.

Mortality rate
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.

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

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

Nucleoside Reverse Transcriptase Inhibitor (NRTI)
Antiretroviral (ARV) 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. A single person-year is 1 year lived by 1 person.

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

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

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

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

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

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

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

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

Seroprevalence
The incidence of disease in a given population based on blood serum specimens.

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

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

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

Viraemia
The presence of a virus in the blood.

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

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

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

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

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