9th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment
Wednesday 18 November 2015
The Royal Tropical Institute (KIT) Amsterdam

Programme & Abstracts
Programme

08:00 Registration

Opening remarks
09:00 Opening and welcome

Session 1: Epidemiology & Prevention I

09:10 Plenary: Pre-exposure prophylaxis for MSM: What have we learned and what are the next steps? Jean-Michel Molina (University of Paris Diderot and Saint-Louis Hospital, Paris, France)

09:40 No decline in hepatitis C virus (HCV) incidence among HIV-positive men who have sex with men (MSM) within CASCADE: 1990-2014 R. Gasius (GGD Amsterdam, Amsterdam)

09:50 Activation of immature Langerhans cells facilitate hepatitis C virus transmission R. Sarrami Foroozhan (AMC-UvA, Amsterdam)

10:00 Modelling the HCV epidemic among HIV positive MSM in the HIV direct-acting antivirals era. Is HCV elimination possible and at what price? S.J. Hullegie (Erasmus MC, Rotterdam)

10:10 The impact of the number of comorbidities and aging on Health-Related Quality of Life (HRQL) in HIV-infected and uninfected individuals N. Langebeek (AMC-UvA, Amsterdam)

10:30 General discussion

10:40 Coffee break

Session 2: Epidemiology & Prevention II

10:50 The HIV epidemic in the Netherlands: an update Peter Reiss (SHM; AIGHD; AMC-UvA, Amsterdam)

11:10 Plenary: Inside the sausage factory: how global HIV estimates and some decisions are made Tim Hallett (Imperial College, London, UK)

11:40 A new method to estimate the first step in the HIV care continuum A.I. van Sighem (SHM, Amsterdam)

11:50 Opportunities for HIV prevention among men having sex with men in the Netherlands O. Ratmann (Imperial College, London, UK)

12:00 On demand PrEP among MSM in the Netherlands: a cost-effective approach for preventing HIV-1 infections B.E. Nichols (Erasmus MC, Rotterdam)

12:10 Home testing for HIV combined with internet counselling in the Netherlands: interim results of the HIVTest@Home trial F.R. Zuure (GGD Amsterdam, Amsterdam)

12:20 General discussion

12:30 Lunch and poster viewing

Themed poster discussion: ‘Test and PrEP’:

Chair: Catherine Hankins (AIGHD)

13:00 Determinants of never having tested for HIV among MSM in the Netherlands C. den Daas (RIVM, Utrecht)

13:55 Factors associated with recent HIV infection among newly diagnosed STI clinic attendees in the Netherlands in 2014 General practitioners’ barriers to and facilitators of HIV testing strategies: a qualitative study S. Parkhaili (RIVM, Utrecht)

14:00 Early experiences from the Amsterdam PrEP project Low knowledge and moderate acceptability towards the prescription of pre-exposure prophylaxis among Dutch healthcare providers of sexual health clinics: a mixed-methods study L.K.C.W. Joore (AMC-UvA, Amsterdam)

14:10 General practitioner’s barriers to and facilitators of HIV testing strategies: a qualitative study E. Hoornenborg (GGD Amsterdam, Amsterdam)

14:20 J.P. Bil (GGD Amsterdam, Amsterdam)

Number
Session 3: Pathogenesis

14:00 Plenary: Towards an HIV vaccine that induces broadly neutralizing antibodies

14:30 Antibodies isolated from an HIV-1 elite neutralizer and BG505 SOSIP vaccinated rabbits target the same epitope on the envelope glycoprotein

14:40 A novel ex vivo HIV-1 vaginal transmission model: dysbiotic microbiota increase HIV-1 susceptibility

14:50 Human TRIM5a restricts mucosal HIV-1 transmission

15:00 G3BP1 binds to HIV-1 RNA transcripts and restricts viral replication in macrophages and T cells

15:10 General discussion

15:20 Tea break

Session 4: Treatment

15:50 Plenary: HIV remission after discontinuing ART: is it achievable?

16:20 Small molecule inhibitors of BAF; a new family of compounds in HIV-1 latency reversal

16:30 Diagnostic value of ultrasensitive HIV investigation in vertically exposed infants with negative routine HIV laboratory results

16:40 Major protease inhibitor resistance in the first three years of second-line antiretroviral therapy for HIV-1 in sub-Saharan Africa

16:50 A 12-week treatment with boceprevir, peginterferon and ribavirin for acute hepatitis C in HIV infected patients. Results from the open-label Dutch Acute HCV in HIV (DAHHS1) Study

17:00 Closing and presentation of Joep Lange & Jacqueline van Tongeren Junior Investigator’s Award

17:10 Drinks
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Organisation

The 9th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV) is organised by:

- Stichting HIV Monitoring
- Centrum Infectieziektebestrijding (Clb) - Rijksinstituut voor Volksgezondheid en Milieu (RIVM) (Centre for Infectious Disease Control - National Institute for Public Health and the Environment)
- Aids Fonds
- Academisch Medisch Centrum - University of Amsterdam (AMC-UvA)
- Amsterdam Institute for Global Health and Development (AIGHD), Department of Global Health
- Nederlandse Vereniging van HIV Behandelaren (NVHB) (Dutch Association of HIV-treating Physicians)

Members of the organising committee include:

- Drs Ton Coenen (Aids Fonds)
- Dr Birgit van Benthem (Clb-RIVM)
- Prof. Suzanne Geerlings (AMC, UvA, NVHB)
- Prof. Peter Reiss (Stichting HIV Monitoring, AIGHD, AMC-UvA)
- Dr Catherine Hankins (AIGHD)

Acknowledgements

This conference is made possible through contributions from:

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Welcome

Dear NCHIV 2015 participant,

On behalf of the Organising Committee, it is my pleasure to welcome you to the 9th Netherlands Conference on HIV Pathogenesis, Epidemiology, Prevention and Treatment (NCHIV 2015).

Once again, NCHIV promises to be a stimulating day, with the familiar key elements of a core programme of four sessions on HIV pathogenesis, epidemiology, prevention and treatment, with invited lectures from four leading international researchers in the field of HIV, and an extended lunch programme with poster presentations. For the first time, this year the lunch programme will include a themed poster discussion session, parallel to the poster session.

The programme will open with a plenary talk by Prof. Jean-Michel Molina, principal investigator of the Ipergay trial of on-demand pre-exposure prophylaxis (PrEP). At NCHIV 2015, Prof. Molina will share his thoughts on the role of PrEP in HIV prevention, against the background of the recently-published Ipergay and PROUD study results. In the second session, Prof. Tim Hallett will join us from Imperial College, London, with a plenary talk on how global HIV estimates are made using mathematical modelling. The plenary talk in the pathogenesis session will be given by Dr. Rogier Sanders of the Academic Medical Center in Amsterdam. Dr Sanders has recently made an important step forwards in broadly neutralising antibody stimulation and vaccine development. In his talk at NCHIV 2015, Dr Sanders will bring us up to date on recent developments in the field of HIV vaccine development. Finally, in the treatment session Dr Jintanat Ananworanich of the US Military HIV Research Program will review progress in the field of post-treatment viral remission in HIV (“HIV cure”). Dr. Ananworanich leads a number of world-renowned research efforts in this field, both in children and adults, in Bangkok, Thailand.

In each of the sessions, the NCHIV Organising Committee has invited researchers to present abstracts on subjects relevant to that session. This year we have increased the number of oral abstract presentations and are pleased to announce that there will be a total of 16 oral abstract presentations during the conference. We are also pleased to have been able to accept 52 abstracts for poster presentation, 5 of which have also been selected for presentation during the themed poster discussion session entitled Test and PrEP, chaired Dr Catherine Hankins. Seats for the lunchtime poster discussion session are limited and places will be allocated on a first-come, first-serve basis. Participants are invited to register for this poster discussion session upon arrival at NCHIV 2015 at the registration desk.

We will also be presenting the Joep Lange and Jacqueline van Tongeren Junior Investigator’s Award for the best oral abstract submitted by a young scientist. The recipient will be awarded a prize to the value of € 1000 to spend on a study or conference trip of their choice, and will be announced at the end of the scientific programme.

Finally, I would like to thank you all for your ongoing support and contribution in making NCHIV a successful conference. As the result of the committed involvement of the Dutch HIV research community, NCHIV has become an established platform for research groups in the Netherlands to discuss results, novel ideas and approaches, as well as an important opportunity for cross-disciplinary networking. I would also especially like to thank our financial sponsors without whose generous contributions organising NCHIV would not be possible.

I trust you will enjoy NCHIV 2015!

On behalf of the organising committee,

Peter Reiss
Chair of the Stichting NCHIV Board
Session 1: Pathogenesis

Peter Reiss
SHM, Amsterdam; AIGHD; AMC-UvA, Amsterdam

Peter Reiss is Professor of Internal Medicine at the Academic Medical Center at the University of Amsterdam. Dr Reiss serves on the Scientific Advisory Boards of the Agence Nationale de Recherches sur le Sida et les hépatites (ANRS) and the Swiss HIV Cohort Study, as well as on the Steering Committees of the D:A:D study, the ART-Cohort Collaboration, and the EuroSida Study. He also is one of the rotating scientific coordinators of the EU-funded EuroCoord collaboration. He has also served on Working Group of the Stichting HIV Monitoring (SHM) until he was appointed as Director of the SHM in February 2013. He is Clinical HIV Section Editor for Antiviral Therapy and editorial board member of a number of other journals. Dr Reiss is immediate past President of the European AIDS Clinical Society, and is the regional representative for Europe & Central Asia on the Governing Council and Executive Committee of the International AIDS Society (IAS). His current research focuses particularly on non-infectious co-morbidity and ageing in HIV.
Opening and welcome

Peter Reiss
Stichting HIV Monitoring, Amsterdam; AIGHD, Amsterdam; AMC-UvA, Amsterdam

Peter Reiss is Professor of Medicine at the Academic Medical Center in Amsterdam, the Netherlands, where he holds a joint appointment in the Department of Global Health and the Division of Infectious Diseases.

Peter Reiss has been Director of the Netherlands HIV Monitoring Foundation since February 2013. He also serves on the Scientific Advisory Boards of the French National Agency for AIDS Research (ANRS) and the Swiss HIV Cohort Study, as well as on the Steering Committees of the D:A:D study, the Antiretroviral Therapy Cohort Collaboration and the EuroSida Study. In addition, Peter Reiss is one of the four rotating scientific coordinators of EuroCoord.

Dr Reiss is clinical HIV section editor for Antiviral Therapy and editorial board member of a number of other journals. He is also Immediate Past President of the European Aids Clinical Society (EACS) and, until 2014, served as the European and Central Asia regional representative on the Governing Council of the International Aids Society (IAS). His current research focuses primarily on the complications of HIV and HIV treatment, and more particularly in relation to ageing.
Session 1: Epidemiology and prevention I

Maria Prins
GGD Amsterdam, Amsterdam

Dr. Maria Prins is a Professor of Public Health and the Epidemiology of Infectious Diseases at the Academic Medical Center (AMC) in Amsterdam. She is a senior epidemiologist. She is the head of the Department of Infectious Diseases Research and Prevention at the Public Health Service of Amsterdam. She is internationally acknowledged as a leading researcher on the epidemiology of sexually transmitted and bloodborne viruses in risk groups and vulnerable populations. She has a highly productive research career and has an active role in several collaborative (inter-)national studies. She coordinates the long-standing Amsterdam Cohort Studies on HIV among people who use drugs and MSM, which are now in their 31th year of follow-up, and the Infectious Diseases network of the Academic Collaborative for Public Health, the Sarphati Initiative. She is a highly successful grantee. Her most recent funding includes the continuation of the Amsterdam Cohort Studies and the MOSAIC study on acute HCV in HIV-infected MSM and the start of AmPREP in H-team study that evaluates the uptake of PrEP among HIV negative MSM.

Andy Hoepelman
UMC Utrecht, Utrecht

Professor Andy I.M. Hoepelman is Head of the Department of Internal Medicine and Infectious Diseases at the University Medical Center Utrecht in the Netherlands. Since August 1st 1998, he has been Professor in Medicine. Prof. Hoepelman received his medical training from the University of Utrecht, receiving his Doctorate in 1978 and his MD degree in 1980. He completed two internships at the University in 1980 and 1985 to earn his board certification as a specialist in Internal Medicine. He received his PhD in 1989. In 1991/1992 he worked at the Rockefeller University, New York (Laboratory Prof. E. Tuomanen) and at the Memorial-Sloan Kettering (Department of Infectious Diseases, Prof. D. Armstrong). In 1993, he was board certified as a specialist in Infectious Diseases. Prof. Hoepelman heads the training programme in Infectious Disease for internal medicine specialists at the University Hospital Utrecht. He is also author/co-author of more than 350 published articles and is a member of several professional associations, including the former European Society for Medical Microbiology and Infectious Diseases. His research interests are pathogenesis and treatment of HIV and viral hepatitis.
Pre-exposure prophylaxis for MSM: What have we learned and what are the next steps?

Jean-Michel Molina
*University of Paris Diderot, Paris, France*

Jean-Michel Molina is Professor of Infectious Diseases at the University of Paris Diderot - Paris 7, France, and Head of the Infectious Diseases Department at the Saint-Louis Hospital in Paris. Professor Molina continues to be involved in basic HIV research and is affiliated to the INSERM U941 directed by Professor F. Clavel in the Saint-Louis Hospital. As Head of the Infectious Disease Department in the Saint-Louis Hospital, Professor Molina mainly treats immunocompromised HIV-infected patients, bone marrow and renal transplant patients, and patients with haematologic malignancies and cancers. Professor Molina’s primary clinical research interest lies in the area of the treatment of HIV infection, and he has been involved in a number of studies assessing new drugs or new strategies for the treatment of HIV infection. A cohort of more than 3,000 patients with HIV infection is followed in his department and is involved in this clinical research. Professor Molina has published numerous papers in a wide variety of scientific journals, including *Clinical Infectious Diseases*, *The Journal of Infectious Diseases*, *The New England Journal of Medicine*, *The Lancet*, *The Journal of Clinical Microbiology*, and *AIDS*. He is Chair of the Clinical Trial Group at the French National Agency for AIDS Research (ANRS), where multicentre clinical trials are reviewed and implemented in France. Working with the ANRS, Professor Molina has been the principal investigator of a number of clinical trials in HIV-infected patients. More recently, Professor Molina has broadened his field of interest to the prevention of HIV infection in men who have sex with men and is leading a PrEP trial in Europe and Canada sponsored by ANRS, the Canadian Trial Network and the Gates Foundation.

No decline in hepatitis C virus (HCV) incidence among HIV-positive men who have sex with men (MSM) within CASCADE: 1990-2014

R. Geskus
*GGD Amsterdam, Amsterdam*

Activation of immature Langerhans cells facilitate hepatitis C virus transmission

R. Sarrami Forooshani
*AMC-UvA, Amsterdam*

Modelling the HCV epidemic among HIV positive MSM in the HCV direct-acting antivirals era. Is HCV elimination possible and at what price?

S.J. Hullegie
*Erasmus MC, Rotterdam*

The impact of the number of comorbidities and aging on Health-Related Quality of Life (HRQL) in HIV-infected and uninfected individuals

N. Langebeek
*AMC-UvA, Amsterdam*
Jean-Michel Molina

*University of Paris Diderot, Paris, France*

Jean-Michel Molina is Professor of Infectious Diseases at the University of Paris Diderot - Paris 7, France, and Head of the Infectious Diseases Department at the Saint-Louis Hospital in Paris. Professor Molina continues to be involved in basic HIV research and is affiliated to the INSERM U941 directed by Professor F. Clavel in the Saint-Louis Hospital. As Head of the Infectious Disease Department in the Saint-Louis Hospital, Professor Molina mainly treats immunocompromised HIV-infected patients, bone marrow and renal transplant patients, and patients with haematologic malignancies and cancers. Professor Molina’s primary clinical research interest lies in the area of the treatment of HIV infection, and he has been involved in a number of studies assessing new drugs or new strategies for the treatment of HIV infection. A cohort of more than 3,000 patients with HIV infection is followed in his department and is involved in this clinical research. Professor Molina has published numerous papers in a wide variety of scientific journals, including *Clinical Infectious Diseases*, *The Journal of Infectious Diseases*, *The New England Journal of Medicine*, *The Lancet*, *The Journal of Clinical Microbiology*, and *AIDS*. He is Chair of the Clinical Trial Group at the French National Agency for AIDS Research (ANRS), where multicentre clinical trials are reviewed and implemented in France. Working with the ANRS, Professor Molina has been the principal investigator of a number of clinical trials in HIV-infected patients. More recently, Professor Molina has broadened his field of interest to the prevention of HIV infection in men who have sex with men and is leading a PrEP trial in Europe and Canada sponsored by ANRS, the Canadian Trial Network and the Gates Foundation.

Birgit van Benthem

*Cib-RIVM, Amsterdam*

Dr Birgit van Benthem is an infectious disease epidemiologist and head of the STI department at the Centre for Infectious Disease Control (Cib), National Institute for Public Health and Environment (RIVM), Netherlands. She is responsible for the surveillance and research on sexually transmitted diseases and national focal point for STI and HIV for European Centre for Disease Control and prevention (ECDC) and member of the ECDC STI-HIV Network Coordination Committee. She previously worked as a senior epidemiologist at the Royal Tropical Institute, Amsterdam in international multidisciplinary studies on malaria, dengue and HIV in Thailand, Vietnam and Rwanda. She started her carrier at the Municipal Health Service Amsterdam, as researcher in epidemiology and coordinator of a European multicentre study on HIV infection in women and completed her PhD thesis on this topic.
The HIV epidemic in the Netherlands: an update

Peter Reiss
Stichting HIV Monitoring, Amsterdam; AIGHD, Amsterdam; AMC-UvA, Amsterdam

Peter Reiss is Professor of Medicine at the Academic Medical Center in Amsterdam, the Netherlands, where he holds a joint appointment in the Department of Global Health and the Division of Infectious Diseases. Peter Reiss has been Director of the Netherlands HIV Monitoring Foundation since February 2013. He also serves on the Scientific Advisory Boards of the French National Agency for AIDS Research (ANRS) and the Swiss HIV Cohort Study, as well as on the Steering Committees of the D:A:D study, the Antiretroviral Therapy Cohort Collaboration and the EuroSida Study. In addition, Peter Reiss is one of the four rotating scientific coordinators of EuroCoord. Dr Reiss is clinical HIV section editor for Antiviral Therapy and editorial board member of a number of other journals. He is also Immediate Past President of the European Aids Clinical Society (EACS) and, until 2014, served as the European and Central Asia regional representative on the Governing Council of the International Aids Society (IAS). His current research focuses primarily on the complications of HIV and HIV treatment, and more particularly in relation to ageing.

Inside the sausage factory: how global HIV estimates and some decisions are made

Tim Hallett
Imperial College, London, UK

Prof. Timothy Hallett is based at the Department of Infectious Disease Epidemiology of Imperial College, London. His work with the Applied HIV Epidemiology research group centres on the development and application of mathematical models for interpreting surveillance data, analysing control trials and planning interventions. The overall aim of this research is to come to conclusions about the optimal use of limited resources in the response to HIV epidemic worldwide.

A new method to estimate the first step in the HIV care continuum

A.I. van Sighem
Stichting HIV Monitoring, Amsterdam

Opportunities for HIV prevention among men having sex with men in the Netherlands

O. Ratmann
Imperial College, London, UK

On demand PrEP among MSM in the Netherlands: a cost-effective approach for preventing HIV-1 infections

B.E. Nichols
Erasmus MC, Rotterdam

Home testing for HIV combined with internet counselling in the Netherlands: interim results of the HIVTest@Home trial

F.R. Zuure
GGD Amsterdam, Amsterdam
Oral sessions

Session 3: Pathogenesis

Charles Boucher
Erasmus MC, Rotterdam, the Netherlands

Charles A. B. Boucher received his MD cum laude at the Academic Medical Center in 1987. In 1993 he finished his PhD in Virology at the University of Amsterdam. He has published over 250 peer reviewed papers that have appeared in Science, New England Journal of Medicine, the Lancet, Nature Medicine, Journal of Infectious Diseases and AIDS. He has coordinated several succesful European-funded programmes. He is the coordinator of a large network (33 countries) in Europe that studies the transmission of drug resistant HIV and chairs the European Society for Antiviral Research (ESAR). His current position is professor in Virology at the Erasmus Medical Center in Rotterdam, clinical microbiologist at the Erasmus Medical Center, coordinator of the Honours Class with the medical curriculum and scientific director at Virology Education, Utrecht, Netherlands. Prof. Boucher is an organiser of international workshops, meetings and conferences, a consultant throughout Europe and the United States, a reviewer for scientific journals and co-chairman of several international committees. He is the author of numerous publications.

Monique Nijhuis
UMC Utrecht, Utrecht, the Netherlands

Monique Nijhuis studied biology and obtained her PhD in 1999 at the University of Utrecht, on the investigation of the impact of antiretroviral therapy on HIV fitness. Following postdoctoral research, she initiated a research line at the interface between fundamental and clinical research and became an associate Professor of Virology at the University Medical Center Utrecht. Her research interest is centered on (I) Viral entry, transmission and pathogenesis (II) Mechanisms of antiviral resistance and viral evolution and (III) Viral-reservoirs and eradication. She was granted the VIDI and ASPASIA awards by the Netherlands Organization for Scientific Research (NWO). She is part of the scientific advisory board of the Aids Fonds and a member of the IAS HIV Cure International Scientific Working Group. She is associate editor of Retrovirology and member of the scientific committee of the Frontiers in Retrovirology meeting and the Frontiers in Drug Development for Antiretroviral Therapies (DART).
Towards an HIV vaccine that induces broadly neutralizing antibodies

Rogier Sanders
AMC-UvA, Amsterdam; Weill Medical College of Cornell University, New York, USA

Rogier studied medical biology at the University of Amsterdam and the Rockefeller University in New York. In 2004 he obtained his Ph.D. (cum laude) from the University from Amsterdam. Rogier currently holds Associate Professor positions at the AMC and at Cornell University in New York, where he spends part of his time. His research focuses on HIV-1 envelope glycoprotein vaccines. He has received several prestigious grants such as the Veni and Vidi grants from the Netherlands Organization for Scientific Research (NWO) and a Starting Investigator grant from the European Research Council (ERC). Rogier has (co-)authored more than 100 articles in scientific journals, including journals such as Nature and Science. In 2011 he received the Dutch Prize for Biochemistry and Molecular Biology.

Antibodies isolated from an HIV-1 elite neutralizer and BG505 SOSIP vaccinated rabbits target the same epitope on the envelope glycoprotein

M.J. van Gils
AMC-UvA, Amsterdam

A novel ex vivo HIV-1 vaginal transmission model: dysbiotic microbiota increase HIV-1 susceptibility

N.H. van Teijlingen
AMC-UvA, Amsterdam

Human TRIM5a restricts mucosal HIV-1 transmission

C.M.S. Ribeiro
AMC-UvA, Amsterdam

G3BP1 binds to HIV-1 RNA transcripts and restricts viral replication in macrophages and T cells

K.A. van Dort
AMC-UvA, Amsterdam
Session 4: **Treatment**

**Anne Wensing**  
*UMC Utrecht, Utrecht*  

Annemarie Wensing, MD, PhD became involved in HIV during her rotations. She worked at the HIV-outpatient clinic in Utrecht from 1998 to 2002 and was subsequently trained as clinical virologist. She advises infectious diseases specialists from multiple HIV-centres. She teaches at the Utrecht Medical and Pharmacy School. She has published over a hundred scientific papers. Her research focuses on HIV drug-resistance, entry, eradication and reservoirs. She is co-PI of EPISTEM investigating potential HIV cure via SCT. She is a founding member of ESAR and the SPREAD program, regional representative for EACS, member of the WHO HIV Drug Resistance Expert Panel and chair of the IAS-USA mutations panel.

**Jan Prins**  
*AMC-UvA, Amsterdam*  

Jan Prins is professor of Infectious Diseases at the University of Amsterdam. He works as Infectious Diseases specialist in the Academic Medical Center (AMC) in Amsterdam, the Netherlands. He is head of the HIV Outpatient Clinic, and head of the Infectious Diseases Fellowship training programme at the AMC.
HIV remission after discontinuing ART: is it achievable?  

Jintanat Anaworanich  
US Military HIV Research Program, Bethesda, USA

Dr Jintanat Ananworanich is Associate Director for HIV Therapeutics Research at the US Military HIV Research Program in Maryland. She is an HIV clinical researcher with interest in acute HIV infection, HIV cure and neuro AIDS. She is principal investigator of acute HIV infection studies in adults (RV254) and children (HIV-NAT 209), and several cure-related trials in Thailand. She is a member of the IAS Towards HIV Cure Initiative steering committee, and the ACTG and IMPAACT cure committees.

Dr. Ananworanich previously served as Director of SEARCH and Deputy Director in Scientific Affairs of the HIV-NAT research units at the Thai Red Cross in Bangkok. She received her medical degree in Thailand and did her PhD in Medicine at the University of Amsterdam with Professor Joep Lange. She is US Board certified in Pediatrics, Allergy and Immunology and Clinical and Laboratory Immunology.

Small molecule inhibitors of BAF; a new family of compounds in HIV-1 latency reversal

M. Stoszko  
Erasmus MC, Rotterdam

Diagnostic value of ultrasensitive HIV investigation in vertically exposed infants with negative routine HIV laboratory results

A. Stam  
UMC Utrecht, Utrecht

Major protease inhibitor resistance in the first three years of second-line antiretroviral therapy for HIV-1 in sub-Saharan Africa

T.S. Boender  
AIGHD, Amsterdam

A 12-week treatment with boveprevir, peginterferon and ribavirin for acute hepatitis C in HIV infected patients. Results from the open-label Dutch Acute HCV in HIV (DAHHS1) Study

S.J. Hullegie  
Erasmus MC, Rotterdam
Themed poster discussion: Test & PrEP

Catherine Hankins
AIGHD, Amsterdam, the Netherlands

Catherine Hankins (AIGHD, Netherlands) is Deputy Director, Science, at the Amsterdam Institute for Global Health & Development (AIGHD), Department of Global Health, University of Amsterdam. She is an Honorary Professor at the London School of Hygiene & Tropical Medicine in the Faculty of Epidemiology & Population Health. She chairs the Scientific Advisory Group of the USA National Institutes of Health HIV Prevention Trials Network and chairs the Scientific Advisory Board for CAPRISA (Centre for AIDS Programme of Research in South Africa) at the University of KwaZulu-Natal. At AIGHD, she leads the HIV prevention research group and the knowledge translation/communication strategy, and represents AIGHD in the Health Insurance Fund Learning and Analysis Unit. She is the Scientific Chair for the International Workshop on HIV Treatment, Pathogenesis, and Prevention Research in Resource-Limited Settings (‘INTEREST Workshop’) held annually in Africa since 2007. A community medicine specialist, she was Chief Scientific Adviser to UNAIDS in Geneva for almost a decade, editing its science blog HIV This Week and heading up the UNAIDS knowledge translation team for proven biomedical HIV prevention strategies. She received her PhD Medicine from the University of Amsterdam in 2014 and was named to the Order of Canada in 2013.
Determinants of never having tested for HIV among MSM in the Netherlands

C. den Daas
RIVM, Utrecht

General practitioners’ barriers to and facilitators of HIV testing strategies: a qualitative study

I.K.C.W. Joore
AMC-UvA, Amsterdam

Factors associated with recent HIV infection among newly diagnosed STI clinic attendees in the Netherlands in 2014

S. Parkkali
RIVM, Utrecht

Early experiences from the Amsterdam PrEP project

E. Hoornenborg
GGD Amsterdam, Amsterdam

Low knowledge and moderate acceptability towards the prescription of pre-exposure prophylaxis among Dutch healthcare providers of sexual health clinics: a mixed-methods study

J.P. Bil
GGD Amsterdam, Amsterdam
Abstracts
Oral Presentations

EPIDEMIOLOGY & PREVENTION I

Pre-exposure prophylaxis for MSM: What have we learned and what are the next steps?
J.M. Molina
University of Paris Diderot and Saint-Louis Hospital, Paris, France

The prevention of infection with the human immunodeficiency virus (HIV) remains a major public health challenge with more than 2 million new infections having occurred worldwide in 2014 according to UNAIDS, underlining the limitations of current prevention strategies to contain the spread of HIV. Due to the lack of an effective HIV-vaccine, consistent condom use remains the cornerstone of prevention, but biomedical interventions such as male circumcision and the use of antiretroviral drugs for the treatment of HIV-infected individuals represent additional strategies to reduce HIV transmission. Pre-exposure prophylaxis (PrEP), represents a new and promising intervention, where antiretroviral drugs are started in non HIV-infected persons before potential exposure to HIV. The efficacy of PrEP was first demonstrated for tenofovir (TFV) vaginal gel in high risk women, but was not confirmed in subsequent larger trials. Daily oral PrEP with either tenofovir disoproxil fumarate (TDF) or the combination of TDF-emtricitabine (FTC) has also been shown to provide protection against HIV infection among men who have sex with men (MSM), heterosexual men and women, intravenous drug users and HIV-negative partners in serodiscordant couples. However two recent trials in heterosexual women failed to show a benefit of daily oral PrEP with TDF or TDF-FTC, most likely because of low adherence to the PrEP regimen. In high income countries such as Europe and North America, the HIV epidemic is concentrated in high risk groups among which MSM and transgender men and women are disproportionately affected. Up to now, there has been a single PrEP efficacy trial in MSM, the Ipex trial, which showed a moderate reduction of 42% of HIV incidence with daily oral PrEP with TDF-FTC due to low adherence.

Recent data from two European trials in MSM (PROUD and IPERGAY) suggest that oral PrEP with TDF/FTC might be more effective than previously anticipated and that non-daily coitally-dependent PrEP might also be very effective. Implications of these results will be discussed as well as implementation challenges for PrEP. Engagement with communities and additional behavioral research are needed to develop methods of counseling that better support PrEP use and adherence to PrEP. While we wait for an effective vaccine, combining effective prevention tools and upscaling testing and early treatment of those infected could contain the spread of the HIV epidemic in high risk populations.

No decline in hepatitis C virus (HCV) incidence among HIV-positive men who have sex with men (MSM) within CASCADE: 1990-2014
R. Geskus, on behalf of D.K. van Santen and the CASCADE Collaboration
GGD Amsterdam, Amsterdam, the Netherlands

Background
Hepatitis C Virus (HCV) incidence increased after 2000 among HIV-positive MSM, as we previously showed using data from CASCADE cohorts up to 2007. Recently, several countries have reported different trends regarding HCV incidence among HIV-positive MSM. Therefore our aims were twofold: 1) to estimate temporal trends in HCV incidence among HIV-positive MSM, overall and by geographical region 2) to assess the association of age, HIV RNA and CD4 cell count with HCV incidence.

Methods
We used data from MSM with a date of HIV seroconversion from 16 cohorts within the CASCADE Collaboration (Concerted Action on SeroConversion to AIDS and Death in Europe). MSM were considered at risk from the latest of: start routine HCV testing, enrolment in the cohort or HIV seroconversion. Two methods were used to calculate follow-up accounting for when MSM were tested for HCV with respect to the moment they became at risk. For those without HCV seroconversion, follow-up ended at the last HCV-negative test. We allowed for smoothly varying trends over calendar time using restricted cubic splines. In the multivariable model we included calendar year, age, CD4 count (lagged), log HIV RNA (lagged) and geographical region.

Results
In total, 5,953/4,326 MSM were included, with 337/279 HCV seroconversions observed (method 1/2). HCV incidence significantly increased over time, irrespective of the method used, ranging from 0.7/1000 person-years (py) in 1990 to 18/1000 py in 2014 (method 1). Preliminary results showed that in the multivariable model a higher HCV incidence was observed in recent years (p=0.02) and, although not significant, among younger MSM (p=0.07). A higher log HIV RNA was associated with an increase in HCV incidence (p=0.03). HCV incidence did not differ by CD4 cell count. Furthermore, although not significant, trends differ by geographical region; in recent years, HCV incidence has not declined in Southern and Northern Europe whereas in Western Europe HCV incidence seems to be declining.
Conclusions
A rise in HCV incidence has been observed among HIV-positive MSM over time. However, trends differ by geographic region.

Activation of immature Langerhans cells facilitate Hepatitis C virus transmission

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Hepatitis C virus (HCV) by a prevalence of about 3% and infecting 300 million people is a major health burden in the world. Little is known about sexual transmission of HCV. HCV mucosal transmission has been observed in HIV-1 infected men. Langerhans cells (LCs) reside in the mucosa and are the first immune components that encounter the viruses. Here we have investigated the role of LCs in sexual transmission of HCV. Virus like particles (VLPs) consisting of HCV envelop glycoproteins and viruses pseudotyped with HCV envelopes were used as models to study HCV/LCs interaction. The result showed that HCV strongly bind to C-type lectin langerin, which is specifically expressed by LCs. Importantly, primary human LCs strongly interact with HCV through Langerin. Confocal microscopic analyses show that HCV colocalises with Langerin and is rapidly internalized into LCs. Thus, Langerin is crucial in the capture of HCV by LCs. Despite efficient capturing and internalization, immature LCs did not transmit HCV particles to the target cells. Our results signify that antiviral activity of LCs is not confined to HIV-1 and imply an important function of LCs on other viral infections. There are reports indicating that HCV sexual transmission is increased in HIV infected men. Since co-infections may cause mucosal inflammation, next we investigated whether immune activation might facilitate HCV transmission by LCs. Immature LCs were induce with different stimuli. Notably activated LCs were able to transmit HCV particles to target cells.

These data strongly suggest that immune activation is an important determinant in sexual transmission of HCV. Immature LCs do not transmit HCV but immune activation changes LC function and activated LCs efficiently capture and transmit HCV to target cells. Our results are crucial to understand how coinfection with other pathogens -that activate LCs, can facilitate transmission of HCV.
Modelling the HCV epidemic among HIV positive MSM in the HCV direct-acting antivirals era. Is HCV elimination possible and at what price?

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Background
Infections with hepatitis C virus (HCV) are common among HIV positive men who have sex with men (MSM). Acute and chronic HCV have traditionally been treated with peg-interferon containing regimens that have major side-effects and low cure rates. During the last year, direct-acting antivirals (DAAs) for chronic HCV treatment have become available. DAAs have limited side-effects and high cure rates. Widespread use of DAAs could therefore not only cure patients but also prevent onward transmission which in turn will reduce the HCV epidemic. Unfortunately, DAAs are expensive and treatment is therefore deferred until later stages of chronic infection. The aim of this study was to assess the epidemiological impact and cost-effectiveness of providing DAAs to all co-infected MSM compared to deferring DAAs until fibrosis stage F2 or F3.

Methods
A deterministic mathematical model was calibrated to the Dutch HIV epidemic among MSM. We first determined the impact of providing DAAs (89%-100% cure) to all patients that were diagnosed. In the counterfactual scenarios, patients were treated with peg-interferon and ribavirin in the acute stage. In patients that failed or refused, treatment with DAAs was initiated in stage F2 or F3. The impact on the HCV prevalence and incidence was calculated to predict the epidemiological impact of DAAs until 2030. Cost-effectiveness ratios were calculated to predict the cost-effectiveness of providing DAAs to all co-infected MSM compared to deferring DAAs until fibrosis stage F2 or F3.

Results
Treating all diagnosed patients with DAAs strongly reduced the epidemic as compared to deferring treatment. The incidence rate declined from 12/1000 to 5/1000 compared to a stable incidence of 12/1000 when treatment was initiated at F2 or F3. The prevalence declined from 5% to 1.4% compared to an increase to 6.5% (F2) or 7.6% (F3). The incremental cost-effectiveness ratio ranged between €40,000 (F3) and €37,000 (F2) per QALY (DAA price €30,000) to €87,000 (F3) and €81,000 (F2) (DAA price €60,000). Providing DAAs to all patients was predicted to be cost-effective for prices of <€50,000 when compared to starting at F2 and F3.

Conclusions
Implementing aggressive treatment of HCV will result in a substantial decrease of the HCV epidemic in the Netherlands, and can be considered cost-effective. However, treating all patients with DAAs will not result in elimination of HCV. The primary determinant for cost-effectivity is the pricing of current DAAs.

The impact of the number of comorbidities and aging on Health-Related Quality of Life (HRQL) in HIV-infected and uninfected individuals

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Background
HIV-infected persons may be at risk for the premature onset of age-associated non-communicable comorbidities (AANCCs) compared to the general population. Such comorbidities are usually accompanied by declines in patients' physical and mental capacities and might thus have a negative impact on patients' HRQL. Previous research has shown that HIV infection itself and aging may also have a negative impact on HRQL. Our objective was to investigate the impact of the number of AANCCs, aging and HIV infection on HRQL.

Methods
The study is conducted among HIV-infected individuals and highly comparable but uninfected controls, aged 45 years or older, participating in the AGhEIV Cohort Study. Participants were screened at enrollment for the presence of AANCCs (including cardiovascular, metabolic, pulmonary, renal, bone and malignant disease). Participants completed the Medical Outcomes Study Short Form 36-item health survey (SF36) to assess their HRQL. We compared HRQL between HIV-infected and uninfected persons using general linear models. Effect sizes for between-group differences were calculated by dividing mean differences by pooled standard deviations. We investigated factors associated with physical- and mental HRQL using linear regression analysis. All models were adjusted for relevant background characteristics (gender, ethnicity, socio-economic status, marital status, educational level, sexual orientation and life style factors, i.e., smoking, alcohol consumption, and drug use).
Results
HIV-infected individuals (n=541) had significantly worse HRQL than HIV-uninfected individuals (n=526) on five out of the eight SF36 scales, i.e., physical- and social functioning, role-physical, vitality and health perceptions, and on the physical and mental health summary score. However, these differences were of a small to moderate magnitude (effect sizes 0.16 to 0.45). There was no evidence that the difference in HRQL between HIV-infected and HIV-uninfected individuals became greater with higher number of AANCs (Figure A and B), or with a higher age (Figure C and D). A higher number of AANCCs and HIV-positive status were each independently associated with a worse physical HRQL (Figure A). HIV-positive status and younger age were independently associated with a worse mental HRQL (Figure D).

Conclusions
HIV-infected individuals have a worse physical and mental HRQL than HIV-uninfected individuals. However, these differences are of a small to moderate magnitude. The difference in HRQL between HIV-infected and uninfected individuals does not become greater with higher number of co-morbidities or with a higher age. Even HIV-infected individuals without AANCCs have statistically significantly worse physical HRQL than HIV-uninfected individuals without AANCCs.
The HIV epidemic in the Netherlands: an update

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Of the cumulative total of 23,303 people living with HIV ever having been registered by Stichting HIV Monitoring, 18,149 adults and 206 children and adolescents remain in active follow-up in one of the 27 HIV treatment centres in the Netherlands as of May 2015. Since 2008 there has been a decreasing trend in the annual number of new HIV diagnoses to approximately 1,000 new diagnoses in recent years, with roughly two-thirds occurring among men who have sex with men (MSM) and one-third as a result of heterosexual transmission. The average age at which newly-diagnosed individuals with HIV enter care in the Netherlands continues to increase gradually (41 years in 2014), as does the age of the population already in care (42% of those in care in 2014 were > 50 years).

Both the proportion of recent infections and CD4 counts at diagnosis have increased among those diagnosed with HIV, indicating that testing for HIV has apparently become more common. As a result, patients are also starting cART increasingly earlier in their infection (at a median of 400 cells/mm³ in 2014 vs. 370 cells/mm³ in 2013). One-third of patients starting cART in 2014 did so at a CD4 count >500 cells/mm³. Nonetheless, late presentation for care remains far too common, and more so among heterosexual men and women than among MSM.

In general the rates of achieving viral suppression are high with most of the currently recommended cART regimens, with superior immunological recovery as treatment is initiated at higher CD4 counts. Regimens have also become increasingly well-tolerated and less toxic, resulting in an increased likelihood of patients to remain on their initial regimen for longer.

Causes of mortality and morbidity have shifted from traditional HIV and AIDS-associated conditions towards conditions such as non-AIDS cancers and cardiovascular and cerebrovascular disease (CVD). Our analyses do show that significant gains may still be achieved in optimising use of secondary and primary CVD risk management.

In terms of treatment for hepatitis C infection, PEG-IFN-containing regimens are rapidly being replaced in clinical practice by a variety of all-oral direct-acting antiviral agent (DAA)-based regimens and more patients with HCV co-infection are being treated. Preliminary data from more than 100 HIV-infected patients treated or undergoing treatment for HCV with one or more of the currently-available novel DAA regimens has shown that 95% of all patients who completed treatment and had sufficient follow-up data achieved a sustained virological response. Over the long term, these treatments are expected to contribute to reducing the burden of severe chronic liver disease, hepatocellular carcinoma, and liver-related mortality among persons living with HIV. In addition, they may be expected to have a beneficial impact on the risk of ongoing HCV transmission which remains substantial as indicated by the stable relatively high incidence of acute HCV infection among MSM. Generally speaking, quality of HIV care across a number of indicators is high with limited variability across the 27 HIV treatment centres. The time between entry into care and starting cART appears to be decreasing across most centres, and high levels of both retention in care and rates of viral suppression on treatment are seen.

Inside the sausage factory: how global HIV estimates and some decisions are made

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We will begin by reviewing the overall state of the global HIV epidemic according to estimates released by UNAIDS and other sources. The methods behind these estimates will then be described, on a region-by-region basis. These estimates make clear three important directions for focus in the next phase of the AIDS response. First, a need to focus on prevention — allocating available resources optimally, according to the great heterogeneity of epidemic conditions within and between countries, and in light of an increasing array of interventions. Second, a need to strengthen the continuum of care, so as to maximise the population level impact of treatment and minimise AIDS deaths. And, third, to prepare for the changing profile of the AIDS epidemic, as people living with HIV age and HIV increasingly becomes one of a number of interacting multi-morbidities.
A new method to estimate the first step in the HIV care continuum

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Background
The total number of individuals living with HIV, including those not yet diagnosed, is crucial information for national public health monitoring and planning, but reliably estimating this number remains a challenge. We present a new method to estimate the first step in the HIV care continuum and subsequently construct the care continuum for the Netherlands in 2014.

Methods
We used a back-calculation method, which was previously validated on simulated data, to estimate the annual number of HIV infections, using national surveillance data on new HIV and AIDS diagnoses from the ATHENA national observational HIV cohort in the Netherlands. At the same time, using CD4 counts at the time of diagnosis, the method could estimate the average time between infection and diagnosis by calendar year of infection. For each calendar year, we could therefore calculate the number of HIV-positive individuals who were still undiagnosed by the end of 2014 and thus estimate the total number of individuals living with undiagnosed HIV. Bootstrap techniques were used to calculate 95% confidence intervals (CI). The number of individuals living with HIV by the end of 2014 was estimated by adding the total number of undiagnosed HIV-positive individuals to the observed number of diagnosed HIV-positive individuals who were registered for care and had not died or emigrated. Subsequent steps in the care continuum were estimated from ATHENA data. Retention in care was defined as ≥1 clinic visit in 2014; viral suppression was defined as HIV RNA <100 copies/ml at the last RNA measurement in 2014, irrespective of treatment.

Results
By the end of 2014, 22,100 (95% CI 21,700-22,800) HIV-positive individuals were estimated to be living in the Netherlands, including 2,700 (2,300-3,400) who were still undiagnosed. Of all 22,100 individuals living with HIV, 88% had been diagnosed and linked to care, 81% were retained in care, 76% were currently on antiretroviral treatment, and 70% were virologically suppressed (Figure).

Conclusion
The estimated proportion of HIV-positive individuals in the Netherlands with viral suppression is close to the UNAIDS 90-90-90 goal of 73%. Since our method to estimate the first step in the HIV care continuum only uses routine surveillance data, estimates can easily be updated annually, in contrast to methods relying mainly on HIV prevalence surveys.
Opportunities for HIV prevention among men having sex with men in the Netherlands

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Background
Several biomedical HIV prevention strategies exist that could be used to reduce the number of HIV infections amongst men having sex with men (MSM) in the Netherlands. Previously, we quantified the sources of infection across the entire infection and care continuum in a cohort of 617 MSM in recent infection at time of diagnosis. With the sources of individual transmission events estimated, we now evaluate and compare the proportion of these infections that could have been averted through prevention strategies in hypothetical modelling scenarios.

Methods
Probable transmitters were previously identified through phylogenetic analysis. Using data from the ATHENA cohort, we described the progression of transmitters through fourteen stages in the infection and care cascade, from before diagnosis to treated infection and loss to follow up. We formulated individual-level intervention models that re-allocate specific transmitters to less infectious stages. This results in an overall lower probability that the corresponding recipient would have been infected, and we average across recipients to calculate the proportion of infections that could have been averted.

Results
Figure 1 quantifies the proportion of transmissions that could have been averted between mid 2009 to December 2010 for thirteen intervention strategies. The majority of new cases could not have been averted through increased annual testing (either with conventional or RNA assays), immediate ART or combinations thereof (test-and-treat) in this period. The impact of PrEP alone is even lower, which agrees with previous modelling analyses (van Sighem, NCHIV2013). We also considered more testing with provision of PrEP to those who test negative (test-and-PrEP). Varying adherence and coverage levels, test-and-PrEP could have averted a similar or higher proportion of transmissions as test-and-treat. Combining both strategies was clearly most effective, and would have lead to a 1.6-2.1 fold improvement over the corresponding test-and-treat strategy.

Conclusion
New HIV infections among MSM in the Netherlands are challenging to prevent at current levels of risk taking behaviour. All evaluated scenarios correspond to considerable improvements to current practice. Substantial reductions in HIV incidence are most likely to achieve with a combination approach that includes more testing with provision of PrEP to those who test negative, plus immediate treatment to those who test positive. This study evaluated prevention opportunities on past transmission events amongst Dutch MSM that could be characterized through phylogenetic methods. Cost-effectiveness was not considered. Forward projections are planned and would account for further indirect prevention benefits that accrue over longer time.

On demand PrEP among MSM in the Netherlands: a cost-effective approach for preventing HIV-1 infections

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Background
Pre-exposure prophylaxis (PrEP) with tenofovir and emtricitabine has been demonstrated to effectively prevent new HIV infections among men who have sex with men (MSM). It has recently been shown that on demand PrEP, in which individuals take PrEP just before and after sexual contact, use can be as effective as daily PrEP in preventing HIV infections. The high cost of PrEP is still a primary limitation in its use for HIV prevention. The aim of this study was to compare the epidemiological impact and cost-effectiveness of both daily and on demand PrEP.

Methods
A deterministic mathematical model was calibrated to the Dutch HIV epidemic among MSM. We aimed to predict the impact of PrEP targeted to 10% of the most sexually active individuals (median 4,500 MSM/year) over the coming 12 years, including two years of scale-up. Cost-effectiveness ratios were calculated to predict the cost-effectiveness of daily (€7,099/year) and on demand (€3,550/year) PrEP, and prevented infections were calculated to predict the epidemic impact. As the future price of PrEP is unknown, we conducted a sensitivity analysis in which the price of PrEP was decreased by 50%. Cost-effectiveness ratios below €20,000 were considered to be cost-effective per Dutch guidelines.

Results
Targeting PrEP to 10% of the most sexually active individuals was predicted to prevent 14.0% (interquartile range [IQR] 11.9%-16.3%) of new infections over the coming 12 years compared to no PrEP usage. Daily PrEP was predicted to cost €36,300 per quality adjusted life year (QALY) gained (IQR €34,000-€45,100). On demand dosing of PrEP has the potential to cut the cost per QALY gained by more than half to €17,700 (IQR €16,500-€22,200) per QALY gained over 12 years compared to no PrEP usage. This cost per QALY can be further reduced to €8,400 (IQR €7,700-€10,700) if the cost of on demand PrEP is reduced by 50%. If increasing numbers of patients are diagnosed and placed on treatment early, PrEP will have a reduced impact on the epidemic. This can result in the cost per QALY gained of on demand PrEP to increase to as much as €32,400 with full-price PrEP, and €16,200 with reduced-price PrEP.

Conclusion
The use of PrEP is only cost-effective when used on demand, and can become far more cost-effective if the price of PrEP decreases. The precise cost-effectiveness estimate is, however, dependent upon the impact of earlier treatment initiation on the HIV epidemic.

Home testing for HIV combined with internet counseling in the Netherlands: interim results of the HIVTest@Home trial

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Background
HIV self-tests (HIVST) may help to increase HIV test uptake by eliminating barriers of testing. The Amsterdam Public Health Service has initiated the HIVTest@Home trial to develop and evaluate a service that provides reliable HIVST in combination with internet counseling for individuals at high risk for HIV, especially men who have sex with men (MSM) and migrants from HIV endemic countries.

Methods
Using MSM and migrant-specific media, a campaign aimed to motivate MSM and migrants to visit our project website (www.time2test.nl) to access our HIV self-testing service. The website included information about HIV self-testing, an optional questionnaire measuring demographics, and the option to buy HIVST packages for 29.50 euro each, either online or via pick-up locations. The test packages included an oral fluid-based test, a manual, and a code to access online instructions and counseling. Website log data and an evaluation questionnaire sent five weeks after website visit measured website use, self-reported HIVST results, user satisfaction, reasons for self-testing, previous HIV-testing behavior and linkage to care.

Results
From August 2014 to July 2015 the website attracted ~30,000 visitors, of whom 2,138 accepted the terms and conditions and answered demographical questions. Of those, 73% were MSM, 88% were born in Europe, and median age was 35 years (IQR=27-45 yrs). A total of 599 tests were sold to 472 persons. Half (52%; 244/472) of participants accessed the online instructions and counseling and 23.9% (113/472) self-reported their HIVST result, of which 0.9% (1/113) tested positive. So far, 11% (52/472) of participants completed the evaluation questionnaire. The majority (92%; 48/52) were satisfied or very satisfied with the service.
Oral presentations

Abstracts

Immediate test results, time savings, anonymity, and no need for a blood draw were the most prominent reasons for using the service. In total, 29% (15/52) were never tested for HIV before, whereas for 17% (9/52) and 17% (9/52) their last test was 1-3 years and more than 3 years ago, respectively. The person who tested positive was confirmed positive and accessed HIV care (CD4 cell count <250 cells/mm³).

Conclusion

The number of website visits is substantial, and our data suggest that almost half of the self-test users has never been tested for HIV before or was not recently tested (>3 years ago). User satisfaction is high. An HIVST service may prove to be an important tool for HIV prevention as it seems to attract individuals who are not sufficiently reached by conventional testing facilities.

PATHOGENESIS

Towards an HIV vaccine that induces broadly neutralizing antibodies

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Most vaccines work by inducing protective humoral immunity and a likely requirement of an HIV-1 vaccine is the ability to induce broadly neutralizing antibodies, i.e. antibodies that can neutralize a large proportion of the HIV-1 strains that circulate worldwide. The HIV-1 envelope glycoproteins, residing in the viral envelope, are the only viral proteins on the outside of the virus and hence the only proteins relevant for the induction of broadly neutralizing antibodies. However, past and current HIV-1 vaccine candidates have thus far not been able to induce such antibodies, because many features of the HIV envelope glycoprotein complex, such as variability, flexibility, instability and glycosylation, limit the induction and binding of neutralizing antibodies. One vaccine approach is to create stable mimics of the 6-subunit envelope glycoprotein complex (termed the “envelope trimer”) that expose as many neutralization epitopes as possible, while occluding epitopes for non-neutralizing antibodies. We have succeeded in generating such trimer mimics, because many features of the HIV envelope glycoprotein complex, such as variability, flexibility, instability and glycosylation, limit the induction and binding of neutralizing antibodies. One vaccine approach is to create stable mimics of the 6-subunit envelope glycoprotein complex (termed the “envelope trimer”) that expose as many neutralization epitopes as possible, while occluding epitopes for non-neutralizing antibodies. We have succeeded in generating such trimer mimics by stabilizing the interactions between the 6 subunits. Trimer vaccines based on the subtype A founder virus BG505, the subtype B founder virus B41, the subtype C virus ZM197M and several subtype B viruses from the Amsterdam Cohort are highly stable and homogeneous, expose most epitopes for neutralizing antibodies and closely resemble native virus spikes when viewed by stain electron microscopy and X-ray crystallography. In contrast to previous vaccine candidates, these trimers induce strong and consistent neutralizing antibody responses against the autologous, neutralization-resistant (“tier 2”) viruses. Heterologous neutralization is limited to relatively neutralization-sensitive (“tier 1”) virus isolates, indicating that future work should be aimed at broadening the neutralizing response. Combined with the detailed structural information on these envelope trimers that is now available, these results will guide structure- and immunology-based improvements to the design of HIV-1 vaccines aimed at inducing broadly neutralizing antibodies.

Antibodies isolated from an HIV-1 elite neutralizer and BG505 SOSIP vaccinated rabbits target the same epitope on the envelope glycoprotein

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Background

HIV continues to cause significant morbidity and mortality around the world, emphasizing the need for an effective preventive HIV vaccine. Broadly neutralizing antibodies isolated from HIV-1 infected individuals have revealed that the human immune system is capable of eliciting antibodies that can protect against infection, as confirmed in macaque challenge studies. The knowledge obtained from elite neutralizers, who very rapidly developed extremely broad and potent serum neutralization capacity, may offer new clues for vaccine design. The BG505 SOSIP trimer has been chosen as the envelope glycoprotein most related to the unmutated common ancestor of the PG9/PG16 patient. This soluble native-like proteins was capable of eliciting neutralizing serum responses against the homologous (Tier-2) virus, however how to broaden the response to target heterologous Tier-2 viruses is still unclear.

Methods

Immunogen-specific IgG+ B cells from 1 elite neutralizer and 3 immunized rabbits were single cell sorted to obtain monoclonal antibodies. The genetic and phenotypic characteristics of these monoclonal antibodies were determined by sequence, ELISA and neutralization assays.

Results

The isolated monoclonal antibodies from BG505 SOSIP immunized rabbits are only capable of neutralizing the homologous virus. Epitope mapping studies showed that these antibodies did not compete with known broadly neutralizing antibodies, indicating that they target a new epitope on the envelope glycoprotein. Interestingly they do compete with newly isolated antibodies from an elite neutralizer of the Amsterdam Cohort Studies. The high-resolution structures of the rabbit antibodies and the human antibodies, described
here, show that they recognize a very similar epitope surrounding the N241 glycan at the gp120-gp41 interface.

The inability of the rabbit monoclonal antibodies to cope with the presence of the N241 glycan is reflected in the narrow neutralization breadth, in contrary to the human monoclonal antibodies, which are able to cope with the N241 glycan and are able to neutralize a range of viruses from different clades.

Conclusion
This unique study shows that antibodies that recognized similar epitope as broadly neutralizing antibodies from HIV-infected patients can be elicited by SOSIP protein immunizations. This knowledge will guide the design of improved immunogens that can be used in a mix of immunogens and/or sequential immunizations to broaden the response after vaccination.

A novel ex vivo HIV-1 vaginal transmission model: dysbiotic microbiota increase HIV-1 susceptibility

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Background
HIV-1 infection is still a global health problem and sexual transmission is the major route of infection. However, the initial events of mucosal HIV-1 infection remain largely unknown. Here we developed an ex vivo model with primary vaginal tissue to investigate the primary targets of HIV-1 and mucosal transmission.

Methods
We have successfully developed a vaginal ex vivo model using primary vaginal tissue. Mucosal sheets were embedded in a transwell system, exposed to TLR ligands or microbiota, and exposed to HIV-1. After culture, the migrated cells were identified and analysed for infection by flow cytometry. Various anti-retroviral agents (indinavir, zidovudine) were used to identify primary vs secondary targets of HIV-1 during mucosal transmission.

Results
In our ex vivo vaginal transmission model, Langerhans cells and T cells (both CD8+ and CD4+ subsets) make up the majority of the emigrated cell fraction. Low levels of infection were observed in either Langerhans cells or T cells when vaginal tissues were treated with HIV-1, supporting our data that immature Langerhans cells are refractory to infection. Treatments of vaginal tissue with Lactobacilli species did not increase HIV-1 infection of Langerhans cells and T cells. Notably, the presence of microbiota associated with vaginal dysbiosis strongly increased HIV-1 infection of both LCs and T cells. To identify the primary target cell we used anti-retroviral agents and identified that LCs are the primary target of HIV-1, and most T cells are infected through transmission of HIV-1 by LCs.

Conclusion
Hence, Lactobacilli do not influence HIV-1 susceptibility but bacteria associated with vaginal dysbiosis enhance HIV-1 transmission by increasing HIV-1 infection of vaginal LCs. Moreover, our data strongly suggest that vaginal LCs, but not T cells, in the vaginal mucosa are primary targets for HIV-1. These studies will provide valuable knowledge to facilitate the design of preventative or therapeutic strategies to combat vaginal HIV-1 transmission.

Human TRIM5a restricts mucosal HIV-1 transmission


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TRIM5α is a host restriction factor that binds incoming retroviral capsid upon viral entry and interferes with the uncoating and reverse transcription processes. Current views hold that TRIM5α restricts HIV-1 infection in a species-dependent manner, i.e. rhesus macaque TRIM5α efficiently blocks HIV-1 infection whereas human TRIM5α fails to inhibit HIV-1 infection. Strikingly, our data show that human TRIM5α potently restricts HIV-1 infection of Langerhans cells (LCs) and that human TRIM5α-mediated restriction is dependent on the virus uptake route. LCs are prime targets for HIV-1 infection during sexual transmission since this dendritic cell subset resides in the mucosal epithelia of vagina, foreskin and colorectal mucosa. LCs cannot become infected by HIV-1; HIV-1 capture by C-type lectin receptor (CLR) langerin and subsequent targeting to Birbeck granules prevents infection. Strikingly, silencing of TRIM5α in LCs by RNA interference strongly increased HIV-1 integration as well as infection of LCs. Our data not only strongly support that human TRIM5α is a cell-specific restriction factor but also challenge the current species-specific TRIM5α restriction paradigm. Little is known about the manner of restriction by TRIM5α. We show that human TRIM5α is associated at steady-state with
autophagosomal molecule Atg16L1 and induced increased Atg5 recruitment upon HIV-1 infection in LCs, suggesting a role for the degradative autophagy pathway in human TRIM5α-mediated restriction. Remarkably, although overexpression of human TRIM5α alone in U87 cell-line marginally restricted HIV-1 infection, co-expression of CLR langerin almost completely abrogated HIV-1 infection. Silencing of either Atg16L1 or TRIM5α abrogated the langerin-mediated restriction. In addition, co-immunoprecipitation and confocal microscopy studies confirmed the co-localization of langerin, autophagosomal molecules and TRIM5α after HIV-1 internalization in LCs. Thus, our data show that restriction by human Trim5α requires HIV-1 uptake by CLR langerin to channel HIV-1 into Trim5α-dependent autophagy pathway. The importance of TRIM5α and innate activation of autophagy in protecting mucosal infections suggest that therapies strengthening these mechanisms in a more targeted way could thus provide methods to prevent mucosal transmission and might be used to confer a superior cell-mediated resistance to HIV-1 in humans.

G3BP1 binds to HIV-1 RNA transcripts and restricts viral replication in macrophages and T cells

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Background
Despite current antiretroviral therapies, total eradication of HIV-1 infection is not achieved due to the existence of the viral reservoir. HIV-1 exploits the cellular machinery of target cells for successful infection, however innate defense mechanisms that inhibit replication may in turn induce latent infection by repressing replication after integration of the provirus. In an effort to identify novel restriction factors, gene transcriptome profiles of permissive macrophages were compared with those of non-permissive IFNγ+TNFα activated macrophages in which HIV-1 is restricted after integration. This resulted in the identification of GTPase-activating protein-(SH3 domain)-binding protein 1 (G3BP1) as one of the cellular factors upregulated in IFNγ+TNFα macrophages in which HIV-1 replication is blocked after integration. Here, we aim to elucidate the effect and mechanism by which G3BP1 affects HIV-1 replication in primary HIV-1 target cells.

Methods
G3BP1 was silenced in primary macrophages and primary CD4+ T-cells by siRNAs or siRNAs targeting G3BP1. These cells were subsequently infected with HIV-1 to analyse the effect of G3BP1 silencing on the different steps of the HIV-1 replication cycle. RNA-immunoprecipitation assays and immunofluorescence microscopy were performed to unravel the mechanism by which G3BP1 affects HIV-1 replication in these primary cells.

Results
Silencing of G3BP1 by RNA interference resulted in increased HIV-1 replication and higher HIV-1 LTR-mediated gene expression in both primary macrophages and T-cells, without affecting other retroviruses. G3BP1 silencing also resulted in lower viral mRNA transcripts, while proviral DNA levels were not affected, suggesting that G3BP1 is able to restrict HIV-1 at a post-integration step. Indeed, we observed that G3BP1 binds to HIV-1 RNA and silencing of G3BP1 resulted in decreased binding to HIV-1 transcripts. Additionally, we
observed increased binding of G3BP1 to HIV-1 RNA in IFNγ+TNFα-stimulated macrophages, in which G3BP1 is highly expressed. G3BP1 is a cellular component of stress granules, yet G3BP1 mediated HIV-1 restriction was not dependent on stress granule formation in macrophages. G3BP1 was highly expressed in resting naïve or memory T-cells from healthy donors and HIV-1 infected patients; however expression decreased significantly upon T-cell activation by IL-2.

Conclusions
Our data suggest that G3BP1 captures viral transcripts, making them unavailable for translation or packaging, and thereby inhibiting viral replication. However, since G3BP1 inhibits HIV-1 after integration, and it is highly expressed in primary cells where HIV-1 replicates poorly, G3BP1 may in turn contribute to viral latency in T-cells and establishment of the long lived macrophage reservoir.

TREATMENT

HIV remission after discontinuing ART: 17 is it achievable?

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Eradication of HIV is extremely difficult and has only been successful in the Berlin patient who underwent transplantation with HIV-resistant stem cells for his cancer. HIV remission is a more achievable near-term goal. It is generally defined as the ability of HIV-infected individuals to maintain blood viral load at undetectable levels after discontinuation of antiretroviral therapy (ART). Such individuals are sometimes referred to as Post Treatment Controllers (PTCs). They are uncommon and usually include individuals treated in early infection and those with low HIV reservoir size. The VISCONTI cohort of PTC adults in long-term HIV remission for over a decade remains unique but provides a basis for the critical role of early ART in achieving remission. Transient HIV remission has been achieved by the Boston patients transplanted with HIV-permissive cells and the Mississippi baby who was treated with ART extremely early. Current evidence suggests that ART instituted during acute HIV infection may be key to containing HIV reservoir establishment particularly in long-lived CD4+ T cells,

Several interventions to eliminate latently infected cells have been studied including latency reversing agents, broadly neutralizing antibodies, therapeutic HIV vaccines, gene editing therapies and cell-based therapies, but none has demonstrated sufficient benefits. Based on current studies, none of these therapies are likely to achieve long-term sustained HIV remission, when used as single interventions. Although there is a general consensus that combinations of interventions will be needed, researchers continue to struggle to identify what these combinations would need to look like.

This presentation will review the status of current research efforts aimed at achieving HIV remission and cure. It will reflect upon the lessons learned from past intervention studies and share information on current studies. It will offer a perspective on priorities for HIV cure research including innovative approaches to studying combination therapies.

Small molecule inhibitors of BAF; 18 a new family of compounds in HIV-1 latency reversal

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Background
Persistence of a reservoir of latently infected cells in presence of cART represents the main obstacle to HIV-1 eradication. Recently, pharmaceutical strategies aimed at HIV-1 eradication have focused on compounds capable to activate latent HIV in order to render infected cells susceptible to viral cytopathic effects and immune clearance. Our group previously identified the BAF chromatin remodeling complex as a key player required for maintenance of HIV-1 latency, highlighting its potential as a molecular target for inhibition in latency reversal.

Methods
We screened a panel of small molecule inhibitors of BAF complex (BAFi’s) for potential to activate latent HIV-1 in different in vitro models of latency including cell lines and ex-vivo infected primary CD4 T cells. Cells were treated with BAFi’s alone and in combination with the HDAC inhibitor Vorinostat and the PKC agonists Prostratin. The specificity and the mechanisms of action of the compounds showing latency reversal activity were investigated by determining the gene expression profile and the status of the BAF complex after treatment with BAFi’s. Nucleosome occupancy and presence of the BAF complex at the HIV promoter following BAFi’s treatment were evaluated by FAIRE assay and chromatin immunoprecipitation, respectively.

Results
Latency reversal was strongly induced by BAFi’s Caffeic acid phenethyl ester (CAPE) and Pyrimethamine (PYR), two
molecules previously characterized for clinical application. We showed that the inhibitory activity of CAPE and PYR against BAF complex is mediated by the degradation of BAF complex-specific subunit BAF250a/ARID1a, and determines a change in the gene expression pattern of BAF target genes mirroring the BAF complex knock-down. Both CAPE and PYR reversed HIV-1 latency in cell lines as well as primary cells models of latency, without inducing T cell proliferation or activation. Moreover, BAFi-induced HIV-1 latency reversal was synergistically enhanced upon PKC pathway activation and HDAC-inhibition. Consistent with the observed latency reversal activity, treatment with BAFi’s resulted in displacement of BAF complex from HIV-1 LTR as well as nucleosome remodeling in HIV-1 promotor region.

Conclusion
We have identified a new family of molecules targeting the BAF complex, that show latency reversing activity alone and in combination with PKC agonists and HDAC inhibitors, molecules under clinical investigation for their effectiveness in HIV-1 latency reversal. Since targeting a previously unexplored pathway, this new class of drugs has high potential for inclusion in latency reversal therapies.

Diagnostic value of ultrasensitive HIV investigation in vertically exposed infants with negative routine HIV laboratory results

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Background
Early cART after vertical HIV infection can prevent the development of HIV specific antibodies and has the potential to restrict the size of the HIV reservoir. One vertically infected baby who retained HIV control for a prolonged period after treatment was discontinued, has become known as the “Mississippi baby”. Although at 27 months off therapy rebound occurred, this particular case has invigorated the hypothesis that HIV cure may be achieved by early cART. Ever since, parents of HIV infected children, who have initiated treatment in an early phase and are seronegative, question if cART should be continued.

Methods
Of a case-series of vertically infected children in whom the presence of an HIV infection was questioned, clinical data and standard diagnostic laboratory data were collected. DNA was extracted from PBMCs or dried blood spots (DBS). Detection and quantification of HIV DNA was performed by different ultrasensitive assays.

Results
7 children were included in this case-series. All children were born in Africa and presented at Dutch hospitals after adoption. At time of presentation all children had negative HIV serology. Child 1 was treated for 8 weeks with monotherapy and had no written documentation of HIV infection. This infant repeatedly tested negative for HIV-RNA during 21 months off therapy and had no detectable HIV antibodies. In this child, ultrasensitive HIV-DNA tests were also negative. All other children had documented records of positive HIV status in the country of origin and had locally initiated cART. In the Netherlands, HIV RNA could only be detected in infant 2. Despite a period low level viremia, no specific HIV antibodies were observed. In child 3 cART was discontinued resulting in a viral rebound (5.64 x 10^6cp/mL) and HIV seroconversion. Retrospective analysis of PBMC obtained before therapy interruption showed a positive ultrasensitive HIV DNA test result. The four other children continued cART after ultrasensitive DNA assays confirmed the HIV infection.

Conclusion
Standard diagnostic tests can provide false hope of a cure and erroneous discontinuation of cART with the risk of viral rebound. By using ultrasensitive tools developed to investigate the viral reservoir, HIV infection could be confirmed in children with negative HIV serology and an undetectable HIV RNA load. In one child, without proper documentation of HIV status, the negative ultrasensitive DNA tests reinforced the decision to stop ART and led to the conclusion that it is unlikely this child was infected with HIV.

Major protease inhibitor resistance in the first three years of second-line antiretroviral therapy for HIV-1 in sub-Saharan Africa

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6Dep. Haematology & Blood transfusion, College of Medicine, University of Lagos, Lagos, Nigeria
7Coast Province General Hospital, Mombasa, Kenya
8MUelman Hospital, Pretoria, South Africa
Background
As antiretroviral therapy (ART) programs in sub-Saharan Africa mature, increasing numbers of HIV-positive people will experience treatment failure, and require second-line or eventually third-line ART. It is yet unclear how many patients will need third-line ART regimens because of major PI resistance. This study aimed to determine the risk factors for virological failure on PI-based second-line ART, and explore potential third-line treatment options for participants with major PI mutations.

Methods
HIV-1 positive adults were enrolled in the PanAfrican Studies to Evaluate Resistance Monitoring (PASER-M) cohort, at the time of switch to second-line PI-based ART, and included in the analysis if they received >180 days of second-line ART. We assessed risk factors for virological failure (viral load >400 cps/ml) after up to 3 years of second-line PI-based ART using Cox models. If viral load ≥1,000 cps/ml, pol genotyping was performed. Drug resistance mutations were scored using the 2014 IAS-USA drug mutation list, and genotype susceptibility was calculated using the Stanford algorithm Version 7.0.

Results
Of 227 included participants, 25.0% (N=54/216) experienced virological failure at some point during follow-up at a rate of 138.9 failures (95%CI: 106.4-181.3) per 1,000 person-years. In multivariable analysis, the risk factors for virological failure on second-line ART were: failing a non-standard non-nucleoside reverse transcriptase inhibitor (NNRTI)-based first-line regimen (hazard ratio [HR] 7.10; 95%CI: 3.40-14.83; p<0.001) or PI-based first-line regimen (HR 7.59; 95%CI: 3.02-19.07; p=0.001) compared to ZDV/3TC/NNRTI, PI-resistance at switch (HR 6.69; 95%CI: 2.49-17.98; p<0.001) and <95% self-reported adherence to second-line ART (HR 3.05; 95%CI: 1.71-5.42; p=0.025).

For 32/43 (74.4%) participants with VL≥1,000 cps/ml during follow-up, genotypic data was available. At least one DRM was found among 22/32 (68.8%) participants: 17 (56.3%) harboured drug resistance to nucleoside reverse transcriptase inhibitors and 7 (21.9%) to PIs (table). Overall, 7/32 (21.9%) participants harboured major PI mutations. The acquired PI mutations conveyed reduced susceptibility to all PIs; 83% of participants with VL>1,000 cps/ml are predicted to remain susceptible for darunavir/ritonavir (figure).

Conclusion
While over 85% had viral suppression after up to 36 months of second-line ART, major PI resistance was detected in 20% of participants failing second-line ART. Future treatment of these individuals require proposed third-line drugs (i.e. darunavir/ritonavir, etravirine and raltegravir), which are currently unavailable in sub-Saharan Africa. To ensure long-term ART success, intensified adherence support through virological monitoring and, if failing, availability of third-line drug options are urgently needed.

Abstract 20: Antiretroviral drug resistance at second-line failure.
Abstracts
Oral presentations

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<th>Viral load (copies)</th>
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Drug resistance mutations were detected using the Stanford algorithm version 7.07. Subtype was determined using the HEGa typing tool V3.

A 12-Week Treatment with Boceprevir, Peginterferon and Ribavirin for Acute Hepatitis C in HIV infected patients.

Results from the open-label Dutch Acute HCV in HIV (DAHHS1) Study


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Objectives
The epidemic of acute hepatitis C virus (AHCV) continues to spread within HIV+ men having sex with men (MSM). In the treatment of AHCV, relatively high cure rates (60-90%) are achieved with 24 weeks of peginterferon(P) (+/- ribavirin(R)). Currently, none of the P-free regimens have been studied or registered for AHCV treatment. Our hypothesis was that addition of a direct-acting anti-viral drug (DAA) to P would allow for a shorter treatment duration. In the DAHHS-Study, the efficacy and tolerability of a 12-week boceprevir, P+R regimen in AHCV genotype-1 was evaluated in 10 Dutch HIV treatment centers.

Methods
HIV+ patients with a new ALAT elevation were screened for the presence of HCV RNA. If positive, stored historical plasma samples were tested to prove that the HCV infection was recent. Boceprevir, P+R for 12 weeks was started without a P+R lead-in and was initiated no later than 26 weeks after the day of infection. Primary endpoint is sustained viral response at week 12 (SVR12) in patients with no HCV RNA detected (Roche, CAP/CTM target not detected) at w4 (RVR4) and in all patients included (secondary endpoint).

Results
From 9/2013 to 1/2015 we screened 127 HIV+ patients with a new HCV infection. We excluded 62 patients because of genotype 4 (n=22), HCV infection >6 months (n=17), spontaneous clearance before inclusion (n=8), refusal to participate (n=13) or other reasons (n=2). 65 patients were included, 8 cleared HCV or refused before treatment initiation and 57 started therapy. RVR4 was 41/57 (72%) and end of treatment response was 52/57 (91%). In the RVR4 population, 41/41 (100%, 95% CI 91%-100%) had a SVR12. In the ITT population SVR12 was 49/57 (86%, 95% CI 75%-93%).

Conclusion
In HIV+ patients with an acute HCV infection, the addition of boceprevir to P+R cured 86% of the patients and as much as 100% of the RVR4 population. At 13.000 euro, this shorter therapy is relatively cheap, reasonably tolerated and therefore a relevant therapy to prevent not only future liver disease but also ongoing transmission of HCV in HIV+ MSM.
Determinants of never having tested for HIV among MSM in the Netherlands*

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2Sigma Research, London, United Kingdom

Background
Men who have sex with men (MSM) who are unaware of their HIV infection are more likely to infect others, and unable to receive treatment. Therefore, we aimed to identify characteristics of Dutch MSM who never tested for HIV, as the ultimate unaware group, assuming that at least some of them have been at risk for HIV.

Methods
We analysed data from Dutch participants from the European MSM Internet Survey (EMIS, NNL=3,787). Uni- and multivariable logistic regression analyses were conducted to investigate associations between ‘never been tested for HIV’ and demographic, behavioural, and social engagement factors.

Results
A total of 774 MSM (20.5%) had never been tested for HIV. Of those, 36.1% reported UAI with a male partner of unknown or discordant status in the last 12 months, thus were at risk for HIV. Demographics associated with ‘never tested for HIV’ were: living outside of Amsterdam (aOR 1.5 95% CI 1.2-2.0 vs Amsterdam), lower education (1.3 CI 1.04-1.6 vs high), and lower knowledge on HIV testing (2.2 CI 1.4-3.6 vs high). Behavioural variables associated with ‘never tested for HIV’ were: less than 5 years sexually active (2.0 CI 1.6-2.7 vs longer), number of sexual partners in the last 12 months (zero: 2.2 CI 1.6-3.0 vs >10), no anal intercourse (AI) ever (6.0 CI 3.0-11.8 vs yes), no sex abroad in the last 12 months (1.6 CI 1.3-2.0 vs yes), no self-reported STIs in the last 12 months (8.6 CI 4.7-15.6 vs yes), no sex/party drugs (2.1 CI 1.6-2.8 vs yes in the last 12 months). Finally, less social engagement was associated with having never been tested: not being out or ‘being closeted’ (1.9 CI 1.6-2.4 vs out), never visiting social venues (1.9 CI 1.4-2.7 vs ever), and having a fewer gay friends (1.8 CI 1.3-2.6 vs most are gay).

Conclusion
MSM who are more assimilated into the gay community seem less likely to never be tested for HIV. Perceived higher sexual risks in the recent past decreased the odds to never be tested for HIV; suggesting that MSM make their own risk assessments that inform their choices about HIV-testing. Nevertheless, MSM who were never tested may have been at risk for HIV, and remain important to target for HIV interventions.

Factors associated with recent HIV infection among newly diagnosed STI clinic attendees in the Netherlands in 2014*

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Background
During 2014, we enhanced HIV surveillance in Dutch STI clinics to differentiate recent from established infections. Identification of recent infections (RI) enables calculating HIV incidence, identification of transmission risk groups, monitoring of HIV trends, and assessment of the impact of preventive interventions. We identified factors associated with RI and compared results with a previous pilot study among men who have sex with men (MSM) in Amsterdam and Rotterdam.

Methods
We collected leftover specimens from persons attending STI clinics who were newly diagnosed with HIV and tested them with the Architect-immunoassay for antibody avidity. RI was defined as avidity index (AI) ≤ 0.80. AI results were linked with epidemiological information from HIV/STI surveillance data. We identified factors associated with RI in MSM using multivariable logistic regression. We estimated HIV incidence among MSM in Amsterdam, using false recent rate (FRR) of 6% obtained from the pilot.

Results
In 2014, 323 STI clinic attendees were newly diagnosed with HIV: 278 MSM, 25 heterosexual men, and 20 women. 179/323 (55%) had a specimen available for AI testing. RIs were more frequent among MSM (39%, 60/153) than heterosexuals (11%, 3/26). Factors independently associated with RI in MSM were: diagnosis with an STI within the previous 2 years (aOR 12.5, 95%CI 4.1-38.4) and Dutch ethnicity (aOR 4.3, 95%CI 1.4-13.2). The percentage of RIs among MSM in this study was higher compared to the previous pilot in 2009-2011. The proportion of recent infections among MSM increased over time from 16% to 25%. The estimated HIV incidence among MSM in Amsterdam in 2014: 1.0 per 100 person years (95% CI 0.6-1.4), lower compared to 2009/2011: 3.3 per 100 person years (95% CI 2.5-4.1).
Conclusions
Specimens were only available for about half of HIV infected STI clinic attendees, which limits the representativeness of our results. MSM more frequently had a RI than heterosexuals. Among MSM, previous STIs and Dutch ethnicity were associated with RI. We recommend targeting interventions to these groups, and to continue testing for recent infections at the STI clinics. Increase in proportion of recent infections in MSM indicate that MSM are being diagnosed earlier. RITA surveillance needs to be expanded to other test locations to improve insights in RI among non STI clinic attendees. The lower incidence among MSM is possibly associated with higher HIV testing rates.

Virological and social outcomes of HIV-infected adolescents and young adults in the Netherlands after transition to adult health care services

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Objectives
To evaluate virological and social outcomes of HIV-infected adolescents and young adults (AYA) on combination antiretroviral therapy (cART) before and after transition to adult health care services and to explore factors associated with virological outcomes of HIV-infected AYA.

Methods
We included AYA who entered care in a paediatric HIV treatment centre and who transferred to adult care. We used HIV viral load (VL) and cART data from the Dutch Stichting HIV Monitoring (SHM)(1996-2014), social and treatment data obtained from patients’ medical records from the four Dutch paediatric HIV treatment centres and 14 Dutch adult treatment centres involved in care of all HIV infected AYA who transitioned from paediatric into adult health care in the Netherlands.

Results
HIV virological failure (VF) occurred frequently among the 59 included HIV-infected AYA and increased significantly from before to after transition (p=<0.001). Characteristics significantly associated with VF after transition were VF during paediatric care, unemployment and receiving a sickness benefit. Lack of autonomy regarding medication intake at the moment of transition and the use of supportive care for cART adherence were associated with VF prior and after transition.

Conclusion
HIV-infected AYA are vulnerable to virological failure after transitioning to adult care. Identification of HIV-infected adolescents at high risk for VF after transition might help to improve treatment success in this particular group.

Keywords
HIV, adolescents, young adults, transition, virological outcomes, social outcomes, cART

The sexual network of men who have sex with men in the Netherlands: who has a relationship with whom?

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Background
In the Netherlands, men who have sex with men (MSM) account for the largest fraction of new HIV diagnoses annually. Despite the availability of successful treatment, there is still ongoing transmission. Research thus far has focused on the impact of several public health measures, such as early initiation of combination antiretroviral therapy or pre-exposure prophylaxis, but the joint impact of combined
strategies is unknown. To assess the effect of combinations of strategies, we developed an individual based model that describes the transmission of HIV and other sexually transmitted infections via sexual relationships among MSM. The aim of this study was to describe the sexual network of MSM in the Netherlands and assess its main characteristics.

Methods
We developed an individual based model that describes sexual relationships among MSM. In the model we accounted for heterogeneity in the rate of partner formation between men, between different age groups, and between periods within the sexual lifetime of a man. Different levels of concurrency in sexual relationships were also included. Parameters relating to sexual behaviour were estimated from data from the Amsterdam Cohort Study among MSM and the Network Study among MSM in Amsterdam.

Results
We found that a large fraction of sexual relationships is of short duration of up to a few days, which agrees with the data. For more than half of sexual relationships, the age difference between the two partners is up to four years, in agreement with data from the Network Study. In the model, the time until the next sexual relationship depends on the average number of partners in the preceding few months and the average number of partners in the preceding few years. In this way, we create a sexual network where the lifetime number of partners has a power-law-like distribution, indicating that men who have had many partners in the past are more likely to have many partners at present.

Conclusions
The sexual network of MSM in the Netherlands can be represented by a scale-free network. This might explain why the HIV epidemic could propagate so fast in the 80’s and why HIV control among MSM has been so difficult thus far.

Acknowledgements
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Failure of donor selection: what can the virus tell us?

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Background
Risk-behaviour based donor selection is used to reduce the number of potentially infectious donors. Nevertheless, 290 Dutch blood donors tested positive for HIV RNA (n=31), HBV DNA (n=212) and HCV RNA (n=47) between 2005 and 2014. During post-test counselling, 12% of infected donors disclosed risk factors which, if revealed during the donor selection procedure, would have caused permanent donor deferral.

Methods
Due to the high-genetic diversity of HIV, HBV and HCV, individual viral strains can be linked to geographic origin and route of infection. Hence, molecular typing might increase our understanding of blood-borne infections among donors without self-reported risk behaviour. Viral typing was based on the HIV pol gene (1200 bp), HBV Core and Surface gene (±1950 bp), and HCV NS5B gene (707 bp). Phylogenies were constructed using HIV, HBV and HCV donor sequences plus HIV pol sequences from the ATHENA cohort (n=8673), HBV sequences from the RIVM acute HBV database (n=552), and closely related sequences on GenBank.

Results
Viral fingerprints were obtained for 24/24 (100%) of HIV-, 97/111 (87%) of HBV-, and 41/41 (100%) of HCV-positive donors for whom serum was available. Amongst HIV-positive donors subtype B (67%) predominated, followed by CRF02_AG (13%) and subtype C (13%). 12/14 (86%) male donors were infected with HIV subtype B; 10/14 (71%) were part of robust MSM clusters. Phylogenetic analysis confirmed heterosexual transmission in 4/4 (100%) female donors with HIV subtype B, and a heterosexual African partner in 5/6 (83%) female donors with HIV subtype non-B. The vast majority of HBV infections among donors was caused by HBV genotypes A (47%) and D (39%). HBV genotype was strongly associated with country of birth: genotype A (the Netherlands), genotype D (Mediterranean/Central Asia), genotypes B and C (South-East Asia). The vast majority (74%) of recently acquired HBV infections among donors was caused by one specific HBV A2 strain that affects MSM and heterosexuals. The HCV genotype distribution in donors is highly diverse: 1a (37%), 1b (22%), 3a (17%), 2b (7%), 4d (5%), others (12%). The association between risk behaviour and HCV subtype is less evident, except for HCV infections with rare subtypes acquired in non-western countries.

Conclusion
Viral typing is a useful tool to improve our understanding on risk factors in donors with unexpected blood-borne infections. It enables us to estimate the relative contribution of various risk factors among donors who do not disclose plausible risk factors or donors who avoid post-test counselling.
High levels of HIV drug resistance in treatment-naïve children in Lagos, Nigeria: original data and a systematic review in sub-Saharan Africa


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Background
Since the roll-out of antiretroviral treatment (ART) in sub-Saharan Africa in the beginning of this millennium, ART coverage has increased substantially. The increased usage of ART, however, is likely to come at a cost, as the levels of HIV drug resistance (HIVDR) are expected to rise. Children who have been exposed to antiretroviral drugs (ARV) for the prevention of mother-to-child transmission are at increased risk of HIVDR prior to ART initiation. Monitoring pre-treatment HIVDR is especially important in children as they have fewer ART options than adults, and will require ART for more years. Data on pediatric HIVDR prevalence, especially from sub-Saharan Africa, are scarce.

Methods
HIV-1 infected ARV-naive children ≤12 years were enrolled at the Lagos University Teaching Hospital, Nigeria. Pre-treatment viral load and population based pol genotypic testing was performed retrospectively. HIVDR mutations were identified using the World Health Organization list for transmitted drug resistance. HIV-1 subtyping was performed using the REGA HIV-1 subtyping tool V3. Nutritional status was assessed using WHO Anthro (version 3.2.2, January 2011) for children ≤5 years and WHO Reference 2007 for children ≥5 years. Results for hemoglobin, CD4 count, CD4 percentage, and HIV RNA load were available for 87, 40, 48, and 82 children, respectively.

Results
Ninety ARV-naive children were enrolled in Nigeria, of whom genotypic testing was successful in 82 children (table). Thirteen of 82 (15.9%) children had pre-treatment HIVDR. All 13 harbored non-nucleoside reverse-transcriptase inhibitor mutations, of whom seven also had nucleoside reverse-transcriptase inhibitor resistance. No protease inhibitor mutations were detected. All 13 children had resistance against one or more drugs of their first-line regimen. The systematic review included 16 studies from...
11 different African countries, including 2,057 children (figure). Among ARV-naïve children, the pooled HIVDR prevalence was 10·8% (95%CI: 4·4-17·1). Meta-regression showed an increase in prevalence from 0·6% (95%CI 0·6-5·4) in 2004 to 36·2% (95%CI 25·5-46·9) in 2011 (p<0·05).

Conclusion
One in six Nigerian children starts a on a sub-optimal ART regimen, which corroborates with other African data. Our systematic review further showed a significant pre-treatment HIVDR increase in ARV-naïve children over the past decade. Our findings stress the importance of protease inhibitor-based regimens in all children <3 years of age. Overcoming practical barriers to implement protease inhibitor-based regimens, and introduction of a population-based HIVDR surveillance system among children should receive priority to ensure optimal treatment for HIV-infected children in sub-Saharan Africa.

Tracing the origin of the high prevalence of the hepatitis C virus NS3 Q80K polymorphism among HIV-infected MSM in the Netherlands


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Background
The naturally occurring Q80K polymorphism in the nonstructural protein 3 (NS3) of hepatitis C virus (HCV) has been associated with a reduced response to simeprevir (a ‘second wave’ first generation HCV protease inhibitor) / peginterferon-alfa/ribavirin triple therapy. This polymorphism is transmissible between hosts, and its prevalence varies geographically and per risk group. This study describes the prevalence of Q80K among various HIV risk groups in the Netherlands, e.g. HIV-1 coinfected men who have sex with men (MSM) and injecting drug users (IDU). Using phylogenetic analysis, we determined whether the presence of Q80K was linked to specific HCV transmission networks.

Methods
Archived samples from 150 HCV genotype 1a infected patients attending two Dutch medical centers, AMC Amsterdam and UMC Utrecht, were used for this study. Data on transmission risk factor and HIV-status were extracted from patient records. All patients were treatment-naïve for NS3/4A protease inhibitors. A 611 bp fragment of the NS3 genomic region including the Q80 amino acid position was amplified and sequenced. The NS3 maximum likelihood (ML) phylogeny was reconstructed using MEGA v6 with the HKY+G substitution model and 1000 bootstrap replicates.

Results
Of the 150 patients, 45% were coinfected with HIV-1, 39% were MSM (all HIV-1 coinfected), 17% IDU, 14% had other risk factors including blood transfusion and for 30% the route of transmission was unknown. The Q80K polymorphism was present in 35% of patients and was stable throughout the time span of sample collection (2000-2015). Q80K was most prevalent among MSM (52%), followed by persons with other or unknown risk factors (30%) and IDU (8%). Robust clustering in the ML phylogenetic tree (figure 1) was only observed for MSM; 5 clusters supported by high bootstrap values were identified. Q80K was present in 100% of sequences in 3 out of these 5 clusters. The largest cluster included 17 patients. Interestingly, sequences did not cluster according to treatment center.

Conclusion
The Q80K polymorphism naturally occurs in 35% of our study population and has persisted over 15 years. Among HIV-1 coinfected MSM, the prevalence of Q80K was highest and distinct transmission networks with and without Q80K were identified. This suggests a founder effect, with the introduction and expansion of Q80K variants in this population which potentially jeopardizes future treatment with simeprevir of HIV-1 coinfected MSM.
Abstract 28: ML phylogenetic tree of the Q80K polymorphis.
Neuropsychological functioning and school functioning of children with HIV in a cohort in the Netherlands


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Background
Combination antiretroviral therapy (cART) has strongly decreased the mortality and morbidity of HIV-infected children. Despite adequate therapy, neuropsychological impairments are found frequently in children with HIV infection. It is unclear what the influence of these neuropsychological impairments are on school functioning.

Objectives
Evaluation of the neuropsychological functioning and school functioning of HIV-infected children in a cohort in the Netherlands and determination of the influence of neuropsychological impairment on school functioning.

Methods
A cross-sectional mixed-method cohort study is being conducted in the Erasmus MC University Medical Center - Sophia Children’s Hospital, Rotterdam, the Netherlands. Forty perinatal HIV-infected children in the age of 5-18 years, as well as their caregivers, and teachers are included in this ongoing study. Assessment consisted of a structured questionnaire on demographic characteristics and neuropsychological questionnaires: the Behavior Ration Inventory of Executive Function (BRIEF), Strengths and Difficulties Questionnaire (SDQ), the Sensory Profile (SP) and the Child Health Questionnaire (CHQ). Results of the HIV-infected children were compared to the results of siblings and the general child population in the Netherlands. (Semi)structured interviews were conducted with caregivers and children with HIV to gain deeper insight in the school functioning (learning difficulties, needing special education services, absenteeism, and disclosure of HIV status).

Results
Data of 22 HIV infected children and 11 siblings have been analyzed so far. Preliminary results show that 55% of the children experience problems with neuropsychological functioning and had at least one score in the clinical range at the neuropsychological questionnaires. Problems are mainly found in concentration, hyperactivity and working memory. Children with HIV and their siblings obtained significantly poorer results compared to Dutch norms on multiple scales of the questionnaires. Alarming problems in school participation were observed in 55% of the HIV infected children and in 64% of their siblings. Children with HIV and their siblings had significantly higher rates of repeating a class, learning disabilities and needing special education services compared to the general child population in the Netherlands.

Conclusions
Children with HIV and their siblings have to repeat a class more often, experience more learning disabilities and need extra support at school, compared with the general child population in the Netherlands. HIV-infected children in the Netherlands and, interestingly also their siblings, need extra attention for their neuropsychological problems and learning difficulties even though the cause of these complications has not yet been fully clarified.

Positive Voices, peer-to-peer research on quality of life with HIV in the Netherlands

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Background
Since HIV became a chronic condition, the focus has shifted towards increased self-management of the infection, with greater emphasis on personal responsibility for a healthy lifestyle. The Dutch HIV Association (board) carried out a large-scale, peer-to-peer study among people living with HIV in the Netherlands. The main research objective was to determine the needs and strategies for a good quality of life among people living with HIV. The outcome was used as input for defining the long-term policies of the Association.

Methods
The research project was set up according the GIPA principle (Greater Involvement of People living with HIV and Aids). All participants involved in setting up and conducting the research were HIV positive: project manager, steering committee, 40 interviewers and the 468 participants. To ensure a stratified sample, interviewers and participants were selected to represent the diversity of the population. Participants were recruited through network organisations and HIV treatment centres, from within the interviewers’ networks, and, finally, by snowball sampling to reach people who would otherwise not have volunteered. The gathered data were analysed by cross sections on gender and sexual identity, cultural background, domestic area and on demographic characteristics.
Results
People with HIV are very consciously engaged with their health and social circumstances after learning their HIV status. Participants consider social interaction with other people with HIV important, to share experiences, seek advice and for partner search. Work is seen as the tool for improving economic conditions, and as having a positive effect on physical and mental health. Perceived stigma and fear of negative consequences of disclosure are important barriers. Lack of awareness about HIV in society is considered to be a serious constraint for living a full life.

Conclusion
On the one hand, this research demonstrates the active role of participants in the management of their chronic illness. On the other hand, certain external factors act as barriers for the participants to raise the quality of life to a desired level. Social cohesion and awareness about HIV in the personal environment, as well as in society, are desired. Stigma reduction in all areas would provide a better quality life for the participants. Facilitating contact between people living with HIV is important as this contact enhances acceptance and self-management, and consequently positively influences their quality of life.

PREVENTION

Let’s talk about sex: Barriers and facilitators for discussing sexual risk behavior with HIV positive MSM by HIV nurse consultants in the Netherlands

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Aim
HIV positive men who have sex with men (MSM) are often diagnosed with sexually transmitted infections (STI), suggesting sexual risk behavior among this group. HIV nurse consultants discussing sexual risk behavior with MSM could improve health promotion in this group. We would like to get more insight in the psychosocial determinants that influence whether HIV nurse consultants discuss sexual risk behavior.

Method
Therefore, an online self-reported questionnaire was conducted among the HIV nurse consultants in the Netherlands. We assessed factors from the theory of planned behavior, and factors from a previous qualitative study. Determinants that were assessed included attitudes, subjective norms, self-efficacy, and also shame, attention for prevention, time concerns. Outcomes were self-reported frequency of discussing sexual risk behavior (5-point likert scale), and intention to discuss sexual risk behavior (sum score 4 items; range 4-24, α = .76).

Results
A total of 60 out of 79 (76%) hiv nurse consultants completed the questionnaire. Overall, participants reported high intentions to discuss sexual risk behavior (M = 17, SD = 3). Intentions to discuss sexual risk behavior was higher among men, non-heterosexuals, participants who followed the Mainline course, had more positive attitudes, had ways to introduce the topic, and had the time or saw it as a priority to discuss sexual risk behavior (R2 = .54). Self-reported discussion was associated with higher intentions to discuss sexual risk behavior, higher experienced knowledge, and being a nurse practitioner (R2 = .60).

Discussion
HIV nurse practitioners in the Netherlands report high intentions and high frequency of discussing sexual risk behavior among HIV positive MSM. However, these MSM increasingly become co-infected with STI. Efforts to improve discussing of sexual risk behavior could focus on getting more insights into what exactly is discussed and what is the effect is of what is discussed on sexual risk behavior among MSM. We could also explore whether the self-reported frequency of discussing sexual risk behavior corresponds with practice or are biased. This study offers insights into the factor that influence discussing sexual risk behavior with HIV positive MSM by HIV nurses, a group that could contribute greatly to their sexual health.

Intention to vaccinate against human papillomavirus among HIV-positive and HIV-negative MSM

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Background
Men who have sex with men (MSM), specifically HIV-positive MSM, have a higher risk for anal cancer caused by the human papillomavirus (HPV). Currently, it is debated whether men should be included in the HPV vaccination programme in the Netherlands. The aim of this study was to assess determinants of HPV vaccine acceptability, and whether HPV
vaccine acceptability differs between HIV-positive and HIV-negative MSM that visit the STI clinic in Amsterdam.

**Methods**

Men aged ≥18 years were recruited from the STI clinic and asked to complete a web-based survey addressing the socio-psychological determinants of their HPV vaccination intention, socio-demographics, and their sexual behaviour. The selected socio-psychological factors were derived from the Theory of Planned Behaviour and Social Cognitive Theory. Univariable and multivariable logistic regressions were performed to assess determinants associated with HPV vaccination intention. Multivariable analysis was performed in two steps, first assessing which socio-psychological variables were associated with HPV vaccination intention (p<0.05), and subsequently assessing which additional socio-demographic variables were significantly associated with HPV vaccination intention. Intention to vaccinate was dichotomized as: certainly wanting to vaccinate versus having any doubts about vaccinating against HPV.

**Results**

Between June and August 2015, 438 MSM participated; 95 (21.7%) were HIV-positive. HIV-positive MSM were significantly older (P<0.001), reported a higher number of anal sexual partners in the preceding six months (P<0.001), and had more lifetime sexual partners (P<0.001). HIV-positive MSM had a higher perceived risk of HPV infection and HPV related diseases (P<0.001), and a higher positive attitude towards HPV vaccination (P<0.001). HIV-negative MSM anticipated a higher degree of regret if they would get infected with HPV in the future (P<0.001). HIV-positive MSM were more willing to get vaccinated against HPV than HIV-negative MSM [80.8% vs 54.5%; crude odds ratio (cOR) 2.5; 95% CI: 1.5-4.4]. In the first step of multivariable analysis, risk perception, anticipated regret when not vaccinating, and attitude towards vaccination were significantly associated with HPV vaccination intention. In the second step, none of the socio-demographics were significantly associated with HPV vaccination intention (neither HIV infection status [adjusted odds ratio (aOR) 1.8; 0.8-4.2]).

**Conclusions**

MSM have a high intention to get vaccinated against HPV, this intention is significantly higher in HIV-positive MSM. However, in multivariable analysis HIV-status did not contribute significantly to the model. Anticipated regret when not vaccinating and risk perception may be important targets for health promotion strategies that aim to increase HPV vaccination acceptability among MSM.

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**A native-like HIV-1 envelope trimer that engages multiple germline precursors of broadly neutralizing antibodies**


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**Background**

The induction of protective immunity against HIV-1 through vaccination remains elusive. To be effective, an HIV-1 vaccine should elicit broadly neutralizing antibodies (bNAbs) targeting the envelope glycoprotein (Env) on the surface of the virion. Since 2009 a wealth of potent bNAbs have been isolated from HIV-infected individuals suggesting that the development of a bNAb-eliciting vaccine is possible. Longitudinal analyses have shown that bNAbs emerge from germline antibody (gAb) precursors through a co-evolutionary process where iterative cycles of viral escape and antibody affinity maturation drive antibody lineages to become bNAbs. There is accumulating evidence that HIV-1 Env and Env-based immunogens usually do not interact efficiently with the inferred germline precursors of known bNAbs. This deficiency may be one reason why these immunogens are not efficient at inducing bNAbs. Env subdomain immunogens have been engineered to interact with inferred germline precursors of bNAbs, but unlike native Env trimers, these subdomains do not impose constraints on the angles of approach. Furthermore, these subdomain approaches only target one specific epitope cluster and do not present quaternary-dependent epitopes. Recombinant native-like Env trimers have the advantage that only gAbs that approach their target with the right angle will be selectively activated. Furthermore, they allow the triggering of germline Abs against diverse epitopes on the trimer. The present work focused on the optimization of a BG505 SOSIP.664 trimer to efficiently bind germline precursors of several bNAbs.

**Methods**

By using a combination of rational design (structural biology), antibody functional studies (neutralization assays),
and literature research, we engineered a native-like Env trimers (BG505 SOSIP.664) with improved germline antibody binding.

**Results**

We designed a native-like BG505 SOSIP.664 trimer containing 18 amino acid changes that collectively allowed efficient binding to the germline versions of several V1V2-apex bNAbs (PG16, PG9, CH01 and PGT145) as well as several CD4 binding site bNAbs (VRC01, PGV19, 12A12). Surface Plasmon Resonance (SPR) assays showed that several germline Abs bound with nanomolar affinity to this new BG505 SOSIP germline trimer.

**Conclusion**

This rationally engineered germline trimer represents a suitable priming protein for vaccine regimens aimed at inducing bNAbs.

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**General practitioners’ barriers to and facilitators of HIV testing strategies: a qualitative study**

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**Background**

European guidelines recommend offering an HIV test to individuals who display HIV indicator conditions. UK guidelines recommend performing ‘routine testing’ in general practices where HIV prevalence exceeds 2 in 1000. Implementation of both strategies in general practice is limited, while the numbers of undiagnosed HIV patients remain high. We aimed to discuss general practitioners’ (GPs) barriers to and facilitators of both strategies.

**Methods**

We combined semi-structured in-depth interviews with focus groups. Nine GPs - key informants familiar with STI prevention and control - were selected for the interviews. Additionally, we organised focus groups with a broad sample of GPs (n=81). Framework analysis was used to analyse the data.

**Results**

Various barriers were found, related to (1) the content of the guidelines (testing the right group and competing priorities in general practice), (2) GPs organisational implementation (lack of time, unclear when to repeat the HIV test and overlong list of indicator conditions) and (3) the patient population (creating fear among patients, stigmatising them and fear regarding financial costs). The majority of GPs stated that performing a risk assessment of patients is important before applying either strategy. Also, they recommended implementing the indicator-guided approach only in high prevalence areas and combining HIV tests with other laboratory blood tests.

**Conclusion**

GPs tend to cling to old patterns of risk-based testing, which alone are not sufficient in reducing the number of undiagnosed HIV patients. Making them aware of the additional value of both strategies could be an important step in achieving implementation.
indicating condition in the five years prior to diagnosis had an OR of 2.4 (95% CI = 1.8 to 3.4) among cases compared to controls, and was stronger for two HIV indicator conditions OR of 8.4 (95% CI = 5.3 to 13.3) and three or more HIV indicator conditions OR of 13.1 (95% CI = 6.6 to 26.8).

Conclusions
This study showed opportunities for HIV indicator condition-guided testing in primary care in the Netherlands. At this stage, HIV indicator conditions are not exploited as triggers for GPs to test for HIV. To move from policy to practice, phasing in this strategy first in high urban areas where HIV prevalence is higher may be the first step for actual implementation.

Tackle the AIDS pandemic through community workers and educators in South Africa, using the blended learning format

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Background
The AIDS pandemic presents a serious threat in South Africa, with a HIV prevalence rate of 19.1 percent among the general population. Given the severe shortage of human resources in the healthcare sector, community workers play an important role in providing health education, provision of primary healthcare, community empowerment and preventing HIV/AIDS. In South Africa community workers function as a bridge between the community and the healthcare system. Health[e]Foundation developed Health[e] Living, a blended learning program that aims to train community workers in viable facilitation skills and knowledge which they use to teach their communities about prevention of HIV.

Methods
In 2014 and 2015, a group of 105 community workers in South Africa completed the Health[e]Living training program, divided in 3 groups. The course content is a combination of 10 modules and interactive activities about various topics related to prevention of HIV. The training consisted of an onsite kick-off workshop followed by a 3 months distance-based self-study period and an onsite follow-up workshop. During the e-learning period participants practiced activities of the program within their community. The individual knowledge gain was assessed via pre- and post-test scores per module. The outreach within communities was assessed through pictures, video material and questionnaires of participating youngsters. During workshops additional data was collected, using questionnaires and focus groups.

Results
The overall increase in knowledge of community workers after completion of the training program was 12.7%. The most significant knowledge gain was found in the modules Substance misuse, Addiction and Global AIDS (21%) and HIV
& Human Rights (18.5%). Due to the low completion rate and low outreach numbers the program was revised after the first two groups. After this revision, the third group showed an increase of 48% in completion and more youngsters within communities were trained. Outreach of the program resulted in a number of 971 trained youngsters. The outcomes of the focus groups confirmed the community workers valued the content of the modules and used the knowledge and skills they gained in daily practice.

Conclusion
The results of this study confirm that blended learning is an effective method to train community workers in up-to-date knowledge and skills in order to educate youngsters in communities on prevention of HIV. However, it is crucial to adapt the program to not only cultural context, but also to the theoretical background of community workers themselves and the specific issues that play a role within communities.

Cervix screening in HIV infected females: adherence with guidelines and development of cervical dysplasia

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Background
Current CDC guidelines based on expert opinion advise yearly screening for cervical dysplasia in HIV infected women by means of Pap smear, but compliance with these guidelines is compromised due to patient- and physician-related reasons. Optimal screening interval and rate of cervical dysplasia development are unknown.

Methodology
We retrospectively analysed all Pap smear results of HIV infected adult women treated in the University Medical Centre Utrecht between 1989 and 2015. We evaluated the potential rate of cervical dysplasia development in patients with more than 3 years of follow-up in whom at least two Pap smears were performed. Mean screening intervals were compared between a group that developed cervical dysplasia (Pap2-5) and the group that did not; Kaplan-Meier regression analysis was used to evaluate a dysplasia-free interval.

Results
Of 324 female patients, 222 (69%) had at least one Pap smear performed. Mean interval between presentation and first Pap smear was 33 months, and shortened from 84 months in 1995-2000 to 7 months after 2010. 165 (51%) patients had at least 2 Pap smears and a follow up of > 3 years. The mean interval between Pap smears was
≤18 months in n= 98 (59%) and ≤12 months in n=38 (23%). CD4 counts were significantly lower in patient with interval <18 months (334 vs 423/mm³; p=0,024).

49 patients (30%) had cervical dysplasia at first screening which left 116 patient for further analysis. Median follow up was 112 months. 93 (80%) patients with Pap 1 at baseline were free of progression during the whole follow-up, 23 (20%) patients showed Pap deterioration, especially in the first 5 years after the diagnosis. Median time to first Pap deterioration was 27 months (IQR 46). The maximum deterioration stage was Pap3b. No cervical carcinoma was diagnosed.

The number needed to screen to diagnose one Pap deterioration after 6 years was 19. For patients with Pap 1 at first screening, no significant difference in deterioration was seen between a screening interval of ≤18 and >18 months.

Conclusion
The interval between consecutive Pap smears in HIV infected women in our hospital shortened over the years and was shortest for patients with a lower CD4 count. Progression to abnormal Pap screening did not differ between shorter and longer screening intervals. Therefore, prolongation of the screening interval may be justifiable for patients with normal Pap smears at first screening.

Early experiences from the Amsterdam PrEP project*

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Introduction
Several RCTs have shown that Pre-Exposure Prophylaxis (PrEP) is effective in preventing HIV infections. However, PrEP is not registered in the Netherlands and Europe and reimbursement of PrEP costs is, contrary to the situation in the US, not organized. As a consequence, PrEP is not available through standard prevention facilities such as STI clinics. The Public Health Service of Amsterdam developed the Amsterdam PrEP (AMPPrEP) project, which is embedded in the H-team. Aim of the project is to evaluate uptake, acceptability and usability of PrEP among MSM and transgender people in the Netherlands.

Methods
The AMPPrEP project aims to include 370 HIV negative men who have sex with men (MSM) and transgender people that meet one of the following criteria: an STI in the previous 6 months, condomless anal sex with casual partners, post-exposure prophylaxis in the previous 6 months or an HIV positive partner with a detectable viral load. Eligible participants will be offered a choice between two PrEP modalities: daily or intermittent oral PrEP. Three-monthly visits will include screening for STI and HIV and completion of questionnaires on acceptability and usability. Data on self-reported adherence will be collected through pill-counts, questionnaires and a newly developed application for mobile phones.

Results
In June 2015 the start of the AmPrEP project was announced and a 4-week application period was set. In the first 24 hours after this announcement, 350 applications were received. Another 185 applications followed, totaling 535 applications. Four transgender people applied. A random number was assigned to each applicant to determine the sequence of screening visits. Screening for eligibility as well as enrolment in AMPPrEP started in August 2015. In the first 5 weeks, 37 people were screened: 15 were eligible and started PrEP, 3 were not eligible (2 because of the lack of high risk sexual exposure; 1 because he was HIV positive) and 19 are still awaiting their screening results. Of the 15 MSM that started PrEP, all chose daily PrEP. Numbers will be updated for the NCHIV conference.

Conclusion
The high number of applications for the Amsterdam PrEP project illustrates the demand for PrEP in the Netherlands. Daily PrEP seems to be preferred among the first participants enrolled. Information on preferred PrEP modality, condom use and adherence to PrEP medication will provide input for clinical guidance and decision making regarding PrEP implementation in the Netherlands and beyond.

Low knowledge and moderate acceptability towards the prescription of pre-exposure prophylaxis among Dutch healthcare providers of sexual health clinics: a mixed-methods study*

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Background
Pre-exposure prophylaxis (PrEP) offers HIV-negative individuals a regimen of lower-intensity antiretroviral therapy to reduce their risk of HIV-infection. Knowledge, beliefs and attitudes of care providers towards PrEP can influence its future implementation. We therefore studied PrEP knowledge, and the association between beliefs about PrEP and personal acceptability of PrEP among healthcare providers in sexual health clinics.
Abstracts
Poster presentations

Methods
We conducted two focus groups in October 2014 among employees of the Amsterdam STI clinic, the largest STI clinic in the Netherlands with over 40,000 visits annually. Results of these focus groups informed an online questionnaire spread among 23 STI clinics nation-wide between March and April 2015. Descriptive analyses were used to measure self-perceived PrEP knowledge in regards to efficacy, frequency and the severity of side effects of PrEP (7-point scale: 1-very insufficient, 7-very sufficient). Multivariate linear regression analyses were used to associate beliefs and attitudes (7-point scale: 1-completely disagree, 7-completely agree) with acceptability of PrEP implementation (7-point scale: 1-low acceptability, 7-high acceptability).

Results
In total, 16 professionals participated in the focus groups (4 doctors, 12 nurses) and 142 employees of 23 clinics (93 nurses, 26 doctors, 13 others) completed the online questionnaire. The mean scores for self-perceived PrEP knowledge were: 3.9 (SD=1.6) for PrEP efficacy, 2.9 (SD=1.5) for frequency of side effects, and 2.8 (SD=1.4) for the severity of side effects. The mean acceptability score for PrEP prescription was 4.2 (SD=1.6) (2 items, r=0.64). Of the beliefs that were obtained in the focus groups, the following were significantly associated (p<0.05) with a higher PrEP acceptability in the quantitative data (table 1): PrEP is an effective intervention to prevent HIV and PrEP prescription is part of the core assignments of the STI-clinic. Beliefs that were associated with a lower PrEP acceptability were: alternative HIV prevention strategies will be more effective; STI clinics are not the right place to prescribe PrEP; use of PrEP will increase STI incidence and; it is unethical to prescribe antiretroviral therapy for healthy individuals.

Conclusion
Overall, self-perceived PrEP knowledge was relatively low and PrEP acceptability was moderate among Dutch healthcare providers of sexual health clinics. In order to successfully implement PrEP in the future, PrEP knowledge should be increased and beliefs that are associated with lower PrEP acceptability need to be addressed in implementation programs.

Internet-based partner notification for HIV: an additional tool for provider and patient, no magic bullet

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Background
An internet-based partner notification system for verified diagnoses of STI/HIV was developed for use at STI clinics (GGD) and general practices (GP). Index patients receive a unique code from their professional to use www.partnerwaarschuwing.nl, sending standard notifications choosing a method per partner (email/sms; anonymous/non-anonymous). Partners receive with their notification a personal link/code, to check out for which STI they are notified.

Methods
Use of the webtool to notify for HIV was evaluated from 14 April 2014 - 2 September 2015. Numbers of created codes, used codes by professional and clients, and number of partners notified were extracted from the notification database.

Results
68 codes were created for clients with HIV/HIV co-infections to notify their partners (Figure 1); 33 clients did not notify their partners by the internet tool (49%), 16 sent notifications themselves (24%), and 19 let the professional send the notifications (28%). Men who had sex with men

| Table 1: Multivariate analyses of beliefs of PrEP associated with attitudes towards PrEP implementation (7-point scale: 1-low PrEP acceptability, 7-high PrEP acceptability) among 142 sexual healthcare providers of 23 STI-clinics, The Netherlands |
|-------------------------------------------------|---------------|-------------|
| Belief                                                                 |
| B     | 95%-CI       | P-value     |
| PrEP is an effective intervention to prevent HIV | 0.35 | [0.23:0.48] | <0.01 |
| PrEP prescription is part of the core assignments of the STI-clinic | 0.38 | [0.26:0.50] | <0.01 |
| Alternative HIV prevention strategies will be more effective | -0.12 | [-0.22:-0.01] | 0.026 |
| STI clinics are not the right place to prescribe PrEP | -0.12 | [-0.21:-0.02] | 0.017 |
| Use of PrEP will increase STI incidence | -0.13 | [-0.23:-0.02] | 0.015 |
| It is unethical to prescribe antiretroviral therapy for healthy individuals | -0.19 | [-0.31:-0.08] | <0.01 |

Note: Beliefs measured on a 7-point scale ranging from 1-completely disagree to 7-completely agree
(MSM) more often notified by themselves than heterosexual men/women (39/53=74% versus 6/15=40%, p=0.015). For non-HIV STI, less clients let the professional send the notifications (134/1929=7% versus 28%, p<0.001). The 16 clients with HIV who send notifications themselves notified 47 partners by the tool (mean 2.9); for the 19 clients for whom the professional send the notifications, 28 partners were notified (mean 1.5). The difference is related to MSM more often notifying themselves and having relatively more partners.

Partners who were notified by professionals more often not checked out the STI they were notified for than partners notified by clients (17/28=61% versus 11/47=23%, p<0.001). This may be explained by MSM more often sending notifications themselves and more often checking out for which STI they are notified than heterosexuals.

**Conclusion**

Clients with HIV often choose to let the professional send notifications by the webtool. 61% of partners notified this way do not check out the STI they are notified for, and thus remain unaware that they are notified for HIV. It is therefore of utmost importance that professionals who use the webtool to notify for HIV additionally try to reach partners by phone. This is in line with the new RIVM draaiboek “Partnermanagement”, which states that the professional has the obligation to make the best effort possible to notify partners, especially for HIV.

Partner notification is an important method to trace undiagnosed cases of (acute) HIV. Our Internet-based system is an additional tool in this, especially for MSM, but no magic bullet.
PATHOGENESIS

Neurometabolite alterations associated with cognitive performance in HIV-infected children

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Background
Despite treatment with combination antiretroviral therapy (cART), cognitive impairment is still observed in perinatally HIV-infected children. We aimed to evaluate potential underlying cerebral injury by comparing neurometabolite levels between perinatally HIV-infected children and matched controls.

Methods
This cross-sectional study evaluated neurometabolites, as measured by Magnetic Resonance Spectroscopy (MRS), in perinatally HIV-infected children stable on cART (n=26) and healthy controls matched for sex, age, ethnicity and socio-economic status (SES) (n=36). N-acetylaspartate (NAA), glutamate (Glu), myo-inositol (mI) and choline (Cho) levels were studied as ratios over creatine (Cre). Group differences and associations with HIV-related parameters, cognitive functioning and neuronal damage markers (neurofilament and total Tau proteins) were determined using age-adjusted linear regression models.

Results
HIV-infected children showed increased levels of Cho/Cre in white matter (+5.8%, p=0.045). Lower nadir CD4+ T-cell Z-scores were associated with reduced neuronal integrity markers NAA/Cr and Glu/Cr, and Center for Disease Control and Prevention (CDC) clinical stage C was associated with higher glial markers Cho/Cr and ml/Cr. Poorer cognitive performance was mainly associated with higher Cho/Cr in HIV-infected children, and with lower NAA/Cr and Glu/Cr in healthy controls. There were no associations between metabolite levels and neuronal damage markers in blood or CSF.

Conclusion
Compared to controls, perinatally HIV-infected children showed increased Cho/Cre in white matter, suggestive of ongoing glial proliferation. Levels of several neurometabolites were associated with cognitive performance, suggesting that MRS may be a useful method to assess cerebral changes potentially linked to cognitive outcomes.

The eye as a window to the brain: retinal structure associated with cerebral injury in perinatally HIV-infected children

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Objectives
While it is increasingly recognized that HIV-infected children are at risk for cerebral injury, retinal structure abnormalities were only recently detected. These deficits may have a shared pathogenesis, which could include HIV-induced impeded maturation, persistent neuroinflammation and (subsequent) neurodegeneration. We aimed to evaluate associations of retinal structure abnormalities with the severity of cerebral injury in perinatally HIV-infected children that were stable on combination antiretroviral therapy (cART).

Methods
Perinatally HIV-infected children (n=29) stable on cART were compared to healthy controls (n=35) matched for age, gender, ethnicity and socio-economic status. All children underwent 3.0 Tesla magnetic resonance imaging, from which gray (GM) and white matter (WM) volumes were determined using a T1-weighted sequence. Diffusion tensor imaging assessed WM diffusivity, thereby determining WM injury as reflected by reduced fractional anisotropy (FA) and increased mean and radial diffusivity (MD and RD). Spectral-Domain Optical Coherence Tomography (Topcon 3D OCT-1000) measured thickness of segmented retinal layers...
Correlations between total retinal layer thickness (RT), segmented layer RT, cerebral volume and WM microstructure were explored using two multivariable linear regression models: model 1 included HIV status and the interaction between HIV and RT, and model 2 included HIV status and separate RT variables for cases and controls.

**Results**

In HIV-infected participants, associations were found between RT and FA (foveal total RT: $\beta=0.062$, $p=0.010$), MD (foveal total RT: $\beta=-0.057$, $p=0.004$; pericentral total RT: $\beta=-0.066$, $p=0.005$) and RD (foveal total RT: $\beta=-0.079$, $p=0.002$; pericentral total RT: $\beta=-0.080$, $p=0.010$; see Figure 1). Further analyses revealed similar correlations for several segmented retinal layers. The majority of associations between pericentral layers and WM diffusivity were significantly different between HIV-infected and healthy participants (as reflected by a significant correlation coefficient for the HIV-RT interaction term). Additionally, the RT of several foveal and pericentral layers was associated with GM and WM volume in healthy participants, but not in HIV-infected participants.

**Conclusion**

Retinal thickness was associated with WM diffusivity in HIV-infected children, and with GM and WM volume in healthy children. Further research is necessary to clarify the pathogenesis behind these in parallel occurring cerebral and ocular deficits and to evaluate the potential role for OCT to noninvasively monitor intracerebral changes in pediatric HIV.

Abstract 43: Association between pericentral retinal thickness and radial diffusivity.
Are patients with well-suppressed HIV-infection at risk for HIV-associated neuroretinal degeneration? A comparative cohort study

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Background

Loss of neuroretinal structure and function has been reported in HIV-infected individuals treated with combination antiretroviral therapy (cART) without ocular opportunistic infections. Whether HIV-infected individuals with prolonged well-suppressed infection are still at risk for neuroretinal degeneration, is unknown.

Subjects and Methods

Ninety-two HIV-infected men with suppressed viremia on cART for at least 12 months and 63 HIV-uninfected, highly comparable, male controls, aged at least 45 years and participating in the ongoing AGEhIV Cohort Study, underwent an extensive ophthalmic assessment, including functional measurements of spatial (Pelli Robson charts) and temporal contrast sensitivity (TCS) and straylight as well as structural OCT based measurements of individual retinal layer thicknesses. Multivariable mixed linear regression models were used to assess possible associations between HIV-related and ocular parameters, while accounting for several known confounders.

Results

Pelli Robson CS was significantly lower in the HIV-infected group (1.89 vs 1.93 logCS, P-value=0.001) while TCS values did not differ among the two groups (2.17 logCS in both groups; P-value=0.888). Straylight values were higher among the HIV-infected individuals (1.15 vs 1.09 log units; P-value=0.026). Peripheral total retinal thickness in the HIV-infected group was slightly increased compared to the controls (279.8 vs 274.4 µm, P-value=0.029).

Conclusions

Pelli Robson CS was significantly reduced in HIV-infected individuals with prolonged well-suppressed infection; although the loss was only 1 letter and not clinically relevant. Instead of an expected neuroretinal thinning, an increase of retinal thickness was detected in the HIV-infected group, possibly due to chronic low-grade (para) inflammation, despite effective viral suppression. These findings should be further explored in longitudinal studies.

Circulating endothelial cells, as a marker for vascular damage, are increased in HIV infected children

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Background

Circulating endothelial cells (CECs) are mature endothelial cells discarded from the endothelium during normal homeostasis. An increased number of CECs is found in vasculitis, sickle cell anemia and several cancers in response to vascular damage. Endothelial damage also occurs in cardiovascular disease, a co-morbidity frequently seen in HIV. We hypothesized that CECs are increased in HIV infection and are correlated to factors associated with cardiovascular disease, such as insulin levels, dyslipidemia and the use of protease inhibitors.

Methods

At the time of abstract submission, a total of 25 patients with HIV at the Sophia children’s hospital in Rotterdam were included. Peripheral blood was collected using EDTA-containing tubes after routine laboratory samples to prevent potential contamination with endothelial cells from the venipuncture. Samples were stored at room temperature and examined within 24 hours after venipuncture. Flowcytometric analysis was performed to enumerate CECs in a total blood volume of 4 mL as described before (J Tromb Haemost 2012; 10: 931-9) for a reliable and validated quantification of this rare cell population. Based on literature and previous experience, we defined CECs as CD34+, CD45neg, CD146+ and CD105+. All patients provided written informed consent and the study protocols were approved by the local research and ethics committee.

Results

The mean age was 11.2 (SD ±4.7) years, 92% had a viral load below 50 copies/ml and the mean CD4 count was 1048 (±320) cells/m³. The median number of CECs was 50,07 cells per 4 ml, which is higher than normal values in adults, and comparable to numbers found in adult patients with metastatic colon cancer and hematological malignancies. Apart from a significant but weak association with bilirubin and alkaline phosphatase, we did not find any correlation with laboratory markers, including insulin, LDL, HDL and triglycerides. There was no correlation of CECs with the use of protease inhibitors, duration of infection, viral load or CD4 cell count.
Conclusion
CECs are increased in children with HIV who are successfully treated with antiretroviral therapy, but no correlation with markers associated with cardiovascular disease was found. We will investigate alternative mechanisms of vascular damage in these patients. Further research is warranted to unravel whether or not the higher CEC levels in children with HIV are associated with cardiovascular events.

Cross-sectional study on drug naive HIV-1 subtype C infected individuals to assess co-receptor tropism in relation to immune activation and TB status in a South African cohort

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Background
Switch from CCR5 (R5) to CXCR4 (X4) co-receptor tropism of HIV-1 subtype B is associated with rapid progression to AIDS, however, it remains largely unknown which factors cause the switch. Preliminary data in subtype B infection shows that the level of CD4+ T-cell activation (HLA-DR/CD38) one year post-seroconversion predicts subsequent R5-X4 switch. If T-cell activation is indeed a predictor of the co-receptor switch, one would expect that co-infection with M.tuberculosis, which is known to induce increased levels of T-cell activation, would lead to increased chances of driving a co-receptor switch. The objective of this study is to assess HIV-1 co-receptor tropism frequencies in a cross-sectional cohort of antiretroviral therapy (ART)-naive South African HIV-1 subtype C infected individuals and to investigate the correlation between host immune activation, TB-status and X4-tropism.

Methods
HIV-infected ART-naive patients, 18 - 45 years of age, have been enrolled at Ndlovu Medical Centre, South Africa. Venous blood has been drawn and plasma and peripheral blood mononuclear cells stored. Viral RNA was extracted from plasma and used for genotypic prediction of HIV co-receptor usage based on envelope glycoprotein sequences (env). Cellular markers for T-cell activation and dysfunction were correlated with TB status and tropism.

Results
116 patients have been enrolled in the study. Of these, 14 patients were retrospectively excluded. Full data is available.
on the first 46 included patients. Successfully deep sequenced env were aligned to a subtype C reference sequence showing 13%-26% of isolates predicted to be X4-tropic with an FPR of 5%-10% respectively. Using a clinical diagnostic algorithm, the TB status of 14/43 included patients (93%) has been determined, indicating the presence of active pulmonary TB in 32% (14/43) of included patients. X4 tropism correlated with CD4 counts (p=0.016), HLA-DR/CD38 in CD4 (p=0.037), HLA-DR in CD4 (p=0.046). TB status correlated with CD57 in CD8 (p=0.058), CXCR4 expression levels in CD4 (p=0.035), CD38 in CD8 (p=0.015), HLA-DR/CD38 in CD8 (p=0.0009).

Conclusion
In this preliminary analysis, X4 tropism prevalence is 13-26% in Subtype C HIV-1 drug naïve individuals. We show a strong correlation between X4 tropism and CD4 counts, immune activation (HLA-DR CD38 in CD4) as well as a strong correlation between TB and immune activation (HLADR CD38 in CD8). This has important ramifications in the way we understand HIV-1 subtype C pathogenesis.

No association between T cell activation and osteopenia or osteoporosis in older HIV-patients

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Background
A higher risk of developing osteopenia and osteoporosis has been seen in HIV-infected patients. Not only traditional risk factors, but also HIV-related risk factors contribute to this low bone mineral density (BMD). We examined the relation between BMD and T cell activation or bone turnover markers (CTX and P1NP) by comparing these in HIV-infected patients with a low BMD (T-score below -1) to those with a normal BMD (T-score above -1).

Methods
In this single visit pilot study, in patients that previously underwent DEXA scanning, bone turnover markers, T cell activation (CD38+HLA-DR+) and senescence (CD57+) of T cells was measured.

Results
Study participants (n=16), all male with a median age of 61 years (IQR 56-66) were enrolled. 3 had osteoporosis (T-score<2.5), 6 had osteopenia (T-score<1). No differences in activation and senescence were found amongst the groups. Furthermore, no relation with BMD was found. Second, no relation between T cell activation and bone markers was found. A relation was seen between higher bone formation (P1NP) and patients longer on cART (β0.26, 95%CI 0.0;0.46, p=0.01). The median length of cART was 5.5 years (IQR 4.5-7.8), with all patients on NRTIs, 88% on tenofovir (TDF), 63% on NNRTI’s and 38% on protease inhibitors (PI’s). A low BMD was seen in 100% of the patients on PI’s versus 30% of those on NNRTIs. A positive relation for current NNRTIs use with BMD was seen (β1.16, 95%CI 0.23;2.09, p=0.02), whereas current PI use was related to a decrease in BMD (β-1.16, 95%CI -2.09;-0.23, p=0.02). A relation for BMD with TDF could not be analyzed, as only two patients were not on TDF.

Conclusion
This study could not confirm a role for activated T cells in the pathogenesis of osteoporosis. The question then remains how to explain this increased osteoporosis prevalence, as activated T cells do not seem to influence its pathogenesis. Interestingly, this small pilot showed that cART influences BMD, with a negative effect for PI’s and a protective effect for NNRTIs. These results warrant further investigation.
Abstract 47: A/B. Differences in expression on CD4/8 CD8+ T cells by BMD. Relation between C. CTX and T score FEM D. P1NP and FEM E. cART use and P1NP.
**TREATMENT**

### First experience with dolutegravir as maintenance antiretroviral monotherapy in HIV-1 patients

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**Background**  
Dolutegravir is recommended as part of combination triple drug antiretroviral therapy (cART) for HIV-1 infected patients. Toxicities, drug interactions and costs related to cART still warrant the search for improved treatment options. Dolutegravir’s high barrier to resistance could make it suitable for antiretroviral maintenance monotherapy. However, the feasibility of this strategy is unknown.

**Methods**  
In this pilot study, we switched 4 consecutive integrase inhibitor naïve HIV-1 infected patients to dolutegravir monotherapy. All were HIV-RNA suppressed <50 copies/mL on their current cART. However, all had contraindications to their current or alternative antiretroviral treatment regimens (including tenofovir, abacavir, non-nucleoside reverse transcriptase inhibitors or CYP3A4-inhibitors) due to comorbidities, comedication or HLAB57-01 positivity. Patients were extensively informed on the experimental nature of dolutegravir monotherapy prior to the switch. They had never failed cART and could therefore be switched back to their original cART if HIV-RNA would rebound.

**Results**  
The four patients were caucasian males, including 3 patients above 60 years of age, who had been HIV-RNA suppressed <50 copies/mL for at least 1.5 years prior to the initiation of dolutegravir monotherapy. The HIV viral loads remained <50 copies/mL at week 4, 8, and 12, with continued virological suppression up to 24 weeks. One patient, with pre-CART HIV-RNA 625,000 copies/mL and CD4 nadir 120 cells/mm$^3$, had a single HIV-RNA 120 copies/mL at week 12 that returned <50 copies/mL afterwards.

**Conclusion**  
The results of this pilot study indicate that dolutegravir monotherapy may be a valuable maintenance option in selected patients, if confirmed by future randomized clinical trials. We are currently conducting a randomized clinical trial (DOMONO) in the Netherlands to evaluate the efficacy and safety this antiretroviral treatment option.

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### Renal toxicity due to concomitant exposure to tenofovir and inhibitors of tenofovir’s renal efflux transporters in HIV-1 infected patients

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**Background**  
Exposure to tenofovir-disoproxil-fumarate (TDF) may cause renal toxicity. Inhibitors of TDF’s apical multidrug-resistance-protein efflux-transporters (MRP) in the renal proximal tubule could enhance this unwanted effect.

**Methods**  
Cohort study with HIV-1 suppressed patients on TDF containing cART. Mean cumulative defined-daily-doses (DDD) of MRP-inhibitors (non-steroidal anti-inflammatory drugs (NSAID)/phosphodiesterase-5 inhibitors (PDE5-i)/salicylates) were collected. The effects of MRP-inhibitors on estimated glomerular-filtration-rate (eGFR) and proximal tubular function were evaluated by generalized-linear-models, adjusting for renal- and HIV-specific factors.

**Results**  
721 HIV-1 patients were included (76.3% males, median 45 years, 600 CD4-cells/mm$^3$). Median TDF exposure was 54 months, and total cumulative exposure was 3484 patient-years. Three-hundred-twenty-one patients had MRP-inhibitor exposure, ranging from 0.02 to 120 mean DDD/month. Exposure to MRP-inhibitors was associated with an additional mean eGFR decline over 12 months of -1.4 mL/min (95%CI: -2.9-0.1) in patients on ≥1 year of continuous TDF exposure. Associations were observed between high MRP-inhibitor exposure and eGFR declines >10mL/min since TDF initiation. The association with >25% eGFR decline since TDF initiation was also consistently observed in the subgroup analyses on patients with higher NSAID exposure (OR: 2.81, 95%CI: 1.21-6.49), or diclofenac exposure (OR: 3.69, 95%CI: 1.63-8.36) only. Overall, both in HIV-1 patients on >1 year of TDF exposure and those <1 year of TDF exposure, no clinically significant associations were found between MRP-inhibitor exposure (including the NSAID and diclofenac subgroups) and abnormal protein, glucose, or phosphate handling in the proximal tubule, or the presence of ≥2 of these markers of proximal tubular injury.

**Conclusion**  
Concomitant incidental exposure to MRP-inhibitors and TDF did not result in major additional TDF related renal toxicity in HIV-1 patients.
Uptake of generic nevirapine and associated cost-savings in a Dutch HIV treatment centre

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Background
Antiretroviral treatment (ART) is used by an increasing number of HIV-infected individuals, and for increasing lengths of time. As such, generic ART could lead to a significant reduction in costs for chronic HIV infection. Nevirapine was the first antiretroviral agent frequently used by patients at the time that generic formulations were licensed. This analysis evaluates the outcome of a pro-active substitution policy, to detect potential hurdles and factors influencing substitution to generics, and to calculate costs savings associated with generic substitution.

Methods
In mid-2013 generic nevirapine (immediate release formulation) became available in addition to Viramune® Extended Release (XR) in our outpatient pharmacy serving approximately 400 HIV-infected patients. Both prescribers and pharmacy assistants proposed patients to use generic nevirapine QD 400mg (2 tablets of 200mg). Interim results were presented to prescribers mid 2014 and consensus on the substitution policy was re-assessed. For this analysis, all patients with nevirapine visiting the outpatient pharmacy between April 1, 2015 and July 31, 2015 were evaluated.

Results
A total of 56 nevirapine users (44 males, 12 females) visited the outpatient pharmacy in the study period. Forty-one (73%) patients used generic nevirapine 400mg QD, the remaining 15 patients used Viramune XR 400mg QD. There were no statistically significant differences in age, gender or ethnicity between patients on generic vs. Viramune XR. Of 15 patients on Viramune XR 4 patients had not (yet) been asked to switch to generic nevirapine, 6 patients refused to switch, and 5 patients had tried the generic nevirapine but switched back to Viramune XR. Projected annual cost savings (assuming similar virological efficacy and tolerability) were predicted 1,826€ per patient, equivalent to a total of 74,868€ in our patient population, or 121,418€ if 100% with complete generic substitution with the cheapest generic manufacturer had been selected. Assuming a similar proportion of patients (73%) at all Dutch treatment centers would be substituted to generic nevirapine, this would save 3.5 million€ in 2015.

Conclusions
A pro-active policy for substituting HIV-infected patients on branded nevirapine (Viramune) to generic was highly successful, acceptable to all subcategories of patients, and cost-saving. Introduction of generic formulations for other ART drugs in the coming years will create opportunities for further cost-saving and rational allocation of available resources for chronic management of HIV, needed in a growing and aging population of HIV-infected individuals.

The effect of rosuvastatin on markers of immune activation in treatment-naive HIV-patients

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Background
Persistent immune activation has been implicated in the excess mortality in HIV-infected patients, due to non-AIDS-defining diseases such as cardiovascular diseases and malignancies. Statins have pleiotropic anti-inflammatory effects and may therefore modulate this immune activation and eventually decrease mortality. The aim of this study was to assess the capacity of rosuvastatin to improve the inflammatory profile of treatment-naive HIV-infected patients.

Methodology
We completed a randomized double-blind placebo-controlled cross-over study to explore the effect of 8 weeks of rosuvastatin 20 mg q.d. in treatment-naive male HIV-infected patients (n=28) on immune activation markers: neopterin, soluble Toll-like receptor (TLR)2, sTLR4, IL-6, IL-1Ra, IL-18, D-dimer, hsCRP and CD38 and/or HLA-DR expression on T-cells. Baseline data were compared with values of healthy male controls (n=10). Furthermore, the effects of rosuvastatin on HIV-1 RNA, CD4/CD8 T-cell count and LDL cholesterol were examined and side effects were registered using the validated MOS-HIV questionnaire and a complaints list. On an intention-to-treat basis, results were adjusted for treatment sequence, age and ethnicity, and analyses using linear mixed models and generalized estimating equations.

Results
Median age of patients was significantly higher than controls (40 vs. 27 yrs, p<0,01). Overall T-cell activation levels were higher in patients (e.g. CD38+HLA-DR+ of CD8+ T-cells 33.4 vs. 5.6%, p<0,01). Also, patients had higher levels of circulating IL-18, sTLR2 (503.5 vs. 322.5 pg/ml p=0.04 and 3.4 vs. 2.0 ng/ml, p=0.04) and of neopterin (19.52 vs. 5.35 nmol/l, p<0,01). Other markers did not differ between
patients and controls. Of 28 randomized patients, 20 completed the study. During rosuvastatin treatment, we observed a significant increase in CD4/CD8 T-cell ratio (RR 1.1, p=0.02). In non-Caucasian patients (n=5), the use of rosuvastatin resulted in a significant increase in IL-18 levels (OR 2.1, p=0.01). No effect on other markers was found. During rosuvastatin, the patients reported more flu-like symptoms (+16/100 points, p<0.01), and we found higher ALT and AST levels (OR 1.5, p<0.01 and OR 1.3, p<0.01).

Conclusions
As expected, HIV-infected patients had elevated T-cell activation markers. Also, circulating neopterin, IL-18 and sTLR2 levels were increased. Daily administration of rosuvastatin had a small but significant positive effect on CD4/CD8 T-cell ratio, but did not influence other markers of T-cell activation or soluble markers of innate immunity. The use of rosuvastatin resulted in more flu-like symptoms and higher ALT/AST levels.

Background
In 2004 a non-selective opt-out screening program for human immunodeficiency virus (HIV) in pregnant women was implemented in the Netherlands. This analysis aimed to evaluate the efficiency of antiretroviral treatment and pregnancy outcomes in patients who were diagnosed through the opt-out program compared to women with known HIV infection at conception.

Methods
This is a single-center retrospective cohort study in HIV positive pregnant women treated at the UMC Utrecht between 01-01-2004 and 01-03-2015. Only first pregnancy after HIV diagnosis was included in this analysis. Demographic, laboratory and pregnancy outcome data were collected from patients’ charts. Possible risk factors for a detectable plasma HIV RNA (viral load, VL) at delivery were analyzed using the chi-square or Fisher’s exact test. Statistically significant risk factors were subsequently analyzed in a multivariate logistic regression analysis.

Results
78 pregnancies were included in the analysis. 32 patients were diagnosed through opt-out screening (group 1), 46 patients had known HIV infection by conception (group 2). 5 (15.6%) patients in group 1 and 3 patients (6.5%) in group 2 had detectable VL at delivery (P = 0.26). Only baseline viral load >100,000 copies/ml was significantly associated with detectable VL at delivery after multivariate analysis (P = <0.05). Patients diagnosed with HIV during pregnancy

Treatment and pregnancy outcome in pregnant women with HIV infection diagnosed through opt-out screening versus patients engaged in HIV care before conception

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underwent significantly more emergency cesarean sections than patients with known HIV infection at conception (respectively 50% vs. 19.6%; P = <0.05), mostly due to a higher rate of (suspected) fetal stress (21.9% in group 1 vs. 10.9% in group 2; P = 0.41).

Conclusion
Although having got the diagnosis of HIV infection through the opt-out screening program was not associated with higher proportion of detectable viremia at delivery, when compared with patients with known HIV infection at conception, emergency caesarean section was necessary in a significantly higher proportion of these patients. These results are of concern and justify further research on a national level.

Development and evaluation of sensitive subtype-tolerant HIV DNA quantification assays using real-time PCR and digital PCR

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Background
Current antiretroviral therapy (ART) is unable to clear HIV, which persists as a latent reservoir of quiescent cells carrying integrated HIV DNA. The latent reservoir is the focus of cure efforts, the success of which is measured by a reduction of HIV DNA in the patient. HIV eradication strategies such as early treatment initiation and stem cell transplantation have led to small HIV DNA reservoirs and as the global availability of ART improves, patients with a wider range of HIV subtypes are being treated. Sensitive, reliable and subtype-tolerant HIV DNA quantification assays are therefore needed to quantify the small reservoirs that make up the barrier to HIV cure. Here, three HIV DNA quantification assays were tested for their sensitivity and subtype-(a) specificity using real-time PCR and digital PCR.

Methods
To evaluate the performance of candidate assays on a wide range of HIV genomic variability, a panel of isolates was cloned to represent subtypes A, B, C, D, F, G and circulating recombinant forms (CRFs) AE and AG, which together are responsible for 94% of HIV infections worldwide. Three assays that target Gag, LTR and Integrase were used to quantify the subtype clones in 5-fold serial dilutions from 15625 to 0.2 copies in a background of HIV-negative donor PBMC DNA using Applied Biosystems’ StepOnePlus Real-Time PCR (qPCR) and Bio-Rad’s QX200 Droplet Digital PCR (ddPCR).

Results
The three assays show disparate sensitivity for the tested HIV subtypes and CRFs. In qPCR, the Gag assay was able to detect 5-copy samples only for subtypes B and G and the Integrase assay detected 5-copy samples only for subtype C.
The LTR assay however proved highly subtype-tolerant, as it was able to detect 5-copy or lower input samples of at least one of two isolates of all subtypes and CRFs. The LTR assay limit of detection is significantly lower than that of the Gag and Integrase assays ($p<0.001$) and this difference holds true in both qPCR and ddPCR as the choice of platform was found not to influence the sensitivity or subtype-tolerance of the assays.

**Conclusions**
The LTR assay was shown to reliably detect 5-copy or lower input samples of all subtypes and CRFs. DdPCR was found not to influence the sensitivity or subtype-tolerance of any of the assays compared to qPCR, but future research should validate this finding and the performance of the LTR assay in clinical isolates.

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**High retention and viral suppression rates across all 27 HIV treatment centres in the Netherlands, but large variation in starting cART within one year after entry into care**

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Abstract 54: The percentage of patients entered into care in 2012 and 2013 who started cART within one year after entry into care are shown.
Background
Data collected by Stichting HIV Monitoring track the outcomes for virtually all individuals infected with HIV cared for across the 27 Dutch HIV treatment centres. We analysed scores of a number of outcome indicators (OI) and process indicators (PI) to gain insight into their variation between centres.

Methods
Indicators were derived from national HIV treatment and monitoring guidelines. OI focused on retention in care (percentage of patients in care on 1-1-2014 of those who entered care in 2012), initiation of cART (percentages of patients starting cART within 12 months of those who entered into care in 2012 and 2013), and achieving viral suppression in 2012, 2013 and 2014 (1. percentage of treatment-naïve patients with a HIV RNA level <400 copies/ml at 6 months after the start of cART, 2. percentage of all HIV-infected patients who received cART for at least 6 months with a HIV RNA level <100 copies/ml). As PI we analysed the proportion of patients who had entered into care in 2012 who were appropriately screened for hepatitis B (HBV) and C (HCV) co-infection within 12 months following entry into care.

Results
1,017/1,117 (91%) of patients who had entered into care during 2012 were retained in care (minimum 81%, maximum 100%). Figure 1 shows the variation in cART initiation between centres, overall and stratified by CD4 count. The median percentage of treatment-naïve patients with a HIV RNA level <400 copies/ml at 6 months increased from 98% in 2012 (minimum 60%, maximum 100%) to 100% in 2014 (minimum 93%, maximum 100%). The median percentage of all HIV-infected patients on cART for at least 6 months with a HIV RNA level <100 copies/ml was above 90% in 2012, 2013 and 2014, with medians varying between 98% and 100%. Percentages of patients screened for HBV and HCV within 12 months following entry into care varied markedly, with a maximum of 100% for both HBV and HCV, and a minimum of 50% and 67% for HCV and HBV, respectively.

Conclusion
Retention in care and both short- and long-term viral suppression rates were high across Dutch HIV treatment centres. Against the background of current guidelines recommending treatment for all patients regardless of CD4 count and screening for HBV and HCV, it is worth noting that in some HIV treatment centres initiating treatment among those entering into care with CD4 counts >350 cells/mm³ and screening for HBV and HCV may be improved.

Maraviroc intensification improves endothelial function in abacavir treated patients
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Background
The increased risk of abacavir on cardiovascular disease (CVD) in HIV-infected patients is still being debated. Maraviroc, a CCR5 blocker, has been shown to decrease immune activation and monocyte infiltration in atherosclerotic plaques, in murine experiments. Therefore, we examined the effect of maraviroc intensification on flow mediated dilatation (FMD) in abacavir-treated HIV-infected patients, and its effect on immunological and inflammatory parameters.

Methods
Open-label prospective crossover study with duration of 16 weeks: 8 weeks intervention (maraviroc intensification) and 8 weeks control (unchanged cART regimen). FMD, HIV-specific variables, expression of HIV co-receptors, markers of inflammation and coagulation, and cellular markers of immune activation were measured at weeks 0, 8 and 16. The changes (Δ) in these variables were compared between intervention and control periods using non-parametric tests. To evaluate the relation with the change in FMD linear regression modeling was used.

Results
21 male patients with suppressed plasma HIV-RNA, on cART, had a known HIV infection for 9.2 years (IQR 6.9-13.5) with abacavir use for 6.5 years (2.8-9.3). A significantly increased FMD of 0.73% (IQR -0.25-1.70) was seen after maraviroc intensification, compared to a decrease of -0.42% (IQR -1.89-0.25; p=0.049) in the control period. There was a negative relation between ΔFMD with ΔD-dimer (β -22.70, 95%CI -39.27:-6.13, p=0.011) and ΔCD95+ CD4+ T cells (β -0.16, 95%CI -0.28:-0.04, p=0.013), adjusted for age and duration of HIV.

Conclusion
Maraviroc intensification modestly improves endothelial function in HIV-infected patients on an abacavir-containing regimen, possibly by directly influencing the endothelium and indirectly by decreasing the activation of immune cells (T cells and monocytes) and coagulation markers.
Abstract 55: Study design (INT = intervention; C = control) B. Changes in the brachial artery FMD after maraviroc (intervention) or after control.

Once daily darunavir/ritonavir in HIV-infected children 6-12 years old: a pharmacokinetic validation of model-based dosing recommendations (DAPHNE)

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Background
Darunavir/ritonavir is one of the preferred agents as part of combination antiretroviral therapy for treatment of HIV-infected adults according to international guidelines. For children 3-12 years old, once daily dosing of darunavir/ritonavir has only recently been approved. Dosing recommendations for children 6-12 years old are based on a modelling and simulation procedure by the company. This pharmacokinetic study is designed to validate the proposed dosing recommendation for once daily darunavir/ritonavir in HIV-infected children 6-12 years of age.

Methods
This pharmacokinetic study is a multicenter phase-1 trial in twelve children on a stable antiretroviral regimen with a viral load <50 copies/mL. It is performed by paediatric HIV-centres in the Netherlands. Children should have taken darunavir tablets for at least 15 days following the approved dose: 600/100mg if 15-30kg; 675/100mg if 30-40kg; 800/100mg if >40kg. A 24h pharmacokinetic curve (7 or 8 samples) was collected after observed intake. Determination of pharmacokinetic parameters [area under the plasma concentration-time curve (AUC), maximum plasma concentration (Cmax), last observed plasma concentration in dosing interval (Clast)] was performed by non-compartmental analysis and are compared to historical data from HIV-infected adults from the ARTEMIS study.

Results
In this analysis we report the results of the first 7 children included, of which 4 are girls. Six have an African origin, one Latin American. Four children used 600mg, two 675mg and one 800mg darunavir. Median (range) AUC0-24, Cmax and Clast for darunavir were 57.2 (30.2-92.7) hr*mg/L, 5.3 (2.9-7.7) mg/L and 1.4 (0.92-2.4) mg/L, respectively. The median AUC0-24 is 65% of the AUC0-24 found in adults (87.9; range: 45.0-219 hr*mg/L). Six children had an AUC below the adult value. Median Clast was comparable to the value found in adults. Clast of all of the children was found to be adequate, since they were above 0.55 mg/L, which is the target for PI-experienced patients.

Conclusion
The overall exposure to darunavir (AUC0-24) was found to be highly variable and significantly lower than in adults. However, target Clast for darunavir was reached in all of the children.

No improvement in endothelial function despite decreased plasma lipids after switching protease inhibitors to raltegravir in HIV-infected patients

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Abstract 57: Study design (INT = intervention; C = control). B. FMD during study (INT:grey; C:black) C. Changes in FMD after switch and in control period

Background
Lipid management is one of the cornerstones of cardiovascular risk reduction. Treatment of HIV-infection with protease inhibitors (PIs) may cause dyslipidaemia, whilst the integrase inhibitor raltegravir (RAL) has a favourable effect on plasma lipids. We examined the effect of switching PIs to RAL on endothelial function, and its effect on immunological and inflammatory parameters.

Methods
We performed a 16-week open-label prospective crossover study; 8 weeks intervention (switch PIs to RAL) and 8 weeks of control (unchanged cART regimen). Flow Mediated Dilatation (FMD), inflammatory plasma and cellular markers of immune activation were measured at weeks 0, 8 and 16.

Results
Study participants with a median age of 50 years (IQR 42-60) and a known HIV-infection of 6.5 years (IQR 5.0-17.3), were on stable cART with undetectable HIV viral loads. After 8 weeks of intervention (RAL) an absolute reduction in FMD of 1.3% was found between the intervention (-0.81%) and the control (+0.54%) period and a significant decrease for total cholesterol (-17% versus +10%; p<0.001), LDL-cholesterol (-21% versus -3%; p=0.026) and triglycerides (-41% versus +18%; p=0.001), compared to the control period. For the intervention a relation between the change in percentage of human B-1 cells and the change in FMD was found (β 0.40, 95%CI 0.16;0.64, p=0.005). Furthermore, surprisingly an increased ALT was seen in 27% of the patients.

Conclusion
Switching PIs to RAL in this short-term study led to a reduction in endothelial function. Nonetheless a significant decrease in lipids was seen, which suggest that longer duration of RAL treatment might reduce the risk of CVD in HIV-infected patients. In patients switching from LPV/r to RAL an unexpected high incidence of ALT elevation was observed, fortunately this elevation was transient. Finally, an association between plasma B-1 cells and endothelial function was found, which warrants further investigation.

HIV care facility characteristics and the cascade of care in the Netherlands

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Background
Successful treatment of people infected with HIV requires that patients are retained in HIV care, use combination antiretroviral therapy (cART) and ultimately reach and sustain viral suppression. Our aim was to identify health facility characteristics associated with these steps in the cascade of HIV care.

Methods
In this retrospective cohort study, we included data from all adult HIV-1-infected patients who entered care in
the Netherlands between 2007 and 2013 (n=7120). Multivariate logistic regression was used to examine the associations between health facility characteristics and the outcomes ‘currently in care’, ‘initiated cART’ and ‘viral suppression’.

**Results**
The proportion of patients ‘currently in care’ was high in all 26 treatment centres. cART initiation was positively associated with the accreditation of the health facility (OR: 1.62; 95% CI: 1.18 - 2.23) and the performance of an internal audit in the preceding 3 years (OR: 1.36; 95% CI: 1.02 - 1.81). The odds of cART initiation were higher in middle-sized (OR: 2.00; 95% CI: 1.25 - 3.21) and large HIV treatment centres (OR: 1.80; 95% CI: 1.14 - 2.84) compared with small centres (<300 HIV-infected patients). The odds of viral suppression were lower in centres with a social worker in the HIV treatment team (OR: 0.62; 95% CI: 0.43 - 0.91).

**Conclusion**
Our results confirm that appointing expert HIV treatment centres facilitates retention in care and that a minimum volume requirement may be desirable. Our findings suggest that quality assessment through accreditation and the measurement of performance benefits the delivery of HIV care.

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**HIV cascade of care: improvements in linkage to care at the STI clinic of the Public Health Service Rotterdam-Rijnmond, The Netherlands**

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**Background**
The hiv cascade of care includes steps from testing to treatment. Once diagnosed, there are several steps determining the time between testing and linkage to care: Algorithm of hiv tests, communication of test results, way of referral to hiv treatment center, and confirmation of being in care. In the course of 2010 - 2015 processes have been changed in the STI clinic to improve linkage to care.

**Objectives**
To evaluate the efficiency of referral to the hiv treatment centers in Rotterdam we investigated the time between date of hiv test, date of referral to and first consultation at the hospital.

**Methods**
We followed newly diagnosed patients from January 2010 - March 2015 until linkage to care and collected data on time of hiv testing, discussing diagnosis, referral to and first consultation in care. Median time was calculated between testing, referral and first consultation in care, and regression analysis performed.

**Results**
We identified 227 newly diagnosed patients, of which six refused referral, nine were referred to hospitals outside Rotterdam, and 212 were referred to an hiv-treatment center in Rotterdam. 41 patients (19%) were lost to follow up, 37 (30%) between 2010 and 2012 versus 4 (4%) between 2013 and 2015. Of the 171 persons in care, the mean time between hiv test and arrival in hospital was 32 days, and decreased significantly (p = 0.004); median time was 39 days in 2010 and 14 days in 2015. The mean time between testing and referral was 18 days and decreased significantly (p< 0.001); (range median 22 - 9 days). There was no significant decrease in time between referral and arrival in hospital.

**Conclusion**
Time to entry into care can be improved in cooperation between STI clinic, laboratory and hiv treatment center. Active follow-up for those referred is needed to facilitate interventions for entry into care.

**Disclosure of Interest Statement**
No grants were received in the development of this study.

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**Changes in renal laboratory parameters and bone mineral density in treatment-naive HIV-1-infected adolescents initiating therapy with INSTI-based single-tablet regimens containing tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF)**

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Abstracts
Poster presentations
Background
EVG/COBI/FTC/TAF [E/C/F/TAF] and EVG/COBI/FTC/TDF [Stribild, STB] are integrase inhibitor (INSTI)-based single-tablet regimens (STRs) in clinical development for HIV-1-infected adolescents. Exposures of all components have been shown to be within the range associated with antiviral activity in adults. Preliminary comparative safety data through 24 weeks are reported.

Methods
Treatment-naive 12 to <18 year-olds weighing ≥35 kg with HIV-1 RNA >1000 copies/mL, CD4 >100 cells/μL and eGFR >90 mL/min/1.73m² received E/C/F/TAF or STB once daily in two ongoing 48-week, single-arm, open-label trials. Adverse events (AE), laboratory tests, bone mineral density (BMD) by dual X-ray absorptiometry and height-age adjusted (HA) Z-scores were assessed through Week 24.

Results
The E/C/F/TAF and STB trials enrolled 50 and 33 adolescents, respectively (median age 15 vs 16 years, 56% vs 30% female, 88% vs 76% Black, 22% vs 27% with baseline HIV-1 RNA > 100,000 copies/mL, median CD4 count 456 vs 407 cells/μL, median eGFR 156 vs 143 mL/min/1.73m²). Most AEs in both trials were mild and unrelated to treatment, with no deaths or AEs leading to treatment discontinuation. At Week 24, the median increase in serum creatinine was +0.08 mg/dL in E/C/F/TAF participants, with and +0.10 mg/dL in STB participants, with median eGFR decreases of -17.0 and -18.0 mL/min/1.73m², respectively, consistent with COBI’s inhibition of renal tubular creatinine secretion. Proteinuria (any grade) occurred in 26% of E/C/F/TAF participants vs 52% of STB participants, with Grade 2 or higher proteinuria occurring in 4% vs 21% of participants, respectively. Of those participants with BMD measurements at Week 24, the median increase in spine BMD was +1.98% in E/C/F/TAF participants, with a decrease of 24% in 3/41 participants (7%), versus a median decrease of -1.29% in the STB cohort, with a decrease of ≥4% in 6/20 participants (30%). Spine HA Z-scores decreased by -0.02 and -0.21 respectively.

Conclusions
Compared with STB, E/C/F/TAF exhibited similar effects on eGFR, a lower incidence and severity of proteinuria, and a median increase in spine mineralization. Both STRs were well-tolerated through 24 weeks. These findings support INSTI-based STRs as initial HIV-1 treatment in adolescents and suggest that TAF could offer safety advantages in pediatric populations.

Training healthcare professionals in resource-limited settings on HIV care and treatment: Implementation of a blended-learning training program in Sub Saharan Africa

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Background
The field of HIV treatment is changing rapidly. It is therefore of great importance that healthcare workers update their knowledge and skills to provide the best care for their patients. In Sub-Saharan Africa continuous medical education remains challenging. Due to the shortage of healthcare workers and the high workload, there is little time to attend trainings. Inadequate knowledge on part of the healthcare worker can become a barrier to initiate ART treatment and retain patients in care. To overcome this problem Health[e]Foundation developed an innovative blended-learning training program. The objective of this study was to enhance clinical knowledge among healthcare workers in Sub-Saharan Africa via a blended-learning training program on HIV care and treatment.

Methodology
In 2014 and 2015 a group of 250 nurses and doctors from Malawi, South Africa and Cameroon completed the Treat’n Care[e]Education training program. The training consisted of an onsite kick-off workshop, a 12 week distance-based self-study period and a two-day follow-up workshop. The program on an USB stick includes 16 modules and focuses on diagnosis and treatment of HIV. In addition there are modules on palliative care, mental health and human rights. The individual knowledge gain was assessed via pre- and post-test scores per module. During workshops additional data was collected, using a clinical case study and focus groups.

Results
The overall increase of knowledge after completion of the program was 11%. The most significant knowledge gain was found in the modules: ‘Initiation of Antiretroviral Therapy’ (14%) ‘Antiretroviral Drug Toxicity’ (25%) ‘Pediatric HIV infection’ (17%) and ‘Palliative care and HIV’ (24%). For each
of these modules the knowledge increase was significant (P < 0.005). At baseline healthcare workers scored on average 9 out of 20 points for the clinical case study, which increased to 12 out of 20 points after the course. The outcomes of the focus groups confirmed this flexible way of learning, via USB sticks and workshops, was highly valued. Although palliative care and drug toxicity were the most difficult topics they were considered very useful in daily clinical practice.

Conclusions
The results of this study confirmed that blended learning is an effective method to offer continues medical education to healthcare workers in resource-limited settings. However, more in-depth training is needed on palliative care and drug toxicity. Staying up to date with the latest development in HIV treatment is essential and can lead to a better quality of care for people living with HIV/AIDS.

Virological suppression among HIV-infected children in low- and middle-income countries: a systematic review and meta-analysis

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Background
Access to antiretroviral treatment (ART) in low- and middle-income countries (LMIC) has increased rapidly over the past ten years. Children on ART in LMIC constitute a vulnerable population to develop treatment failure, due to variability in pharmacokinetics, previous exposure to prevention of mother- to-child transmission, and limited experience of health workers with pediatric HIV-infection. Achieving virological suppression on ART is especially important in children, for whom few pediatric formulations are available and who will need adequate treatment for the rest of their lives. This review and meta-analysis aims to provide global summary estimates of virological suppression rates in HIV-infected children in LMIC, up to five years after initiation of non-nucleoside reverse transcriptase (NNRTI)- or protease inhibitor (PI)-based first-line treatment.

Methods
We systematically searched Medline, Embase, the Cochrane Central Register for Controlled Trials (CENTRAL) and the Literatura Latino Americana de Ciencias de Salud (LILACS) for randomized controlled trials, cohort studies, and cross-sectional studies published between January 2005 and May 2015. We extracted data on virological suppression six to 60 months after first-line treatment initiation and summarized the proportion of children with virological suppression at six-monthly time intervals using random-effects meta-analysis.

Results
Seventy-two papers, reporting on 51,347 children, were included in the analysis. Summary estimates of virological suppression (viral load <1000 cps/ml) after six, 12, and 24 months of ART were 71.3% (95%CI 67.9-74.6), 69.6% (95%CI 66.3-72.9), and 78.3% (95%CI 75-81.6), respectively (table). For NNRTI-treated children these rates were 65.5% (95%CI 56.7-74.3), 64.6% (95%CI 57.0-72.2), and 76.8% (95%CI 71.7-82.0), and for PI-treated children 77.2% (95%CI 66.8-87.6), 70.3% (95%CI 61.0-79.6), 74.2% (95%CI 58.6-89.7), respectively (figure).

Conclusion
In the most comprehensive literature overview of first-line ART in children in LMIC to date, virological suppression rates were 70-80% in the first two years of treatment, and 60-80% up to five years after ART initiation. These rates are considerably lower than the rate of approximately 85% found in adults in LMIC, and of >95% found children in high-income countries. Despite current efforts, such as the implementation of more potent PI-based treatment for all children <3 years of age, children in LMIC still have poorer treatment outcomes than adults. More attention should be given to strategies to increase virological suppression rates, including improved monitoring, increased access to and accelerated development of adequate and affordable first- and second-line ART.
Abstract 62: Summary estimates of the proportion of children with virological suppression at 6 to 60 months after treatment initiation

<table>
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First experience with interferon-free HCV treatment of HCV/HIV infected patients in the Netherlands


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Abstract

Background
In 2014 new direct-acting virals (DAAs) against hepatitis C became available in the Netherlands, enabling interferon-free treatment for patients in highest need. Furthermore phase-2 studies suggested similar outcomes for patients with or without co-infection with HIV. Here we describe our experiences in a cohort of HIV/HCV co-infected patients in our hospital.

Methods
We selected all patients with chronic HIV-HCV co-infection, who started the new DAAs that became available by compassionate use or licensing: sofosbuvir(SOF), daclatasvir(DAC), simeprevir(SIM) or ledipasvir(LED). We collected information on age, sex, previous HCV treatments, disease stage (cirrhosis, level of fibrosis (measured by fibroscan)), genotype, HIV status, HIV medication (cART) and need for cART change at baseline and the effects on both HCV and HIV infection during treatment. The primary endpoints were end-of-treatment response (EOT) and the sustained response 12 weeks after stopping HCV treatment (SVR12). The secondary endpoint was the amount and severity of adverse events (AEs) during treatment and the sustainability of the effect of the HIV treatment.

Results
From August 2014 eighteen HIV/HCV co-infected patients started DAA-treatment, at the moment of abstract submission twelve patients finished treatment and will be reported below: mean age was 55 years, there were eleven males and eight were HCV treatment naive. DAAs used: SOF/SIM (n=8), SOF/DAC (n=2), SOF/DAC/ribavirin (n=1) and SOF/LED (n=1). Ten had a METAVIR score higher than F2 (mean liver stiffness 14.3 kPa (SD 7.2)) and one had symptomatic cirrhosis. Genotype distribution: GT 1a (n=7), GT 1b (n=1), GT 3 (n=1) and GT 4 (n=3). All patients used cART with full HIV suppression, mean CD4 658/mm³ (SD 375). Six had to switch cART, because of potential interactions with the DAAs; 10/12 used integrase inhibitors.

All twelve patients had mild AEs (grade 1, fatigue, headache and nausea). There were two serious AEs, unrelated to the DAAs: fever due to Bartonellosis (grade 3) and ribavirin-related anaemia (grade 3). All twelve patients had an undetectable HCV at EOT. Six of them reached the SVR12 endpoint and all had undetectable HCV. HIV suppression was maintained for all patients during the entire period as well.

Conclusion
This small analysis confirms the claims from studies that DAAs appear to be very effective in HIV/HCV co-infected patients, with minor adverse events and no compromise of HIV-treatment. Future follow-up is necessary to demonstrate whether this virological success will translate into improved liver histology and better quality of life.
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Gilead Sciences doet onderzoek naar medicijnen om de behandeling van hiv, hepatitis B en C te verbeteren, met als ultieme doel deze aandoeningen te kunnen genezen.
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RETHiNK+

‘Toen ik in de eerste jaren trots aan buitenstaanders vertelde dat ViiV het enige bedrijf is dat voor honderd procent gefocust is op hiv, was de reactie vaak: ‘Leuk, maar wat is het verschil?’ Als ik nu aan buitenstaanders vertel wat ViiV allemaal doet, is de reactie: ‘Dat is een heel ander verhaal! ViiV probeert echt verschil te maken.’

‘ViiV lanceert de campagne RETHiNK+. Hiv-zorg in Nederland is goed, maar we willen onszelf en andere organisaties uitdagen: wat kan nog beter? Kunnen we de kwaliteit van leven van mensen met hiv verhogen door iets een beetje anders aan te pakken? RETHiNK+ stimuleert het uitwisselen van ervaringen door personen en organisaties voor het voetlicht te brengen die een rol spelen op het gebied van hiv.’

Bernhard Daut, directeur
ViiV Healthcare Nederland

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