



Rigshospitalet



UNIVERSITY OF COPENHAGEN



Centre of Global Excellence



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CHIP

Copenhagen HIV Programme

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Global Excellence



CHIP has been recognized as a Centre of Global Excellence by the hospitals of the Capital Region of Copenhagen and on 28 September 2010 was presented with an award of 1.5 million Danish kroner. As one of 10 centres in Denmark to receive the award, CHIP was acknowledged as a hub for international world-class research in the area of HIV. CHIP, active for many years in the dissemination of results, training and patient care, appreciates the recognition on a national level and hopes this award will lead to further development of national collaborations. The direct collaboration with both the University of Copenhagen and clinical departments at Rigshospitalet, namely the Finsen Centre, is one of CHIP's strengths and reinforces the high quality results produced by the various projects and studies conducted and coordinated by CHIP. In addition, CHIP's innovative work and large international network prove useful in other areas of infection and viruses, such as influenza preparedness for H1N1.

Foreword

During the fall 2010, Rigshospitalet – Copenhagen University Hospital has developed its vision and goal to become the international hospital of Denmark by 2020. The strategy focuses on specific elements: Global Excellence, Partnership, Research, Productivity & Resource Optimising and the Good Working Life.

The Global Excellence strategy will assist Rigshospitalet to offer patients a highly specialised treatment on an international level and aims to ensure that Rigshospitalet will be among the 10 best research hospitals in Europe by 2020. The global excellence strategy is a collaborative effort between the Capital Region of Copenhagen and the Copenhagen University with the aim to support competent academic groups with a recognised high international research profile. Ten Global Centres of Excellence were announced in October, of which Rigshospitalet houses six – and we are very proud that Copenhagen HIV Programme is one of the six Global Excellence in Health Centres. The strategy implies that these centres of excellence will act as lighthouses to inspiration for other groups striving to reach an international level of their research.

CHIP has a long history of top-end research in HIV, but we find it very inspiring that CHIP has been able to extend its activities to include research in H1N1 influenza as well



Jannik Hilsted, MD
Chief Medical Officer, Rigshospitalet

as the innovative set-up of monitoring viral infections in transplant patients to ensure optimal treatment and improved organ survival in the recipient as effectuated in the MATCH initiative described elsewhere in this annual report. We are convinced that CHIP will fulfil the expectations inherent in being awarded the Global Excellence in Health status.

From the Director

The future mission and vision for CHIP

CHIP aims to perform front-line research that informs the clinical handling of persons suffering from infectious diseases in general and specifically HIV, while the scientific methodology applied has to be state-of-the-art. All proposed projects are evaluated against these overall aims and only research ideas that fulfill both will be considered for further development.

The name CHIP encompasses HIV and a large section of research within CHIP will remain focused on this virus, including the ongoing effort to disseminate the results of our research in training and outreach, not least in developing e-learning and e-tools. But our aim has all along been to also focus on other pathogens. This is exemplified in the ongoing CHIP research projects on infectious (tuberculosis and viral hepatitis) and non-infectious (cardiovascular disease, diabetes, renal disease) co-morbidities seen in HIV-infected persons, on bacterial infections in the intensive care setting (the PASS and CASS studies), on pandemic influenza, on post-transplant infections (the MATCH initiative). I have the distinct impression that CHIP's research profile will continue to diversify in the years to come.

So why diversify? Firstly, the innovation potential for HIV research is now reduced compared to what was the case 10 years



Jens D. Lundgren

ago. Critical research questions of strategic relevance for the clinical management of the HIV infection itself have been resolved. The only pending question that is realistic to solve is: When in the course of the HIV infection should antiretroviral therapy be initiated? We are currently addressing this question in the START study. Secondly, challenges in infectious disease are wider reaching than merely HIV. Hence, it is actually an ideal situation to apply to other areas the research capabilities and infrastructure that have been built to get HIV research where it is now.

History

The Copenhagen HIV Programme (CHIP) was developed on the basis of the international network originating from AIDS in Europe and the EuroSIDA study. Since 1994 European research activities have been coordinated from our group. In 1998 this effort was further developed into a trial unit with the capabilities of planning and execution of randomized, controlled trials according to the ICH-GCP guidelines. CHIP was also designated as a research section within the department of infectious

diseases at Hvidovre University Hospital, which had a long tradition for clinical management of HIV-infected persons and was among the first to diagnose and treat AIDS patients when the epidemic first broke out.

In 2002 CHIP became an independent research department. CHIP's main office is now located at the University of Copenhagen, the Faculty of Health Sciences in Copenhagen, Denmark - with cooperating offices in Germany, UK, Spain and Portugal.

International position and affiliation

CHIP has developed substantial expertise and is internationally recognized for leadership, coordination and support of clinical research and consulting, teaching and outreach. CHIP is collaborating with more than 200 clinical departments, research teams and institutions in Europe, USA, Canada, Argentina and Australia including the National Institutes of Health (NIH), USA; University of Minnesota, USA; Medical Research Council, Clinical Trials Unit, UK and The National Centre in HIV Epidemiology and Clinical Research, (NCHECR) Australia.

Presently, CHIP has a full-time staff of 47 persons consisting of physicians, PhD students, statisticians, IT experts, clinical monitors, laboratory technicians and administrative staff, as well as a group of part time physicians and students. CHIP has 5 local employees at the Site Coordination Centres in Frankfurt, Germany and Madrid, Spain and funding through CHIP allows University College London, Royal Free Hospital, to secure statistical resources for CHIP activities corresponding to 3 positions.



Aim & Function

The aim of CHIP is the execution of front-line research related to infectious diseases, in particular HIV, in order to improve the treatment and management of patient care. The direct collaboration with Rigshospitalet ensures a constant linkage to patient care and management so that experiences from the clinic can be directly translated into research and teaching. CHIP's activities include international randomized studies in management of treatment strategies and cohort studies focusing on epidemiology, treatment, side effects and development of resistance.

Early detection and treatment of HIV as well as dissemination of knowledge via web-based tools, training, and curriculum devel-

opment (namely, a Master in HIV education) are prioritized areas. Recently, CHIP's core theme of clinical HIV has been complemented with research on other communicable diseases including the pandemic influenza virus (H1N1v). Other high impact research accomplishments include the design and implementation of the "Data Collection on Adverse Events of Anti-HIV Drugs" (D:A:D) study (+50,000 patients followed since 1999), and the EuroSIDA study (a prospective observational study of over 16,000 patients in over 100 clinics in 33 countries).

International Randomized Trials

CHIP takes on the responsibility of coordinating international trials for other scientific groups, where the knowledge and experience of working in the Scandinavian and European countries can contribute and ensure the quick and safe set-up of the trials.

Study	Objective	Number of patients	Number of centres	Number of countries
The ESPRIT Study	The main objective of the study was to compare the effects of subcutaneous recombinant interleukin-2 (SC rIL-2) and no SC rIL-2 on disease progression and death over a 5 year follow-up period in HIV-1 + patients who have a CD4+ cell count above or equal to 300 cells/mm ³ . The study was completed in 2009.	4150	73	23
The START Study	The main objective of the START study is to determine whether starting antiretroviral therapy (ART) early (before the CD4 count drops to less than 500 cells/mm ²), rather than waiting until the CD4 count drops to less than 350 cells/mm ² as current guidelines recommend, reduces the occurrence of serious morbidity and mortality.	900	58	22
The SMART Study	A large, long-term, randomized trial comparing two anti-retroviral treatment strategies. Patients were randomised equally (1:1) to either the Drug Conservation (control) group or the Viral Suppression (experimental) group. The primary endpoint was clinical HIV-related disease progression or death.	5472	318	23
The H1N1v Studies	FLU 002 (An international observational study to characterize adults with Influenza A - Pandemic H1N1 [H1N1v]) and FLU 003 (An international observational study to characterize adults who are hospitalized with complications of Influenza A - Pandemic H1N1 [H1N1v]) opened in September 2009 and enrolled patients in order to follow the pandemic.	988	73	20
National Randomized Trials				
The PASS Study	The PASS study is a randomized, singleblinded, multi-centre trial to investigate if clinical management guided by daily standardized procalcitonin measurements can reduce mortality in critically ill patients.	1200	9	Denmark
The CASS Study	Cooling and Surviving Septic Shock is a randomised trial to determine whether mild induced hypothermia via apoptosis-inhibition, metabolism-lowering, anti-coagulation and inhibition of bacterial growth can improve survival among patients with septic shock.	560	15	Denmark



START

Strategic Timing of AntiRetroviral Therapy (START) is an international randomized trial comparing early antiretroviral therapy (ART) vs. deferred ART. The purpose of START is to determine whether the immediate initiation of ART in HIV-1 infected persons, who are antiretroviral naïve with a CD4+ lymphocyte count above 500 cells/mm³, is superior in terms of reducing the occurrence of serious morbidity and mortality, compared to deferral of ART until CD4+ lymphocyte count declines below 350 cells/mm³, as most of the current guidelines recommend.

The pilot phase of the START study was successfully completed in September 2010 and based on the pilot phase performance, funding for the definitive phase of the START study has been granted by the Division of AIDS (DAIDS, NIH).

CHIP is one of four international coordinating centers (ICC) within the INSIGHT network. For the pilot phase of the START study, CHIP was responsible for coordinating 28 sites in Belgium, Denmark, Finland, Germany, Poland and Spain. In the definitive phase of the study CHIP will be expanding to 59 sites in 13 countries, enlarging the study group to include Austria, Czech Republic, Estonia, Luxembourg, Norway, Portugal and Sweden.

The aim is to recruit a total of 4000 participants worldwide by the end of 2012:





Sub-studies

There are 5 sub-studies in START to which the sites are committed to engage and contribute: Informed Consent, Neurology, Genomics, Arterial Elasticity Pulmonary and Bone Mineral Density. Sub-study participation is based on recruitment potential and geographical diversity.

START has major scientific merits and all the sub-studies raise appealing supplementary research questions focusing on various organ dysfunctions, which HIV and antiretroviral therapy may either improve or further deteriorate.

FLU 002 and 003

Observational studies to characterize adults with influenza A pandemic (H1N1v)

FLU 002 and FLU 003 are two international observational studies on the pandemic Influenza virus (H1N1v) with the objective of describing the outcome of patients who seek medical care for an influenza-like illness (FLU 002) and those who are hospitalised with severe or complicated influenza A (FLU 003). Both studies are funded by the U.S. National Institutes of Health.

As one of four International Coordinating Centres (ICCs) within the International Network for Strategic Initiatives in Global HIV trials (INSIGHT), CHIP is responsible for the imple-

mentation and conduct of the FLU studies at 28 sites in 10 European countries: Austria, Belgium, Denmark, Estonia, Germany, Lithuania, Norway, Poland, Portugal and Spain. Depending on how the H1N1v pandemic unfolds, the goal is to enrol 5000 patients in FLU 002 and 1000 patients in FLU 003. As of November 2010, the total numbers of enrolled patients are 1047 in FLU 002 and 315 in FLU 003.



NEAT

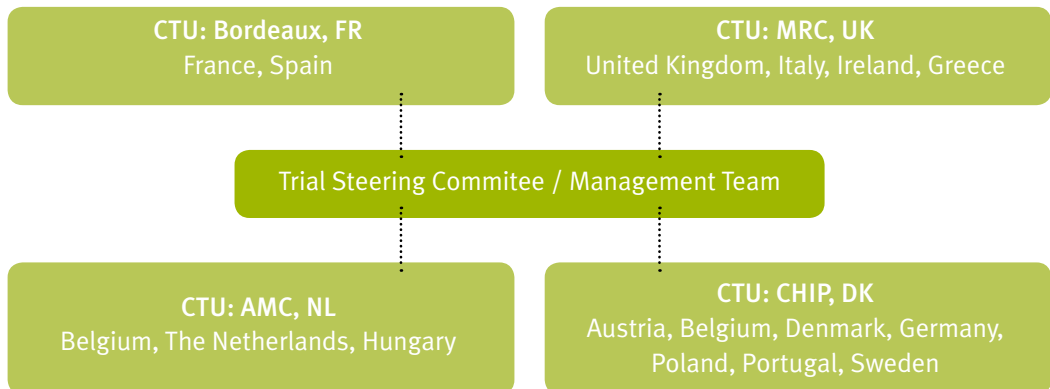
NEAT 001/ANRS 143 is a phase III, multicentre open-label randomized trial comparing the efficacy and safety of two first-line regimens in HIV-1-infected antiretroviral naïve subjects: darunavir (DRV)/ritonavir(r) + tenofovir (TDF)/emtricitabine (FTC) vs. DRV/r + raltegravir (RAL).

Throughout 2010 extensive preparations have been ongoing, including the set-up of trial logistics and obtaining approvals from Ethics Committees and Competent authorities. CHIP is one of four Clinical Trials

Units (CTU) within the NEAT network and is responsible for the implementation and conduct of the trial at 22 sites in 7 countries, as well as for establishing an Endpoint Review Committee.



NEAT 001 Organization



PASS

The Procalcitonin And Survival Studies

The PASS study was completed on 30 June 2009 and the primary results were presented at the Infectious Diseases Society of America Meeting, Philadelphia, October 2009. Since then, several studies exploring organ failure, life quality and mortality in critically ill patients have begun to use the PASS database and biobank.

- Use of medical ventilation until day 28
- Antibiotic prescriptions until day 28
- Creatinine, carbamide, platelets and bilirubin until day 28

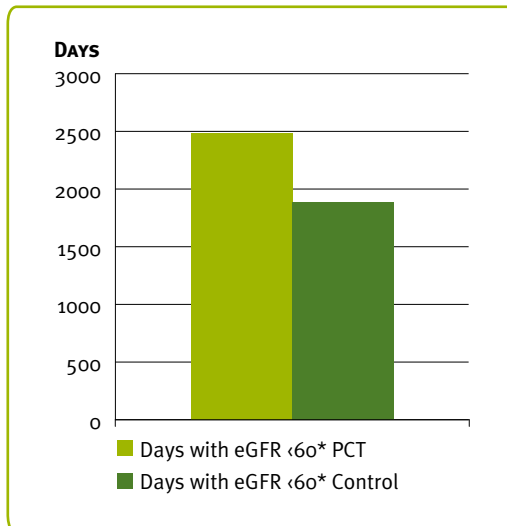
Studies currently conducted focus on renal organ failure, lung failure, fungal infections and quality-of-life after admission to the intensive care unit.

Status

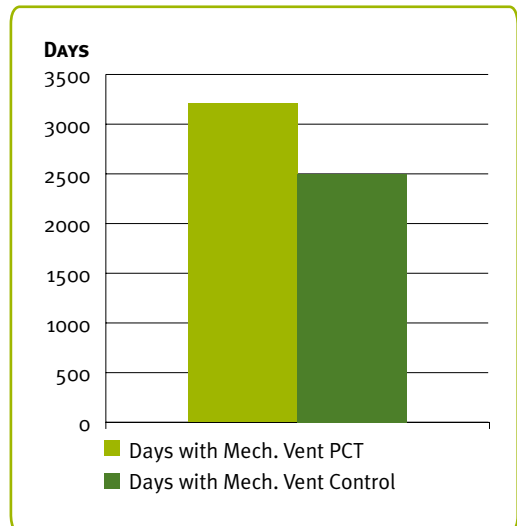
Follow up is now complete for:

- All data from the ICU
- Microbiology from baseline to day 28
- Vital status until 180 days after discharge
- All admissions in Denmark until day 180
- Use of dialysis until day 28

Renal failure (biochemically defined)



Respiratory failure



ICU-division at CHIP: Jens-Ulrik Jensen, MD, PhD, Kristian Reinholdt, med.stud., Maria E. Johansen, med. stud., Marie Louise Jakobsen, RN, Clin. Monitor, Zoe Fox, MSc, PhD, Jesper Kjær, MSc, Jesper Grarup, DVM, Jens D. Lundgren, MD, DMSc





The Cooling And Surviving Septic Shock study is a randomized trial to determine whether mild induced hypothermia via apoptosis-inhibition, metabolism-lowering, anti-coagulation and inhibition of bacterial growth can improve survival among patients with septic shock.

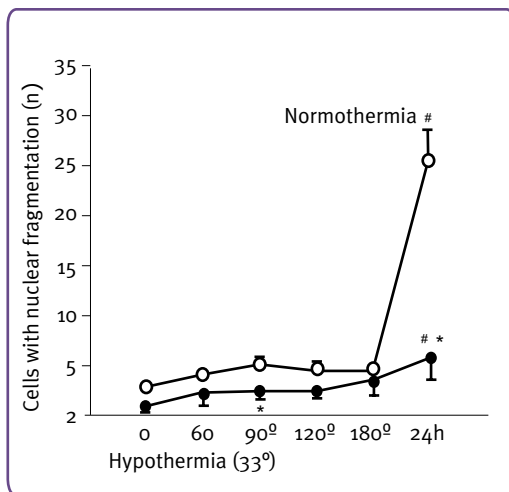
- In the US, about 750,000 sepsis cases per year
- Mortality of 35-60%

Despite numerous randomized trials, only few evidence-based effective therapies have been developed and mild induced-hypothermia has so far only been used sporadically.

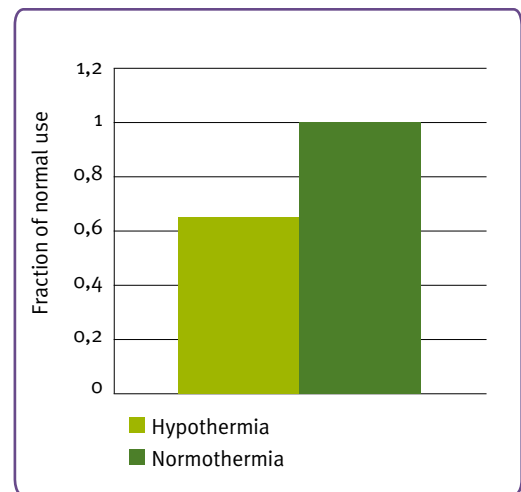
Facts about severe sepsis and septic shock

- In Denmark, about 1/5 of all ICU patients develop severe sepsis or septic shock

Anti-Apoptosis (2)



Metabolism lowering (o2-consumption) (1)



References

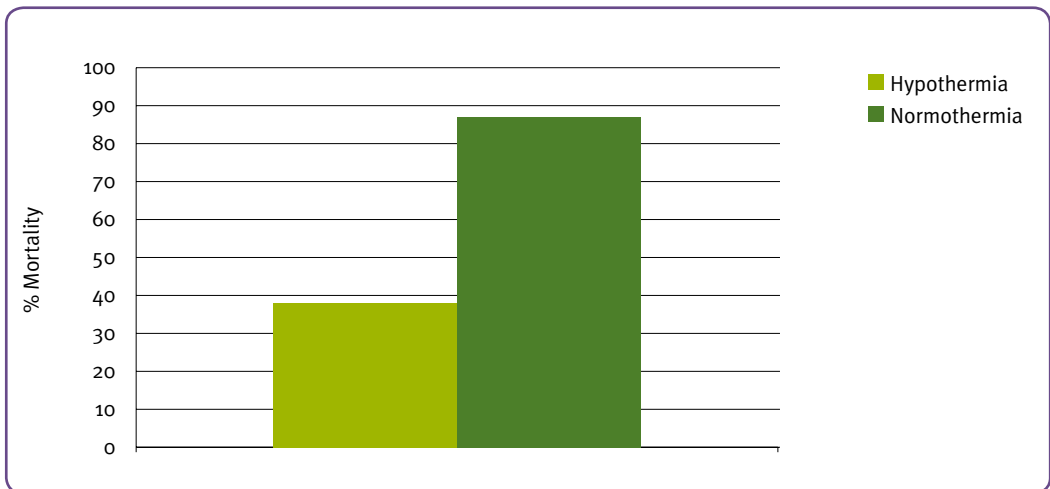
1 Mechanisms of action, physiological effects, and complications of hypothermia. KH Polderman.

Crit Care Med. 2009 Jul;37(7 Suppl).S186-202

2 Surface cooling inhibits tumor necrosis factor-alpha induced microvascular perfusion failure, leukocyte adhesion, and apoptosis in the striated muscle. S Westermann, B Vollmar, H Thorlacius, MD Menger.

Surgery. 1999 Nov;126(5):881-9.

Mortality - animal experiments



CASS – Steering Committee & Principal Investigators

- Else Tønnesen (Chair, Århus)
- Niels-Erik Drenck (Roskilde)
- Hamid Tousi (Herlev)
- Morten Steensen (Hvidovre)
- Peter Søre-Jensen (Herlev)
- Jesper Løken (Hvidovre)
- Morten Bestle (Hillerød)
- Hans Christian Boesen (Glostrup)
- Lars Hein (Hillerød)
- Jens-Ulrik Jensen (Hvidovre/Panum)
- Thomas Mohr (Gentofte)

- Christian Østergaard (Hvidovre)
- Kim Michael Larsen (Århus)
- Bettina Lundgren (RH)
- Mads Holmen Andersen (Århus)
- Jens D. Lundgren (Panum)
- Maria Johansen (Panum)
- Palle Toft (Odense)



Ongoing Cohort Studies

Study	Objective	Number of participants	Number of centres	Number of countries
The EuroSIDA Study	The main objective of the study is to assess the impact of antiretroviral drugs on the outcome of the general population of HIV-infected patients living in Europe.	16,505	103	33
The D:A:D Study	The objective of the study is to assess the incidence of myocardial infarction and other serious adverse drug reactions on HIV/AIDS patients who are receiving anti-retroviral therapy.	50,000	188	21
The PARTNER Study	The main objective of the study is to precisely estimate the rate of transmission of HIV to an ongoing unprotected sex partner in persons with current plasma viral load <50 copies/mL on ART, and to assess factors associated with transmission.	1650	52	16
The HIV/TB Study	The main objective of this project is to describe and analyse the best clinical approach to interactions between HIV and TB therapies in Eastern and Western Europe, the overlapping toxicity between these treatments and the role of prophylaxis against TB.	1075	12	12
Indicator Disease Guided Testing	The objective of this project is to identify which of eight indicator diseases have an HIV prevalence of over 0.01% in order to better inform testing guidelines.	7500	14	18
COHERE	The main objective is to conduct epidemiological research on the prognosis and outcome of HIVinfected people from across Europe including pregnant mothers, children, and adults which require a large sample size.	246,600	110	33

D:A:D

At a glance

Study Overview (status as of November 2010)	
Patients enrolled	>49,000
Number of clinics	212
CD4 count measurements	1013478
Total Person-years of follow-up	300,004
Triglycerides measurements	516,224
Centrally validated endpoints, MIs	718
Non-AIDS defining malignancies	971

The D:A:D study expanded in 2010 with the inclusion of more than 16,000 patients in cohort III and initiated the collection of 3 new end-points (non-AIDS defining cancers, chronic liver disease and end-stage renal disease) for central validation at the D:A:D coordinating centre at CHIP.

What's next?

Due to its large size, the D:A:D study will have the potential for exploring possible relationships with drug exposure and rare outcomes such as end-stage renal disease and chronic liver disease in the years to come. From 2010 onwards the study will focus on the associations with long-term drug exposure and long-term complications, in particular non-AIDS defining cancers and risk factors for the development of chronic kidney disease. Additionally, the D:A:D study will assess the relationship between immunodeficiency and non-fatal cancer outcomes.

EuroSIDA

At a glance

Study Overview (status as of November 2010)	
Patients enrolled	16 500
Number of countries	35
Number of clinics	103
Total Person-years of follow-up	108 908
Viral load measurements	318 816
Plasma samples collected	59480

What's next?

EuroSIDA received renewed funding for a 5-year period from the European Commission under their 7th Framework Programme. One of the unique contributions of the EuroSIDA study is the ongoing follow-up in patients from Eastern Europe. Today EuroSIDA is fol-

lowing 4000 patients from Eastern Europe.

This follow-up provides unique information about clinical care and disease progression in the region as well as allowing for comparisons to other regions in Europe.

The study has produced a total of 137 articles in peer-reviewed journals, of which 13 were published in 2010.



The CoDe Project ("Coding of Death in HIV")

Scientific purpose

The CoDe project was initiated in 2004 out of the need to harmonize and standardize the approach taken when collecting data and reviewing the causes of death in HIV-1 infected patients. This has become increasingly necessary as a significant proportion of deaths in HIV-1 infected persons are now caused by non-AIDS events. Many illnesses that are related to HIV-infection are poorly identified in the ICD system, and some diseases (e.g. CNS diseases, renal disease) have a different aetiology in HIV patients and are therefore not covered by the ICD system, or are at great risk of mis-classification.

Methods

CoDe is a uniform coding system that can be applied to studies of individuals with HIV infection, including:

- A detailed data collection on the causes of death and contributing factors, and
- A centralized review process of the data collected.

All study documents, CRFs, and other materials are free to use and accessible online at www.cphiv.dk/CoDe.

TB:HIV project

In 2010 the retrospective phase of the "Co-infection with Mycobacterium tuberculosis among HIV-infected patients in Europe" or HIV/TB project was completed.

In 2009 the HIV/TB project has documented pronounced differences in survival of HIV/TB patients in Eastern compared to the other regions Europe: HIV/TB patients in EE, compared to those in the other regions, were at 3-5-fold increased risk of death within the first year after TB diagnosis.

Detailed analysis of causes of deaths revealed that patients in Eastern Europe were more likely to die of TB whereas patients from other regions were more often dying of causes other than TB. We hypothesized that the reasons for differences in survival

may include access to and use of health care across Europe.

Funding from EuroCoord provided the opportunity to extend the HIV/TB project into the prospective phase starting from 2011. During this phase we plan to enroll at least 1200 HIV-infected patients with active TB disease from existing and new collaborative centers. The two main objectives to address will be various clinical aspects and management of HIV/TB patients and temporal trends in the epidemiology of the co-infection.

TB:HIV 



- This compared with 44% in sub-Saharan Africa (UNAIDS, 2008, 5a)
- To support the implementation of the consensus definition of late presentation and the use of multiple methods to estimate the number of undiagnosed
- To initiate audits to evaluate whether HIV testing is being conducted in situations where there is an obvious indicator (and if not, why?)
- To increase interaction and raise awareness among clinicians within different specialities and implement indicator disease guided testing
- To develop and implement evidence-based strategies to reduce the barriers to testing due to stigmatisation, discrimination and criminalisation
- To stimulate health professionals, policy-makers, civil society and PLHIV to advocate and collaborate

HIV in Europe

The HIV in Europe Initiative

HIV in Europe is a pan-European initiative with the overall objectives to:

- 1) Determine and work towards reducing the number of people living with HIV in Europe who are unaware of their serostatus;
- 2) Identify political, structural, clinical and social barriers to achieving optimal counselling and testing and earlier access to care;
- 3) Promote evidence based practices and guidance on HIV testing in Europe;
- 4) Study the proportion of people living with HIV presenting late for care.

Achievements 2010

- Consensus definition of late presentation published and used in several presentations and publications (ex. European Centre for Disease Prevention and Control (ECDC) 2010 Special Report).
- Improved methods to estimate the number of infected not yet diagnosed people living with HIV.
- Indicator disease guided testing on the European (testing) agenda.
- Initiatives started to develop and implement evidence-based strategies to reduce the barriers to testing due to stigmatization, discrimination and criminalization.
- Communications policy and strategy 2010-2012.
- On December 1st 2010, World AIDS Day, the European Centre for Disease Prevention and Control (ECDC) launched its new HIV testing guidelines in the European

Parliament to support countries to improve their national HIV testing strategies. HIV in Europe and Jens Lundgren have been part of the ECDC Technical Advisory Group on HIV testing and presented at the launch of the guidelines with participation of the Belgian Minister of Social Affairs and Public Health for the Belgian EU Presidency, Laurette Onkelinx, Member of the European Commission John Dalli, ECDC Director Marc Sprenger among others.

The HIV Indicator Diseases Across Europe Study

In autumn 2009, a pilot study was initiated to develop and evaluate the best methods to estimate HIV prevalence of conditions handled by the health care system and to estimate which of 8 conditions have an HIV prevalence of >= 0.1% in various settings in Europe.

Throughout 2009-2010, the 38 surveys were launched in 17 centres in 14 countries. As of December 2010, 2700 patients were enrolled into the different surveys. The surveys were intended to capture the number of patients who tested HIV positive when they went to the clinic or hospital department with one of the indicator diseases (listed in the graph below). We know that many HIV patients are being diagnosed late and are entering care when the disease has advanced. We also know that some have been in contact with the health system for other symptoms prior to an HIV test and diagnosis.

EuroCoord

The EuroSIDA, COHERE and HIV-TB activities coordinated or managed by CHIP are being conducted under the umbrella of EuroCoord for the period of the five-year funding circle which began 1st January 2011. The successful achievement of securing the funding has been a challenge, but we are now eager to get started to ensure that the many deliverables we are responsible for can be met in a timely manner.

EuroCoord CHAIN

The EuroCoord founding networks have been responsible for a resistance project through CHAIN. This project is now under finalization and a publication is expected shortly. The merger and analysis of resistance data from a large number of individuals has allowed for presentation of results beyond what each independent cohort would have been able to achieve individually. The project was made possible due to a valuable contribution from Gilead.

ACTIVATE

The founding networks behind EuroCoord have been collaborating on a finalization of the ACTIVATE project activities. ACTIVATE (capACity building and Training in HIV/Aids Treatment and management across Europe) was funded until 2010 by DG SANCO. The experience CHIP gained through developing and conducting training sessions for infectious disease physicians in Minsk, Belarus has contributed to the extension of CHIP's network in Eastern Europe and will form the basis for continued activities within EuroCoord. The experience has also been utilized in CHIP's collaboration with the WHO on

establishing an electronic platform for training under the Monitoring Medicines project funded by the EU and focusing on benefits and risks of antiretroviral therapy.

IWHOD (International Workshop on HIV Observational Databases)

In 2009, EuroCoord, in partnership with the scientific committee (SC) of the IWHOD, took over the organisation and administration of the cohort workshop.

The cohort workshop involves cohorts from Europe, Australia, North America and resource limited countries. The presented data at this workshop is not made public, thereby allowing for discussion of work-in-progress.



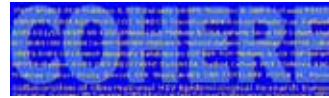
COHERE

COHERE (Collaboration of Observational HIV Epidemiological Research Europe)

Established in 2005, COHERE is a cohort collaboration which focuses on scientific questions requiring a large sample size of patients which the contributing cohorts cannot answer individually and which do not overlap with existing COHERE collaborations.

CHIP acts as one of two regional data management and coordinating centres for

COHERE. In 2009, COHERE formalised the relationship with EuroCoord and is now one of the founding networks applying for the Network of Excellence funding under the European Commission.



MATCH



Management of Post-Transplant Infections in Collaborating Hospitals

Following solid organ or bone marrow transplantation, treatment with immunosuppressive drugs used to prevent rejection renders patients susceptible to several opportunistic infections. Among these is the post-transplant cytomegalovirus infection - a potentially serious complication which puts the patient at risk for progression to CMV disease associated with increased morbidity, mortality and reduced graft survival. CHIP, in collaboration with the liver, kidney, heart and lung transplantation clinical departments at Rigshospitalet have established a prospective transplantation database to monitor and evaluate the risk of developing viral infections among transplant patients. Intended as a patient safety and monitoring tool, the data will be collected centrally for the clinical management, care, and shared expertise for the care of patients.

The platform will also be used for collaborative scientific purposes.

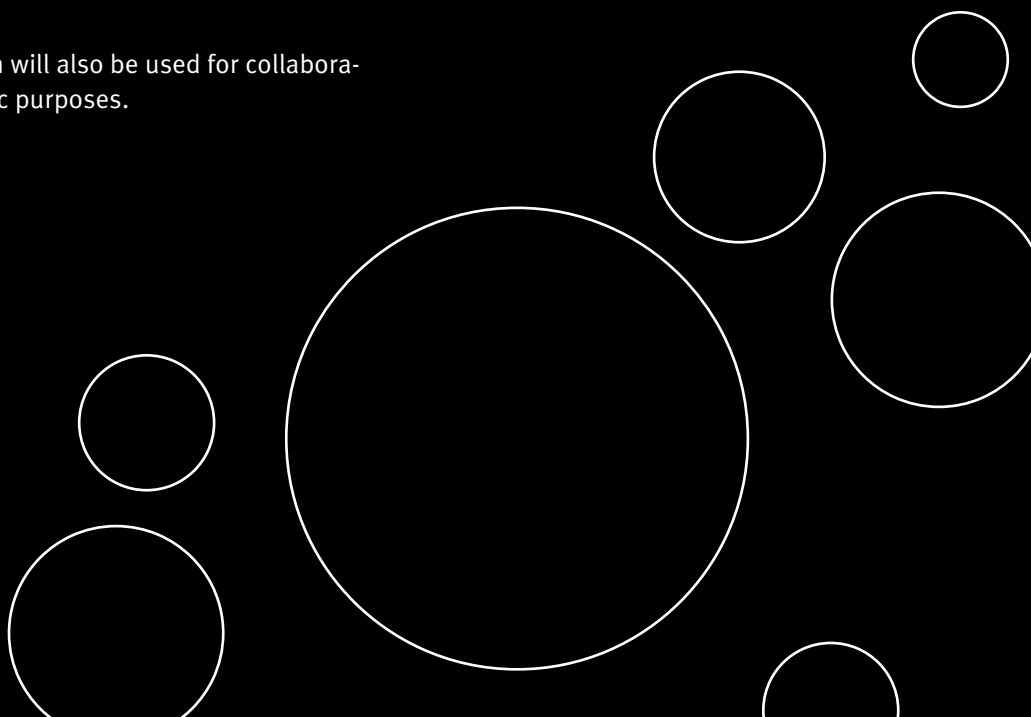
The major focus for 2010 has been on the development and implementation of the database so that the transplant departments can start to use the tool. The clinical departments have started to implement the standardized viral screening for the patients' individual planned monitoring.

The project initiated monitoring of the kidney and liver transplanted patients and the infrastructure is being adapted so that the lung and heart transplanted patients can be followed by the end of 2011.

Participating departments:

Epidemiklinikken, Nefrologisk Klinik, Kirurgisk Gastroenterologisk Klinik, Hjertemedicinsk Klinik, Hæmatologisk Klinik, Klinisk Mikrobiologisk Afdeling og Blodbanken

Monitoring: 350 transplant patients/year



CHIP at a glance

Research and Development 2005 - 2010

Original articles in English language peer-reviewed journals	187 (til 2010)
Average journal impact factor	8.053 (til 2009)
Review articles in journals with peerreview	5
Other publications	13
Number of researchers with > 1000 citations	4
Number of researchers with H-index > 25	3

National and International Researchers

Professors	1
Associate professors	2
Postdocs	5
Research Fellow	1
PhD students	6
Medium higher education	2



Teaching

CHIP has continued to grow and professionalize activities related to teaching both within the University environment as well as outside. An important component to research is disseminating and applying the scientific results. Teaching is and will remain an important priority for the group.

In 2010 the activities included lectures, facilitating group work, as well as supervising OSVAL (Medical students), MIH, and other thesis work.

OSVAL students

- **Predictors of a sustained virologic response in chronic hepatitis C treatment; a comparison between HCV mono-infected and HCV/HIV coinfecting.**
Josefin Eklöf, medical student, OSVAL 2.
- **Mechanisms of CD4+T-lymphocyte depletion in HIV-1 infected individuals.**
Bojan Kovacevic, medical student, Bachelor of Science in Medicine.
- **Epstein-Barr virus and post-transplant Lymphoproliferative disorder.**
Marie Bangstrup, medical student.
- **Genetic variations in the CCR5 gene associated with HIV-1 resistance.**
Karina Juhl, humanbiology student.
- **Evolution of HIV-1 co-receptor tropism.**
Pernille Nilsson, humanbiology student.
- **Clinical characteristics of stroke and stroke-like events in HIV-1 patients.**
Karin Skullman, medical student.

CHIP's PhD Programme

CHIP has an extensive history of PhD and Post Doc teaching and supervising. The environment allows for a good exchange and shared experience as well as

providing teaching and supervising experience internally within CHIP. The organisational structure allows for the facilitation of the administrative and operational work so that the PhDs and Post Docs can focus on the research components as well as maintaining an operational overview of the research conducted.

CHIP has a long-standing collaboration with the University College London, Royal Free Hospital's HIV Epidemiology and Biostatistics Research Group. The group under the leadership of Professor Andrew Phillips as well as Caroline Sabin and Amanda Mocroft also supervises PhD and Post Doc work on the studies coordinated by CHIP. The group of statisticians at Royal Free and the clinicians at CHIP are able to learn and share experience and expertise to the benefit of both groups. This is a dynamic exchange, strengthened even more by international collaboration.

Currently active within the PhD program

Justyna Kowalska, MD, PhD student, CHIP
Caspar da Cunha-Bang; MD, PhD student, CHIP
Lene Ryom, MD, PhD student, CHIP
Joanne Reekie; PhD Student, Royal Free Hospital, London
Alim Kamara; PhD Student, Royal Free Hospital, London
Daria Podlekareva, MD, PhD; Active Post Doc, CHIP
Signe Worm, MD, PhD; Active Post Doc, CHIP
Lars Peters, MD, Research Fellow, CHIP

Internal education sessions

CHIP continues to prioritize employee training and has for the last 5 years provided a

Master of HIV

An important activity for CHIP in 2010 has been establishing a Master program for HIV, and in April 2010 the Faculty of Health Sciences approved the Master of HIV curriculum.

The interest and need for the Master of HIV is evident. More than 400 people across the world have expressed sincere interest, however most of them are looking for scholarships. We admitted 20 students within only 3 months in the beginning of 2010. All applicants fulfilled the admission criteria and had a definite need for the education (many of them from low-income countries with a severe HIV burden). Unfortunately the majority could not afford the tuition fees.

In June 2010 it was thus decided to postpone the launch of the Master of HIV programme until September 2011. A Master of HIV scholarship fund has now been established and we have intensified marketing and fundraising for future annual Master of HIV programmes. We will launch one of the modules: "HIV-related Diseases, Treatment and Care" (5 weeks) under the Master of International Health Programme in April 2011.

In addition CHIP has established a one-week course in collaboration with Copenhagen University's summer programme. The course entitled "Effective Response to Major Infectious Diseases - where Medicine meets Public Health Policy" will be lead by Professor Jens Lundgren and Dr. Jeffrey Lazarus from The Global Fund.

weekly internal education and update session. The topics, identified by staff, are presented by CHIP staff as well as other guest lecturers, both national and international.

Danish Institute for Study Abroad (DIS)

Drs. Lars Peters and Signe Worm and others from CHIP have been active in teaching at DIS (affiliated with Copenhagen University). Lars and Signe coordinate the course entitled 'A biomedical exploration of HIV and AIDS', offered in the spring and autumn. This course includes an overview of the complexity of HIV/ AIDS from a biological and medical perspective. The course also includes biological

characterisation of HIV (virology, immunology and epidemiology), and medical and clinical aspects of HIV/AIDS (development of HIV infection, opportunistic infections, treatments, complications and co-infections).

Outreach

As the activities at CHIP all involve collaborative projects, an important component is outreach and communication. This involves communication internally within the studies as well as externally to all stakeholders. We realise that research does not end with publication in peer-reviewed journals and that coordinating the experience from patient care and research results into teaching, policy making and action is also an important priority.

Activities in 2010 included:

- International consultancy
- Annual international conference coordination
- International Scientific and Operational Steering Committee and Advisory Board participation
- National networking activities related to HIV
- Developing and implementing a communication strategy

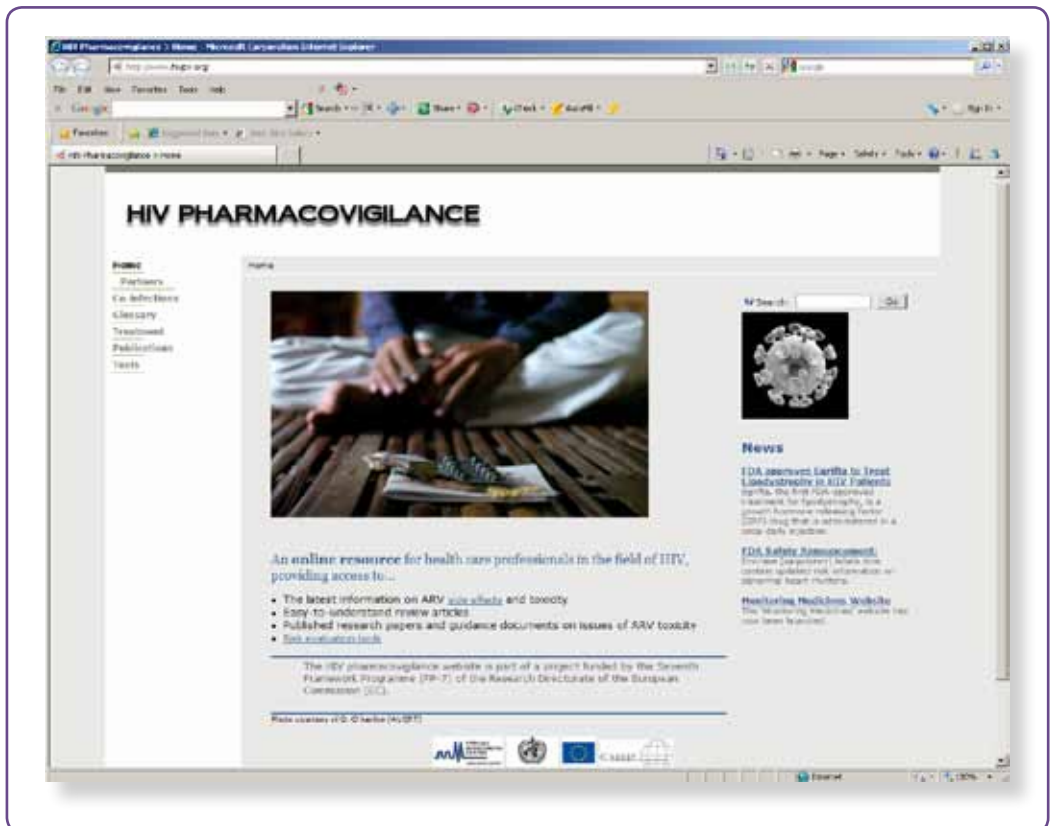
HIV

Pharmacovigilance Website

In partnership with the WHO and Uppsala Monitoring Centre, CHIP is currently developing an HIV pharmacovigilance website. As part of a project funded by the Seventh Framework Programme (FP-7) of the Research Directorate of the European Commission (EC), the website

will provide access to the latest information on ARV side effects and toxicity, e-learning modules, and risk calculator tools to aid physicians in patient management.

Please visit the website at www.hivpv.org.



Financial contributors 2010

Study/activity	Public	Private
EuroSIDA (EuroCoord)	EU Commission Danish Council for Independent Research	Gilead Sciences Merck & Co Inc Pfizer Inc
D:A:D	The Oversight Committee for The Evaluation of Metabolic Disorders of HAART Danish Council for Independent Research EMeA FDA	The Oversight Committee sponsors: Abbott Laboratorie Boehringer-Ingelheim Pharmaceuticals Inc Bristol-Myers Squibb Gilead Sciences GlaxoSmithKline Merck & Co Inc Pfizer Inc Roche Pharmaceuticals Tibotec/ Janssen-Cilag International NV
INSIGHT network	National Institutes of Health, USA (NIH)	
INSIGHT START	Agence Nationale de Recherches sur le SIDA et les Hépatites Virales (ANRS), Australian National Health and Medical Research Council (NHMRC); Bundesministerium für Bildung und Forschung (BMBF), Division of Clinical Research, NIAID, NIH; National Institute for Mental Health (NIMH), NIH; National Institute of Neurological Disorders and Stroke (NINDS), NIH; National Cancer Institute (NCI), NIH; European AIDS Treatment Network (NEAT); Department of Bioethics, NHI, Clinical Center	Study drug sponsors: Gilead Sciences Bristol-Myers Squibb Merck & Co Inc Abbott Laboratorie GlaxoSmithKline Tibotec/Janssen-Cilag International NV
INSIGHT FLU	NIAID, NIH	
NEAT	EU Commission	Study drug sponsors: Gilead Sciences Janssen-Cilag International NV Abbott Laboratories Ltd Merck Inc.
Monitoring Medicines, WHO	EU Commission	Bill & Melinda Gates Foundation
ACTIVATE	EU Commission	
EuroCoord-CHAIN	EU Commission	Gilead Sciences
COHERE	ANRS	
PARTNER	National Institute for Health Research, UK (NIHR)	
IWHOD	NIH Office of AIDS Research NEAT ANRS, Agence nationale de recherches sur le sida	Boehringer-Ingelheim Pharmaceuticals Inc Gilead Sciences GlaxoSmithKline Pfizer Inc Roche Pharmaceuticals Tibotec/ Janssen-Cilag International NV
HIV in Europe	Endorsed by AIDS Action Europe WHO Europe European AIDS Treatment Group (EATG) University of Copenhagen	Abbott Laboratorie Boehringer-Ingelheim Pharmaceuticals Inc Bristol-Myers Squibb Gilead Sciences GlaxoSmithKline Merck & Co Inc Schering-Plough Tibotec/ Janssen-Cilag International NV
CASS	Danish Council for Independent Research	Lundbeck Foundation



International Conference Presentations 2005 – 2010

Year	Oral	Poster
2005	11	11
2006	7	10
2007	6	18
2008	11	13
2009	17	20
2010	6	13

10 selected publications

CHIP has published more than 150 articles in peer-reviewed journals over the last 5 years, predominantly within clinical management of HIV infection, but also to an increasing extent covering other infectious diseases and co-infections such as tuberculosis, hepatitis and meningitis.

Both randomized controlled trials and observational studies have been published, presenting national as well as international data.

A complete list of CHIP publications is available at www.cphiv.dk.

A randomised trial to evaluate lopinavir/ritonavir versus saquinavir/ritonavir in HIV-1 infected subjects. The MaxCmin2 trial. UB Dragsted, J Gerstoft, M Youle, Z Fox, M Losso, J Benetucci, DT Jayawwera, A Rieger, JN Bruun, A Castagna, B Gazzard, S Walmsley, A Hill, and JD Lundgren for the MaxCmin2 trial group. *Antivir Ther.* 2005;10(6):735-43.

CD4+ count-guided interruption of antiretroviral treatment. The Strategies for Management of Antiretroviral Therapy (SMART) Study Group. Writing Group: WM El-Sadr, JD Lundgren, JD Neaton, F Gordin, D Abrams, RC Arduino, A Babiker, W Burman, N Clumeck, CJ Cohen, D Cohn, D Cooper, S Emery, G Fätkenheuer, B Gazzard, B Grund, J Hoy, K Klingman, M Losso, N Markowitz, J Neuhaus, AN Phillips, and C Rappoport. *N Engl J Med* 2006; 355(22); 2283-2296.

Class of antiretroviral drugs and the risk of myocardial infarction. Writing committee: N Friis-Møller, P Reiss, CA Sabin, R Weber, A D'Arminio Monforte, W El-Sadr, R Thiebaut, S de Wit, O Kirk, E Fontas, MG Law, A Phillips, JD Lundgren on behalf of the D:A:D study group. *N Engl J Med.* 2007 April 26;356:1723-35.

Normalisation of CD4 counts in patients with HIV-1 infection and maximum virological suppression who are taking combination antiretroviral therapy: an observational cohort study. A Mocroft, AN Phillips, J Gatell, B Ledergerber, M Fisher, N Clumeck, M Losso, A Lazzarin, JD Lundgren for the EuroSIDA study group. *Lancet.* 2007 Aug 4;370(9585):407-13.

Impact of bacteremia on the pathogenesis of experimental pneumococcal meningitis. CT Brandt, D Holm, M Liptrot, C Østergaard, JD Lundgren, N Frimodt-Møller, IC Skovsted and IJ Rowland.

J Infect Dis. 2008 Jan 15;197(2):235-244.

Use of nucleoside reverse transcriptase inhibitors and risk of myocardial infarction in HIV-infected patients enrolled in the D:A:D study: a multi-cohort collaboration. Writing group: CA Sabin, SW Worm, R Weber, P Reiss, W E I Sadr, F Dabis, S De Wit, M Law, A D´Arminio Monforte, N Friis-Møller, O Kirk, C Pradier, I Weller, AN Phillips, JD Lundgren. Lancet. 2008 Apr 26;371(9622):1417-26.

Outcomes from monitoring of patients on antiretroviral therapy in resource-limited settings with viral load, CD4 cell count, or clinical observation alone: a computer simulation model. AN Phillips, D Pillay, AH Miners, DE Bennett, CF Gilks, JD Lundgren.

Lancet. 2008 Apr 26;371(9622):1443-51.

The Procalcitonin And Survival Study (PASS) - a randomised multi-center investigator-initiated trial to investigate whether daily measurements biomarker Procalcitonin and pro-active diagnostic and therapeutic responses to abnormal Procalcitonin levels, can improve survival in intensive care unit patients. Calculated sample size (target population): 1000 patients. JU Jensen, B Lundgren, L Hein, T Mohr, PL Petersen, LH Andersen, AO Lauritsen, S Hougaard, T Mantoni, B Bømler, KJ Thornberg, K Thormar, J Løken, M Steensen, P Carl, JA Petersen, H Tousi, P Sjøe-Jensen, M Bestle, S Hestad, MH Andersen, P Fjeldborg, KM Larsen, C Rossau, CB Thomsen, C Ostergaard, J Kjaer, J Grarup, JD Lundgren. BMC Infect Dis. 2008 Jul 13;8:91.

Interleukin-2 therapy in patients with HIV infection. INSIGHT-ESPRIT Study Group; SIL-CAAT Scientific Committee, D Abrams, Y Lévy, MH Losso, A Babiker, G Collins, DA Cooper, J Darbyshire, S Emery, L Fox, F Gordin, HC Lane, JD Lundgren, R Mitsuyasu, JD Neaton, A Phillips, JP Routy, G Tambussi, D Wentworth.

N Engl J Med. 2009 Oct 15;361(16):1548-59.

Mortality from HIV and TB coinfections is higher in Eastern Europe than in Western Europe and Argentina. DN Podlekareva, A Mocroft, FA Post, V Riekstina, JM Miro, H Furrer, M Bruyand, AM Pantelev, AG Rakhmanova, E Girardi, MH Losso, JJ Toibaro, J Caylá, RF Miller, N Obel, A Skrahina, N Chentsova, JD Lundgren, O Kirk; HIV/TB Study Writing Group.

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