

CASCADE:
Concerted Action
on SeroConversion
to AIDS and Death
in Europe
2006-2010

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Foreword

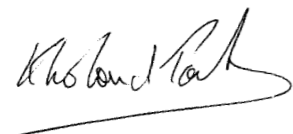
Before the introduction of combination antiretroviral therapy in the mid-1990s, the average life expectancy of an HIV-infected individual was in the order of 10-15 years. cART has been, quite literally, life-saving for the millions infected and affected by HIV. In countries where such treatment became available, we witnessed dramatic reductions in illness, hospitalisation, and death.

Although there have been vast improvements in our knowledge of HIV infection, we still have limited information on the long-term consequences of treatment, especially if started close to the time of infection. Indeed, the optimal time to initiate therapy is still not known and neither is the value of initiating it close to the time of being infected, or "seroconverting". As new HIV drugs are introduced and management practices improved, it is only through the follow-up of HIV cohorts that we are able to continually assess risk factors for success and failure, the likely impact of such changes on the HIV population, and the introduction and consequences of changes in the virus itself.

The CASCADE Collaboration was first established in 1997 with European Commission funding - and with subsequent renewal through competitive bids - to pool data from cohorts of people with well-estimated dates of HIV infection, so called "seroconverters" across Europe. It has been a highly successful collaboration due to an ethos of inclusiveness and not least because it comprises so many internationally-esteemed researchers.

This booklet showcases just some of the research achievements of CASCADE during the current funding term 2006-2010. This period has seen many developments in our understanding of HIV infection and treatment and CASCADE data have made a vital contribution. The work has been truly collaborative and has included a number of staff exchanges and training courses, from PCR techniques and genotypic resistance testing, to phylogenetics, marginal structural models and analyses of genetic data.

Obviously it would not be possible to include all of the research that CASCADE has carried out to date. On page 18 is listed all of our published research since the start of our current funding term in 2006, after a list of our collaborators on page 17. If you would like to know more about CASCADE since its inception in 1997, please visit our website www.CASCADE-Collaboration.org.



Kholoud Porter, Project Leader



CASCADE Collaboration

About CASCADE

CASCADE was established in 1997 as a collaboration between the investigators of European cohorts of people with well-estimated dates of HIV infection, known as seroconverters.

Funded by the European Commission, it is currently a network of epidemiologists, statisticians, virologists, and clinicians from lead HIV institutions in 15 European countries. The network has expanded to now include cohorts from Australia, Canada and Sub-Saharan Africa.

CASCADE's main aim is to monitor newly-infected individuals and those already enrolled in studies, covering the entire duration of HIV infection. Seroconverters are recruited into the individual cohorts locally and nationally and are typically followed up for life. Through pooling data from so many different cohorts, we are able to address issues which cannot be reliably addressed from single studies alone.

Follow-up data from seroconverters are valuable in being able to allow us to relate events to the same time since an individual first became infected with HIV. Seroconverters thus provide a unique opportunity to study HIV throughout its whole infection period, to enable researchers to examine the characteristics of recently-acquired HIV infection in the population and changes over time.

CASCADE currently contains data from over 20,000 HIV-infected individuals, drawn from more than 300 clinics across Europe, Canada and Australia as well as 13 sites in Sub-Saharan Africa. The people that make up the CASCADE dataset are those who have had their HIV diagnosed early so have the best chances of access to treatment. These seroconverters therefore represent the ideal of what may be achieved through early testing and presentation, and set a gold standard against which to compare the outcome of all infected individuals.



Participating cohorts

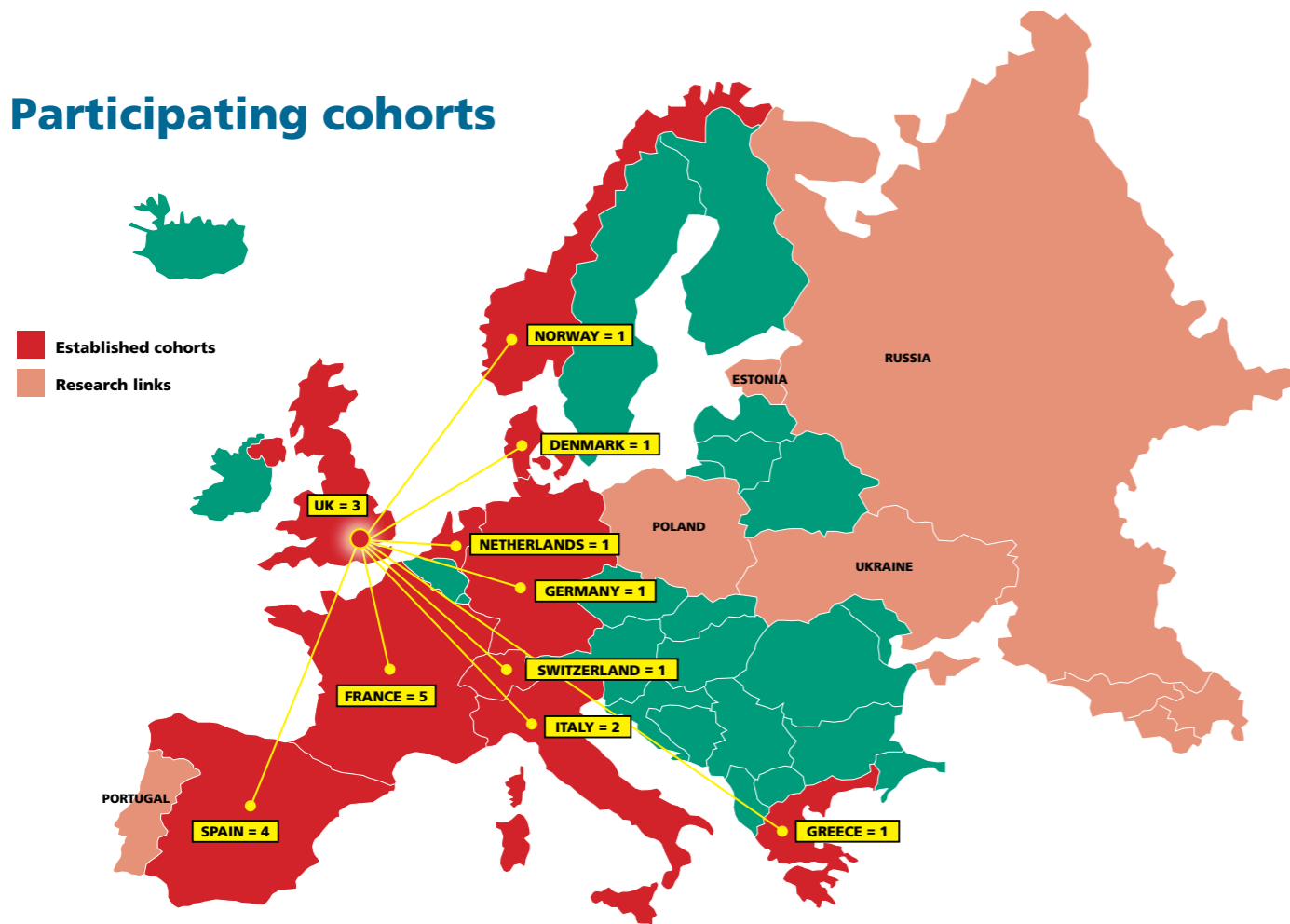


Figure 1: Map showing the European cohorts that contribute to CASCADE with the number of different cohorts. The Collaboration also has links with researchers in Estonia, Poland, Portugal, Russia, and Ukraine.

European cohorts:

Denmark

Danish HIV Cohort

France

Aquitaine Cohort
French Hospital Database
Lyon Primary Infection Cohort
SEROCO Cohort
French PRIMO Cohort

Germany

German Cohort

Greece

Greek Haemophilia Cohort

Italy

Italian Seroconversion Study
ICoNA cohort

Netherlands

Amsterdam Cohort Studies in Homosexual Men and IDUs

Norway

Oslo and Ullevål Hospital Cohorts

Spain

Badalona IDU Hospital Cohort
Barcelona IDU Cohort
Madrid Cohort
Valencia IDU Cohort

Switzerland

Swiss HIV Cohort Study

UK

Edinburgh Hospital Cohort
Royal Free Haemophilia Cohort
UK Register of HIV Seroconverters

Non-European cohorts also contribute to CASCADE:

1. Sydney AIDS Prospective Study, Australia
2. Sydney Primary HIV Infection Cohort, Australia
3. Southern Alberta Clinic Cohort, Canada
4. Genital Shedding Study, Uganda, Zimbabwe
5. Early Infection Cohorts, Kenya, Uganda, Rwanda, Zambia, South Africa.

CASCADE research highlights 2006-2010

Changes in the risk of death after HIV seroconversion compared with mortality in the general population

Background

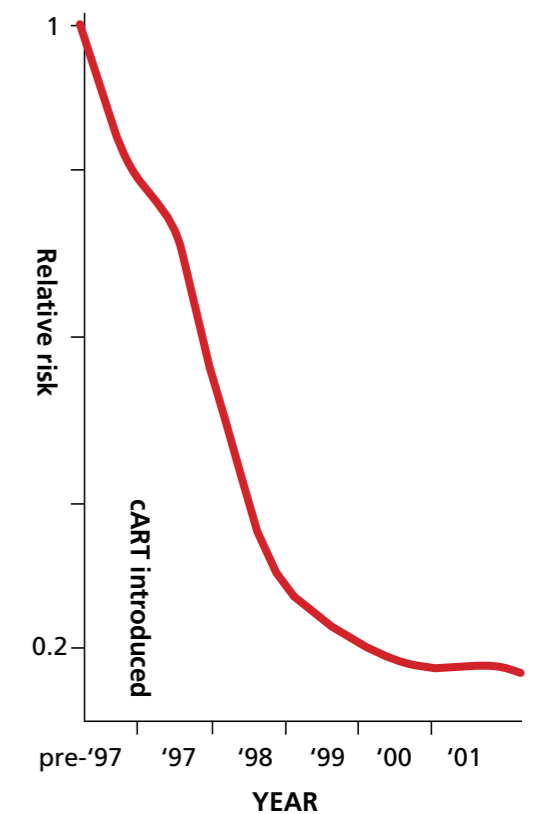
The decrease in mortality following the introduction of cART is well-documented and some previous studies have compared mortality in HIV-infected and uninfected populations in industrialised countries. However, these studies have not been able to adjust for duration of HIV infection, which is a key factor influencing mortality risk and one which can confound other relationships.

This analysis was the first to make a comparison of mortality among HIV-infected and uninfected individuals taking account of duration of HIV infection. The results have therefore provided estimates, previously unavailable, of the cumulative excess probability of death as duration of HIV infection lengthens.

Results

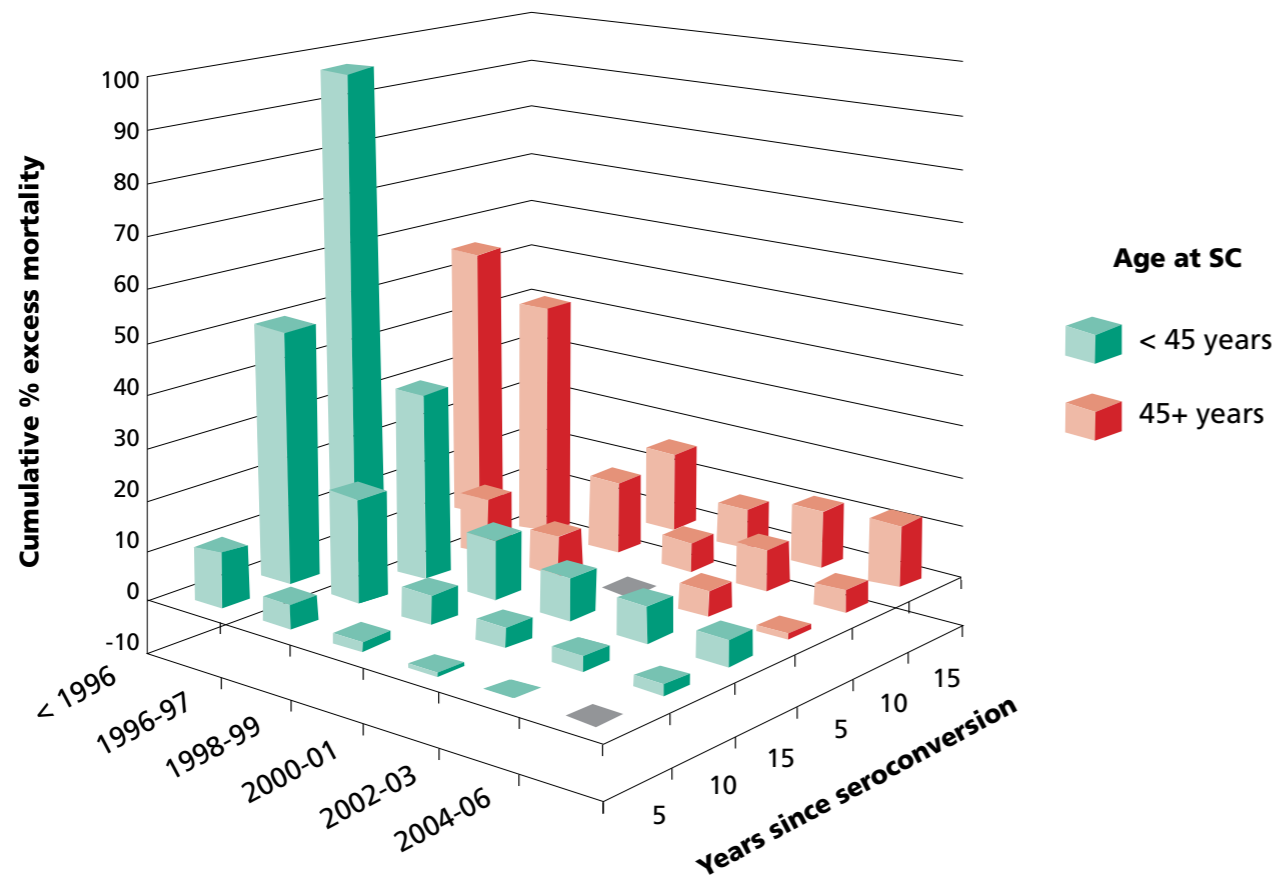
Of 16,534 individuals with median duration of follow-up of 6.3 years, 2,571 died, compared with 235 deaths expected in an equivalent general population cohort. The excess mortality rate (per 1000 person-years) decreased from 40.8 before the introduction of cART (pre-1996) to 6.1 in 2004. By 2004-2006, no excess mortality was observed in the first 5 years following HIV seroconversion among those infected sexually, though a cumulative excess probability of death remained over the longer term. See figure 1.

Overall, this study estimated an 88% reduction in excess mortality in 2000-2001 compared with pre-1996. Reductions have continued to 2004-2006, with excess mortality in this period 94% lower than pre-1996 levels.



Change in the risk of death after becoming HIV positive

Figure 1: Cumulative excess mortality (sexual exposure only) by age group



Conclusion

Mortality rates for HIV-infected people have become much closer to general mortality rates since the introduction of cART.

In industrialised countries, people who were infected sexually with HIV now appear to experience mortality rates similar to those of the general population in the first 5 years following infection, though a mortality excess remains as duration of HIV infection lengthens.

Bhaskaran K, Hamouda O, Sannes M, Boufassa F, Johnson A, Lambert P and Porter K on behalf of the CASCADE Collaboration. Changes in the risk of death after HIV seroconversion compared with mortality in the general population. JAMA 2008; 2;300:51-9

Comment in: ACP J Club. 2008 Nov 18;149(5):15. Evid Based Med. 2009 Feb;14(1):23. Evid Based Nurs. 2009 Jan;12(1):26.

CASCADE research highlights 2006-2010

Effective therapy has altered the spectrum of cause-specific mortality following HIV seroconversion

Background

Due to the introduction of cART, the life expectancy of HIV-infected people has greatly improved. This means that they are increasingly likely to die from non-HIV related causes such as infection with hepatitis viruses and therapy-related toxicities including cardiovascular side-effects.

Before effective therapy was available, the risk of pre-AIDS mortality increased as the CD4 cell count (a measure of how healthy the immune system is) decreased and HIV RNA level (a measure of the amount of virus in the blood) increased. The risk of death in those being treated has been shown to be associated with CD4 cell count. However, it is not clear whether these relationships are the same for all causes of death, or whether any relationship with CD4 count or HIV RNA level may simply reflect a longer duration of infection.

This study evaluated the impact of the introduction of cART on cause-specific mortality and investigated the relationships between CD4 cell counts and HIV RNA levels and specific causes of death.

Results

A total of 1,938 of 7,680 HIV-seroconverters died during follow up. Prior to cART, the most common cause of death was opportunistic infections, followed by unknown and HIV/AIDS-unspecified. In the cART era, the cumulative incidence for all AIDS-related causes of death decreased, with opportunistic infections remaining the most important. Large reductions in death due to other infections and organ failure were seen.

Cumulative death risk decreased in the cART era for most causes. The effect of cART was not the same for all risk groups. The cumulative risk of death from AIDS-related malignancies, opportunistic infections, and non-AIDS-related malignancies decreased significantly among homosexual men, whereas the risk of dying from (un)-intentional death (accidents, suicide, overdose) increased significantly among injecting drug users. A non-significant increase in hepatitis/liver-related death was seen in homosexual men, injecting drug users, and haemophiliacs. See figure 2.



CASCADE research highlights 2006-2010

Non-AIDS defining deaths and immunodeficiency in the era of combination antiretroviral therapy.

Background

Due to the decrease in HIV-related mortality, non-AIDS defining conditions specifically malignancies, end stage liver disease, cardiovascular disease, severe infections, and kidney disease now account for between 50 to 66% of deaths that occur.

The incidence of a variety of non-AIDS conditions may be associated with longer duration of immunodeficiency, even in cART-treated patients. Establishing if HIV infection itself explains these conditions, because of exposure to uncontrolled viral replication or to persistent immune suppression, might have important implications in terms of the optimal timing of antiretroviral treatment.

Prior to this, most studies looking at this issue used data from prevalent cohorts (where the date of infection is not known), and measured immunodeficiency by using the latest CD4 cell count. By using data from CASCADE, and different ways of measuring and accounting for immunodeficiency, this study aimed to investigate the relationships between non-AIDS defining deaths and HIV-associated immunodeficiency in the era of cART.

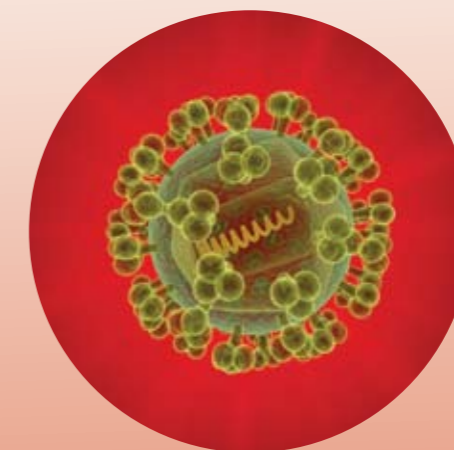
Results

Latest CD4 count, nadir (lowest) CD4, and time spent with a CD4 count of <350 cells/mm³ were used to measure immunodeficiency. The outcomes were specific causes of death using a standardised classification. Among 9,858 patients, 597 died, 333 (55.7%) of whom died from non-AIDS-defining causes.

Non-AIDS defining infection, liver disease, non-AIDS defining malignancy, and cardiovascular disease accounted for 53% of non-AIDS deaths.

For each 100 cells/mm³ increment in the latest CD4 count, there was a 64% (95%CI 58-69%) reduction in risk of death from AIDS defining causes and significant reductions in death from non-AIDS infections (32% reduction, 18-44%), end-stage liver disease (33% reduction, 18-46%), and non-AIDS malignancies (34% reduction, 21-45%). See figure 3.

These risks were also associated with nadir CD4 count among those who had not received cART and duration of exposure to immunosuppression. No relationship between risk of death from cardiovascular disease and CD4 count was found although there was an increased risk associated with elevated HIV RNA.



Mortality in the pre-cART era

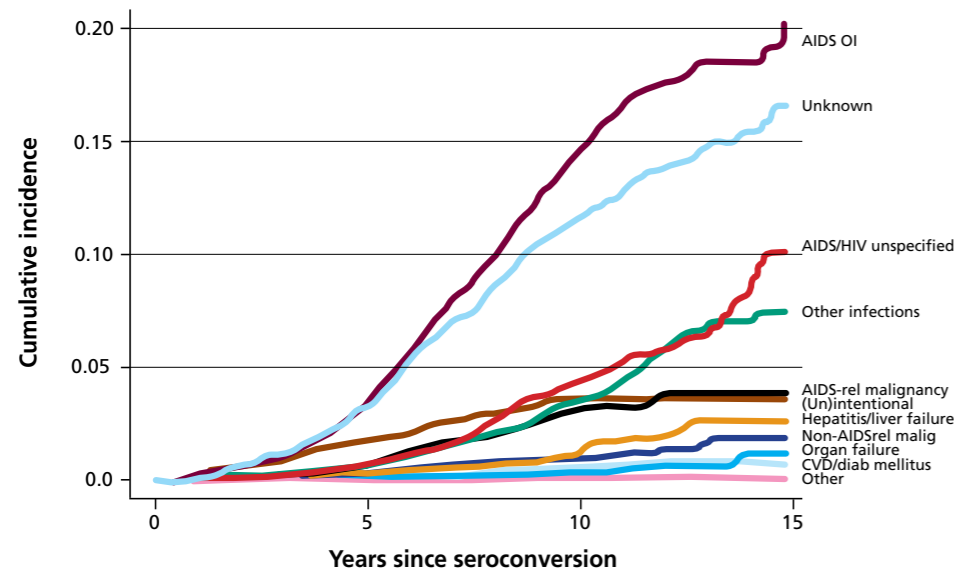
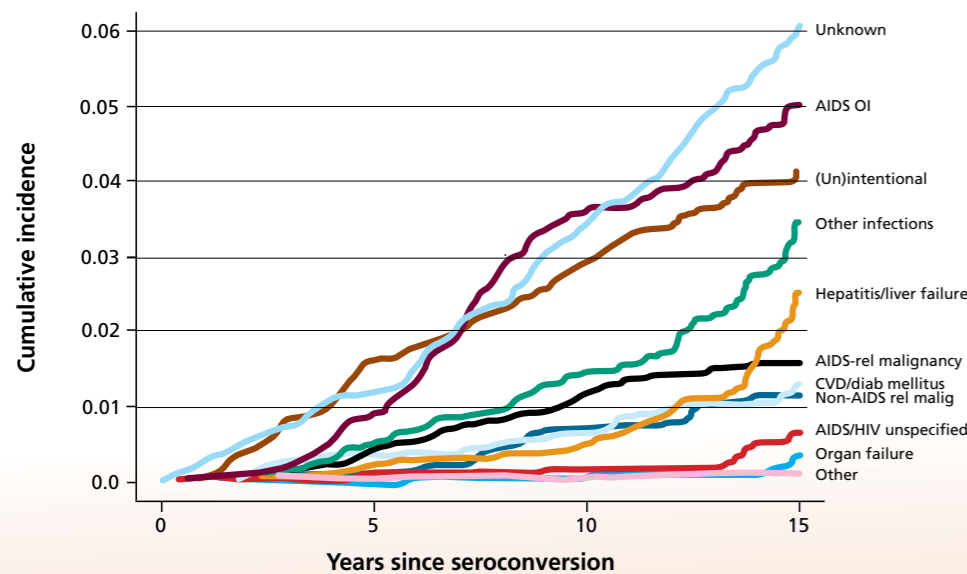


Figure 2:
(a) Cumulative incidences in the CASCADE Collaboration of each specific cause of death in the pre-cART, according to time from seroconversion.
(b) Cumulative incidences in the CASCADE Collaboration of each specific cause of death in the cART era, according to time from seroconversion. CVD, cardiovascular disease: OI, opportunistic infection.

Mortality in the cART era



a

b

Conclusion

This study was the first to show a general reduction in the risk of dying from specific causes in seroconverters in the era of cART.

Overall mortality as well as cause-specific mortality has substantially decreased following the introduction of cART. However, AIDS opportunistic infections remain the most common cause of death, suggesting that AIDS-related events will continue to be an important cause of death in the future.

Smit C, Geskus R, Walker S, Sabin C, Coutinho R, Porter K, Prins M on behalf of the CASCADE Collaboration. Effective therapy has altered the spectrum of cause specific mortality following HIV seroconversion. AIDS 2006; 20:741-9.

CASCADE research highlights 2006-2010

Conclusion

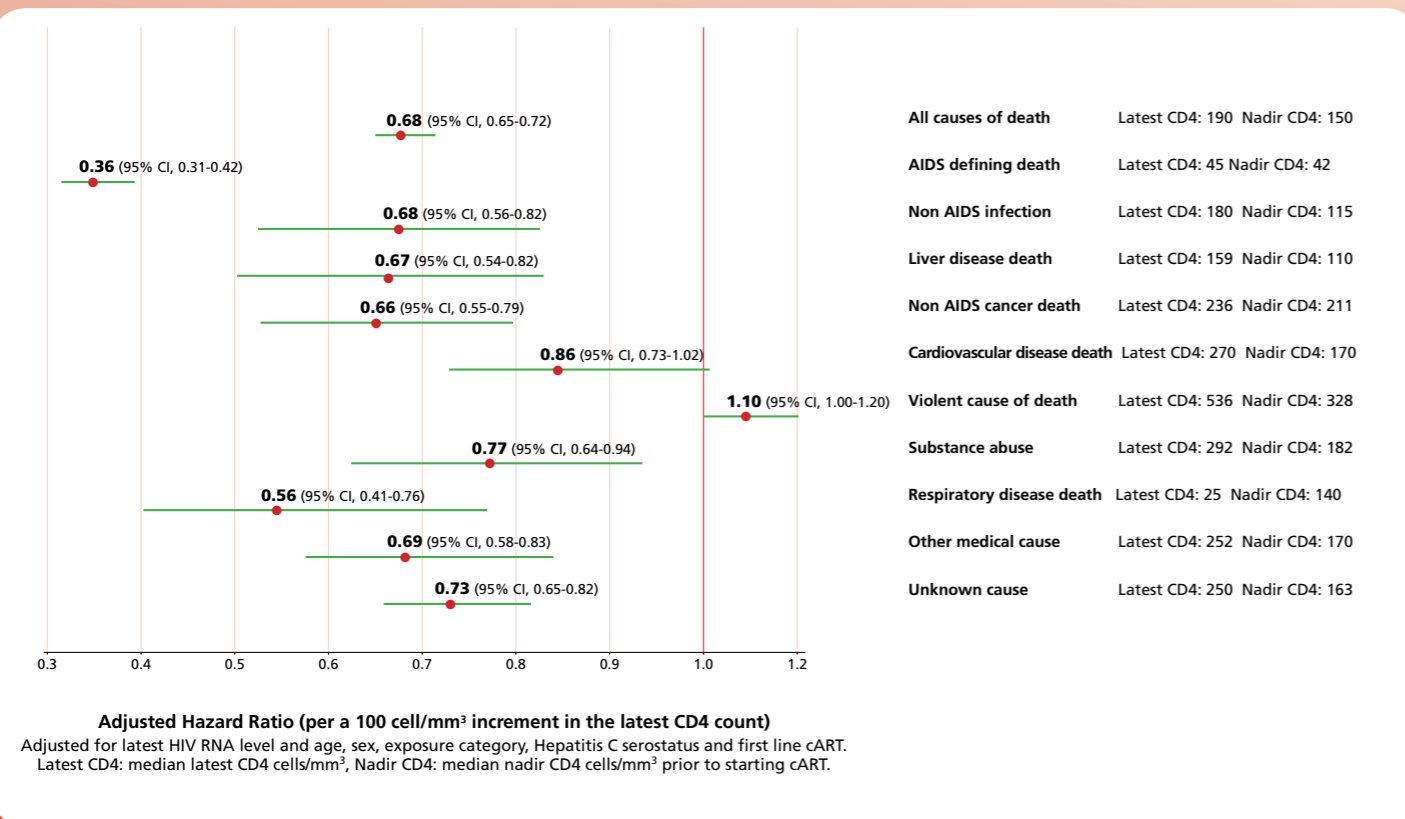
In the cART era, the most frequent non-AIDS-defining causes of death are associated with immunodeficiency. Only cardiovascular disease is associated with high viral replication.

Avoiding immunodeficiency through earlier initiation of cART, may impact on the morbidity and mortality of HIV infected patients.



Marin B, Thiébaud R, Bucher HC, Rondeau V, Costagliola D, Dorrucchi M, Hamouda O, Prins M, Walker AS, Porter K, Sabin CA, Chêne G on behalf of the CASCADE Collaboration. Non-AIDS defining deaths and immunodeficiency in the era of combination antiretroviral therapy. *CASCADE 1996-2006. AIDS 2009; 23; 1743-53*

Figure 3: Adjusted cause-specific hazard ratios of progression to death associated with a 100 cell/mm³ increment in the latest CD4 count.



Pre-treatment CD4 cell slope and progression to AIDS or death in HIV-infected patients initiating antiretroviral therapy

Background

Knowledge of CD4 cell count can be used to predict the subsequent risk of AIDS or death in untreated patients, and those starting cART. It is, therefore, an important tool for clinicians when deciding whether to initiate cART in patients who are not yet experiencing any symptoms from their HIV (asymptomatic individuals).

In the absence of evidence from randomised controlled trials, recent data from cohort studies have indicated that starting cART at a CD4 cell count above 350 cells/mm³ may reduce the risk of AIDS and death. However, it is not known whether the dynamics of CD4 cell decline, represented by the pre-cART CD4 cell slope, can give further clues to outcomes after cART initiation.

This analysis considered whether CD4 cell decline is related to prognosis in patients starting cART as well as those not treated, and whether it is, therefore, relevant to the decision on whether to initiate therapy in asymptomatic patients.

Results

Survival analyses were undertaken of patients with a known date of HIV seroconversion and at least two CD4 measurements prior to starting cART. For each patient, a pre-cART CD4 slope was estimated using a linear mixed effects model. The primary outcome was time from starting cART to a first new AIDS event, or death. A total of 2,820 patients were included who were treatment-naïve and initiating cART with a median (interquartile range) pre-cART CD4 cell decline of 61 (46–81) cells/mm³ per year. A total of 125 patients died, and 255 patients experienced either a new AIDS event or death.

In an analysis adjusted for established risk factors, the hazard ratio for AIDS or death was 1.01 (95% confidence interval 0.97–1.04) for each 10 cells/mm³ per year reduction in pre-cART CD4 cell decline. There was also no association between pre-cART CD4 cell slope and survival. Alternative estimates of CD4 cell slope gave similar results.

In 1,731 AIDS-free patients from the pre-cART era with >350 CD4 cells/mm³, the rate of CD4 cell decline was also not significantly associated with progression to AIDS or death (hazard ratio 0.99, 95% confidence interval 0.94–1.03, for each 10 cells/mm³ per year reduction in CD4 cell decline).

Conclusion

The CD4 cell slope does not improve the prediction of clinical outcome in patients with a CD4 cell count above 350 cells/mm³.

Knowledge of the current CD4 cell count is sufficient when deciding whether to initiate cART in asymptomatic patients.

Wolbers M, Babiker A, Sabin C, Dorrucchi M, Chêne G, Mussini C, Porter K, Bucher HC, on behalf of the CASCADE Collaboration. Pre-treatment CD4 cell slope and progression to AIDS or death in naïve HIV-infected patients initiating combination antiretroviral therapy: The CASCADE Collaboration. *PLoS Med.* 2010; 7:e1000239.

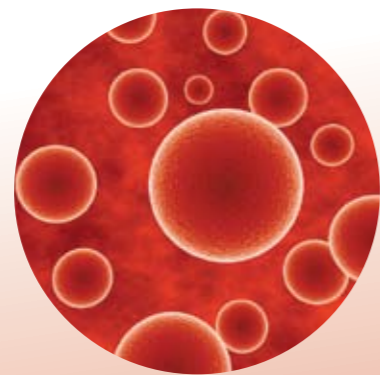
CASCADE research highlights 2006-2010

Current CD4 cell count and the short-term risk of AIDS and death before the availability of effective antiretroviral therapy in HIV-infected children and adults

Background

An important consideration when deciding whether a patient should start cART is their short-term risk of disease progression in the absence of treatment, which is assessed by measuring the number of CD4 cells. Clinically-relevant estimates of the risk of disease progression based on the most recent CD4 cell count have only recently become available. These were derived for adults and children using data from CASCADE and the HIV Paediatric Prognostic Markers Collaborative Study (HPPMCS) respectively. However, because of the differing statistical approaches used in these studies, a direct comparison of the results was not possible.

This analysis aimed to use common methodology to assess data from these studies to gain a more complete picture of how, for a given CD4 cell count, the risks of AIDS and death vary across the age range of the patients. The main focus was to determine whether for children, there is an age threshold at which the association between the CD4 cell count and the rate of disease progression approximates that noted in adults.



Results

A total of 1,260 deaths and 1,894 initial AIDS events were observed among 6,741 patients (3,244 children [i.e., patients ≥ 15 years of age] and 3,497 adults). Young children (aged >5 years) experienced high morbidity and mortality rates. After adjustment for the CD4 cell count, the effect of age on disease progression was not significant among older children, whereas the risk increased markedly in association with increasing age among adults.

Death rates were similar among older children, and adults aged approximately 20 years, as were the rates of progression to AIDS/death when cases of serious recurrent bacterial infection (which has a more restrictive case definition in adults) were excluded. See figure 4.

Conclusion

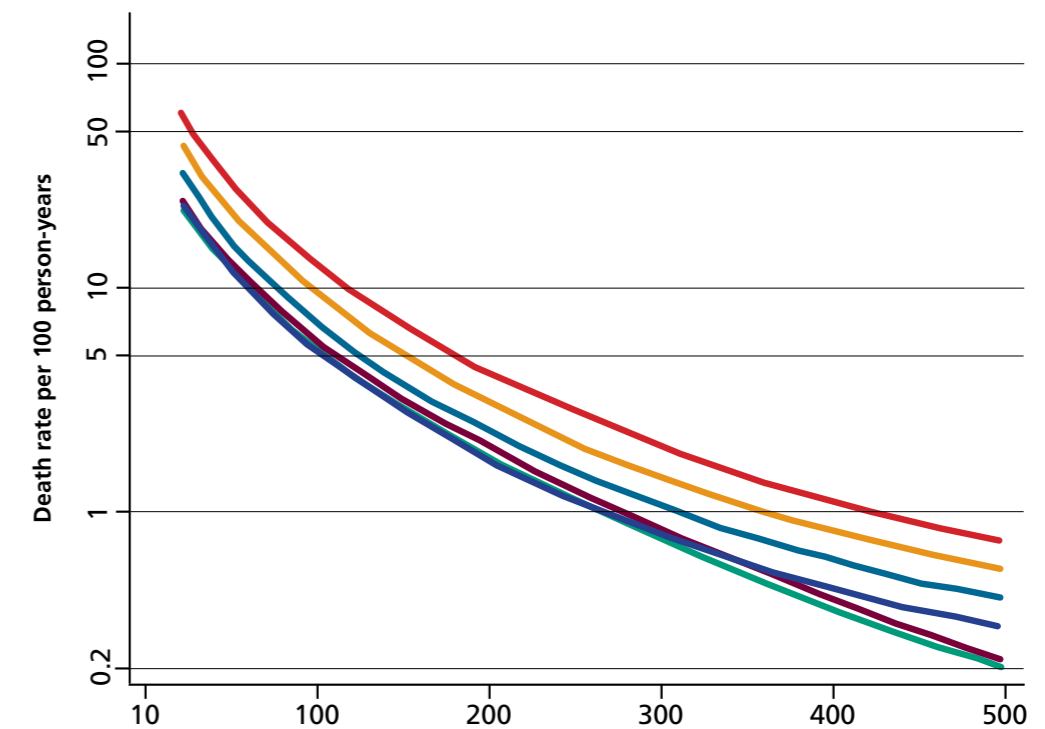
Current treatment guidelines for the initiation of cART differ for adults and children. This study demonstrated that similar CD4 cell count criteria for initiation of antiretroviral therapy can be applied to both adults and children of more than 5 years of age.

Dunn DT, Woodburn P, Duong T, Peto J, Phillips A, Gibb D, Porter K on behalf of HIV Paediatric Prognostic Markers Collaborative Study (HPPMCS) and the CASCADE Collaboration. Current CD4 cell count and the short-term risk of AIDS and death before the availability of effective antiretroviral therapy in HIV-infected children and adults. J Infect Dis 2008; 197:398-404.

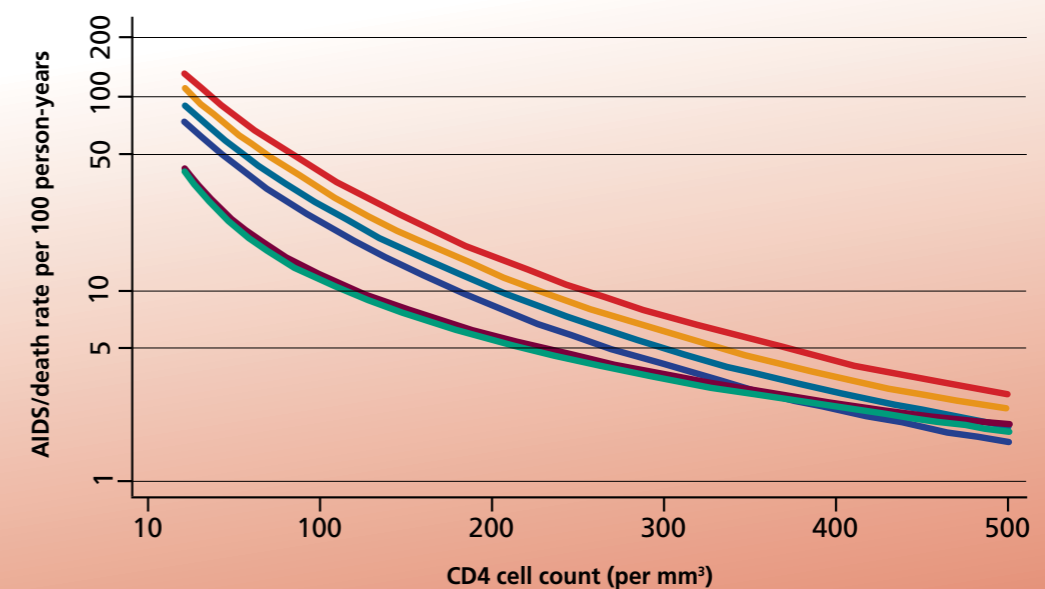
Figure 4: Estimated event rate (per 100 person-years), according to the most recent CD4 cell count and patient age, by use of fractional polynomial models: death (a), or AIDS excluding serious recurrent bacterial infection or death (b).

5 years (purple), 10 years (green), 20 years (blue), 30 years (teal), 40 years (yellow), 50 years (red)

a



b



CASCADE research highlights 2006-2010

Gender differences in HIV progression to AIDS and death in industrialised countries: slower disease progression following HIV seroconversion in women

Background

Reports on gender differences in HIV progression in both the pre- and post-cART era are contradictory. This study was the first to look at sex differences in time to individual AIDS-defining conditions, and changes over time in AIDS and non-AIDS mortality in male and female seroconverters in the same transmission category.

Results

While no significant sex differences were found before 1997, from 1997 onward, women had a lower risk of AIDS (cumulative relative risk (CRR) = 0.76, 95% confidence interval (CI): 0.63, 0.90) and death (adjusted hazard ratio = 0.68, 95% CI: 0.56, 0.82) than men.

Compared with men, women also had lower risks of AIDS dementia complex (CRR = 0.23, 95% CI: 0.07, 0.74), tuberculosis (CRR = 0.60, 95% CI: 0.39, 0.92), Kaposi's sarcoma (CRR = 0.27, 95% CI: 0.07, 0.99), lymphomas (CRR = 0.47, 95% CI: 0.23, 0.96), and death without AIDS (CRR = 0.74, 95% CI: 0.56, 0.98). See figure 5.

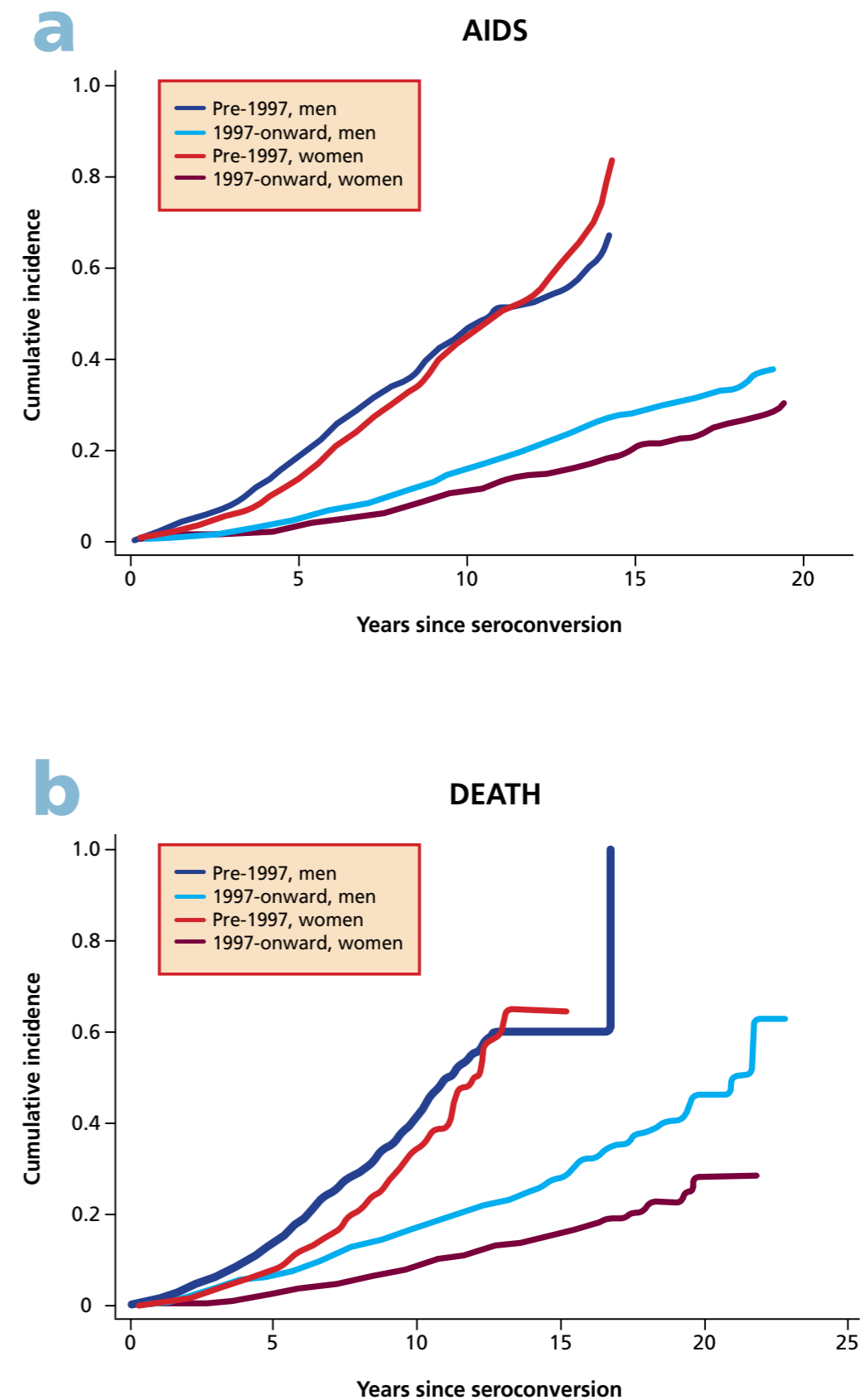
Conclusion

Sex differences in HIV disease progression have become larger and statistically significant in the era of cART, supporting a stronger impact of health interventions among women.

Compared with men, HIV-infected women in industrialised countries survive longer following HIV seroconversion.

Jarrin I, Geskus R, Bhaskaran K, Prins M, Perez-Hoyos S, Muga R, Hernández-Aguado I, Meyer L, Porter K, del Amo J and CASCADE. Gender differences in HIV progression to AIDS and Death in industrialised countries: Slower disease progression following HIV seroconversion in women. AJE 2008; 168:532-40.

Figure 5: Cumulative incidence of a) AIDS and b) death according to number of years from seroconversion and stratified by calendar period (pre-1997 and 1997–2006), and gender.



CASCADE research highlights 2006-2010

The effect of antiretroviral treatment of different durations in primary HIV infection

Background

With long-term exposure to cART being associated with various clinical disorders and adherence problems, the initiation of fixed duration therapy in the early stages of HIV infection (termed primary HIV infection or PHI) has been suggested as an alternative. Whether cART initiation, or at least transient treatment, during primary HIV infection could have a long-lasting beneficial effect is unknown.

In this study, individuals from CASCADE were identified during primary HIV infection. Comparisons were made between CD4 cell, HIV-RNA, and clinical disease rates in those who initiated 'early' cART of different durations during the first 6 months after seroconversion, and those who 'deferred' treatment for at least 6 months following seroconversion.

Results

Of 348 'early treated' patients, 147 stopped cART following treatment for at least 6 months (n=38), more than 6-12 months (n=40), or more than 12 months (n=69). CD4 cell loss was steeper for the first 6 months following cART cessation, but subsequent loss rate was similar to the 'deferred' group (n=675, P=0.26).

Although those treated for more than 12 months appeared to maintain higher CD4 cell counts following cART cessation, those treated for 12 months or less had CD4 cell counts 6 months after cessation comparable to those in the 'deferred' group. See figure 6.

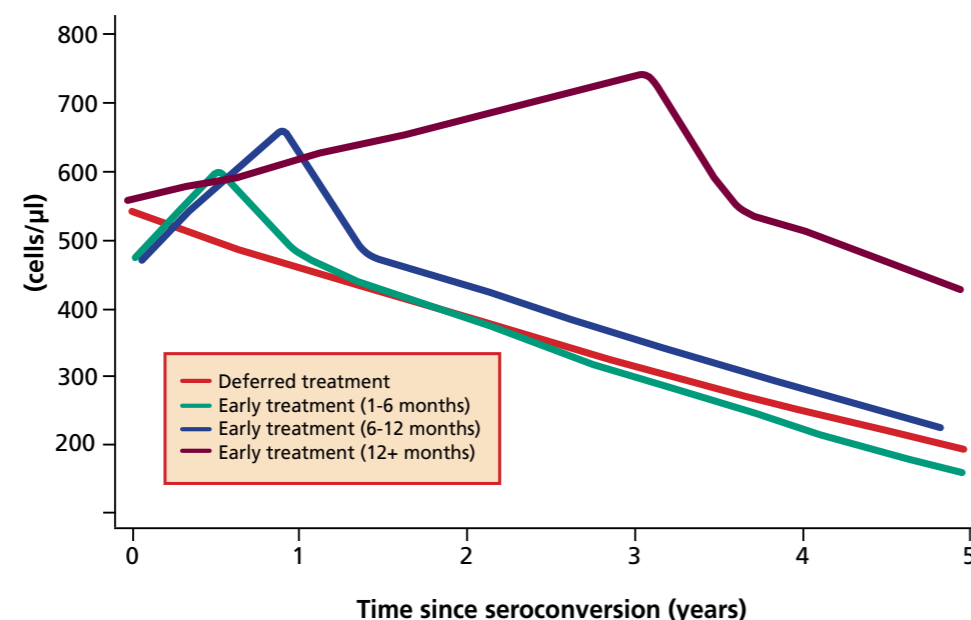
There was no difference in HIV-RNA set points (a term used to describe the stabilisation of viral load) between the 'early' and 'deferred' groups (P=0.57). AIDS rates were similar but death rates, mainly due to non-AIDS causes, were higher in the 'deferred' group (P=0.05).

Conclusion

Transient cART, initiated within 6 months of seroconversion, seems to have no effect on viral load set point, and limited beneficial effect on CD4 cell levels in individuals treated for more than 12 months. Further investigation into its long-term effects is needed.

Pantazis N, Touloumi G, Vanhems P, Gill J, Bucher H, Porter K on behalf of the CASCADE Collaboration. The effect of antiretroviral treatment of different durations in primary HIV infection. AIDS 2008; 22:2441-50.

Figure 6. Predicted average CD4 cell count trends by group ('early' and 'deferred' treatment) and duration of first cART.



Study organisation

CASCADE 2006-2010 was funded through the European Commission's Framework Programme 6 (LSHP-CT-2006-018949)

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Australia Sydney AIDS Prospective Study and Sydney Primary HIV Infection cohort (Tony Kelleher, Tim Ramacciotti, Linda Gelgor, David Cooper, Don Smith); **Canada** South Alberta Clinic (John Gill); **Denmark** Copenhagen HIV Seroconverter cohort (Louise Bruun Jørgensen, Claus Nielsen, Court Pedersen); **Estonia** Tartu Ülikool (Irja Lutsar); **France** Aquitaine cohort (Geneviève Chêne, Francois Dabis, Rodolphe Thiebaut, Bernard Masquelier), French Hospital Database (Dominique Costagliola, Marguerite Guiguet), Lyon Primary Infection cohort (Philippe Vanhems), French PRIMO cohort (Marie-Laure Chaix, Jade Ghosn), SEROCO cohort (Laurence Meyer, Faroudy Boufassa); **Germany** German cohort (Osamah Hamouda, Claudia Kücherer, Barbara Bartmeyer); **Greece** Greek Haemophilia cohort (Giota Touloumi, Nikos Pantazis, Angelos Hatzakis, Dimitrios Paraskevis, Anastasia Karafoulidou); **Italy** Italian Seroconversion Study (Giovanni Rezza, Maria Dorrucchi, Claudia Balotta), ICoNA cohort (Antonella d'Arminio Monforte, Alessandro Cozzi-Lepri, Andrea De Luca.) **Netherlands** Amsterdam Cohort Studies among Homosexual Men and Drug Users (Maria Prins, Ronald Geskus, Jannie van der Helm, Hanneke Schuitemaker); **Norway** Oslo and Ullevål Hospital cohorts (Mette Sannes, Oddbjørn Brubakk, Anne-Marte Bakken Kran); **Poland** National Institute of Hygiene (Magdalena Rosinska, Joanna Gniewosz); **Spain** Badalona IDU Hospital cohort (Roberto Muga, Jordi Tor), Barcelona IDU Cohort (Patricia Garcia de Olalla, Joan Cayla), Madrid cohort (Julia Del Amo, Jorge del Romero), Valencia IDU cohort (Santiago Pérez-Hoyos); **Switzerland** Swiss HIV Cohort Study (Heiner C. Bucher, Martin Rickenbach, Patrick Francioli); **Ukraine** Perinatal Prevention of AIDS Initiative (Ruslan Malyuta); **United Kingdom** Edinburgh Hospital cohort (Ray Brettell), Health Protection Agency (Valerie Delpech, Sam Lattimore, Gary Murphy), Royal Free Haemophilia cohort (Caroline Sabin), UK Register of HIV Seroconverters (Kholoud Porter, Anne Johnson, Andrew Phillips, Abdel Babiker, Valerie Delpech), University College London (Deenan Pillay), University of Oxford (Harold Jaffe), **African cohorts:** Genital Shedding Study (US: Charles Morrison; Family Health International, Robert Salata, Case Western Reserve University, Uganda: Roy Mugerwa, Makerere University, Zimbabwe: Tsungai Chipato, University of Zimbabwe); International AIDS Vaccine Initiative (IAVI) Early Infection Cohorts, Kenya, Uganda, Rwanda, Zambia, South Africa (Susan Allen, Pauli N. Amornkul, Omu Anzala, Linda-Gail Bekker, Pat Fast, Jill Gilmour, Mumbiana Inambao, Etienne Karita, Pontiano Kaleebu, Anatoli Kamali, William Kilembe, Shabir Lakh, Lawrence Mwananyanda, Matt Price, Eduard Sanders).

Publications & presentations 2010

Publications

1. Lodi S, Phillips A, Touloumi G, Pantazis N, Bucher HC, Babiker A, Chêne G, V Philippe, Porter K. CD4 decline in seroconverter and seroprevalent patients in the pre-cART era. *AIDS. In press.*
2. Lodi S, Guiguet M, Costagliola D, Fisher M, de Luca A, Porter K and the CASCADE Collaboration. Incidence of Kaposi's Sarcoma and survival following its diagnosis in HIV-infected homosexual men followed up since HIV seroconversion. *J Natl Cancer Inst.* 102:784-92.
3. Wolbers M, Babiker A, Sabin C, Dorrucchi M, Chêne G, Mussini C, Porter K, Bucher HC, on behalf of the CASCADE Collaboration. Pre-treatment CD4 cell slope and progression to AIDS or death in naïve HIV-infected patients initiating combination antiretroviral therapy: The CASCADE Collaboration. *PLoS Med.* 2010 Feb 23;7(2):e1000239.

Conference presentations

1. Wolbers M, Babiker A, Porter K, Bucher HC, on behalf of the CASCADE Collaboration. CD4 cell slope and AIDS - a case study in longitudinal data analysis and prediction. *ISCB 2010, 29 August - 2 September Montpellier, France*
2. Funk M, Fusco JS, Cole SR, Thomas JC, Porter K, Kaufman JS, Davidian M, White AD, Hartmann KE, Eron JJ, CASCADE Collaboration. HAART initiation and clinical outcomes: insights from the CASCADE cohort of HIV-1 seroconverters on 'When to Start'. *XVIII International AIDS Conference, 18-23 July 2010, Vienna, Austria.*
3. Madec Y, Boufassa F, Prins M, Sabin C, d'Arminio A, Amournkul P, Venet A, Lambotte O, Porter K, Meyer L on behalf of the CASCADE Collaboration. HIV controllers with a known date of seroconversion - What happens before and during HIV control? *XVIII International AIDS Conference, 18-23 July 2010, Vienna, Austria.*
4. van der Helm J, Geskus R, Sabin C, Meyer L, del Amo J, Muga R, Porter K, Prins M. The effect of HCV co-infection on cause-specific mortality. *XVIII International AIDS Conference, 18-23 July 2010, Vienna, Austria.*
5. van der Helm J, Jansen I, Porter K, Geskus R, Lodi S, Meyer L, Sabin C, Schuitemaker H, Gunzenheimer-Bartmeyer B, d'Arminio Montforte A, Prins M, on behalf of the CASCADE Collaboration. The characterisation of long-term non-progression of HIV-1 infection since seroconversion. *XVIII International AIDS Conference, 18-23 July 2010, Vienna, Austria.*

6. van der Wal WM, Prins M, del Amo J, Perez-Hoyos S, Porter K, Geskus RB, Urbanus A. Trends in the causal effect of AIDS defining conditions on mortality. *XVIII International AIDS Conference, 18-23 July 2010, Vienna, Austria.*
7. Jarrin I, Gill J, Geskus R, Meyer L, Touloumi G, Prins M, Hamouda O, Pantazis N, Perez-Hoyos S, Porter K, del Amo J, and the CASCADE Collaboration. Differences in time from HIV seroconversion to HAART initiation according to geographical origin. *XVIII International AIDS Conference, 18-23 July 2010, Vienna, Austria.*
8. Lodi S, Phillips A, Touloumi G, Geskus R, Meyer L, Thiebaut R, Pantazis N, del Amo J, Babiker A, Porter K, on behalf of the CASCADE Collaboration. Proportion of individuals likely to need treatment for CD4 thresholds <200, <350, and <500 cells. *The 17th Conference on Retroviruses and Opportunistic Infections, San Francisco, February 2010.*
9. Lodi S, Murphy G, Rosinska M, Smolen J, Zalewska M, Janiec J, Marzec-Boguslawska, Porter K. Concordance of recent HIV infection between three STARHS assays is not dependent on patient characteristics. *The 17th Conference on Retroviruses and Opportunistic Infections, San Francisco, February 2010.*
10. Pantazis N. Longitudinal CD4 cell count evolution during HIV natural history: comparison between European and sub-Saharan African seroconverter cohorts. *The 17th Conference on Retroviruses and Opportunistic Infections, San Francisco, February 2010.*
11. Jarrin I, Gill J, Geskus R, Meyer L, Touloumi G, Prins M, Hamouda O, Perez-Hoyos S, Porter K, del Amo J. Differences in time to AIDS and death following HIV seroconversion according to geographical origin. *The 17th Conference on Retroviruses and Opportunistic Infections, San Francisco, February 2010.*
12. van der Helm J, Geskus R, del Amo J, Chêne G, Gill J, Hamouda O, Sannes M, Porter K, Prins M, on behalf of the CASCADE Collaboration. The hepatitis C epidemic among HIV-positive men who have sex with men started before 2000. *The 17th Conference on Retroviruses and Opportunistic Infections, San Francisco, February 2010.*

Publications & presentations 2009

Publications

1. Marin B, Thiébaud R, Bucher HC, Rondeau V, Costagliola D, Dorrucchi M, Hamouda O, Prins M, Walker AS, Porter K, Sabin CA, Chêne G on behalf of the CASCADE Collaboration. Non-AIDS defining deaths and immunodeficiency in the era of combination antiretroviral therapy. *CASCADE 1996-2006. AIDS 2009; 23; 1743-53*
2. Brown AE, Gifford RJ, Clewley JP, Kucherer C, Masquelier B, Porter K, Balotta C, Back NK, Jorgensen LB, de Mendoza C, Bhaskaran K, Gill ON, Johnson AM, Pillay D on behalf of the CASCADE Collaboration. Phylogenetic reconstruction of transmission events from individuals with acute HIV infection: toward more rigorous epidemiological definitions. *JID 2009; 199:427-431*

Conference presentations

1. van der Helm J, Geskus RB, del Amo J, Porter K, Prins M on behalf of CASCADE Collaboration. The hepatitis C epidemic among HIV-positive men who have sex with men started before 2000. Accepted as a poster presentation at the 18th International Society for STD Research Conference, 28th June - 1st July 2009, London.
2. Lodi S, Porter K, Phillips A, on behalf of the CASCADE Collaboration. Time to reaching CD4 \leq 500 for individuals followed up since HIV seroconversion. Accepted as a poster to the 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention, July 19th-22nd July 2009, Cape Town.
3. Ewings F, Walker AS, Porter K, Copas A. Using causal models to determine optimal dynamic treatment regimes with a time-to-event outcome. Accepted as an oral presentation at the 30th Annual Conference of the International Society for Clinical Biostatistics, 23rd - 27th August 2009, Prague. Abstract reference: S11.4.

4. van der Wal W, del Amo-Valero J, Porter K, Perez-Hoyos S, Prins M, Geskus RB, on behalf of the CASCADE Collaboration. Causal effect of AIDS-defining conditions on mortality modified by HAART use and calendar time. Accepted as an oral presentation at the 30th Annual Conference of the International Society for Clinical Biostatistics, 23rd - 27th August 2009, Prague. Abstract reference S27.3.
5. Drylewicz J, Walker S, Commenges D, Pillay D, Venet A, Masquelier B, Meyer L, Chêne G, Porter K, Thiébaud R, and the CASCADE Collaboration. Plasma HIV RNA and CD4+ count dynamics during acute infection in 761 HIV-1-infected patients: The CASCADE Collaboration. *The 16th Conference on Retroviruses and Opportunistic Infections, Montreal, February 2009, San Francisco, February 2010.*



Publications & presentations 2008

Publications

1. Pantazis N, Touloumi G, Vanhems P, Gill J, Bucher H, Porter K on behalf of the CASCADE Collaboration. The effect of antiretroviral treatment of different durations in primary HIV infection. *AIDS* 2008; 22:2441-50
2. Touloumi G, Pantazis N, Stirnadel AH, Walker AS, Boufassa F, Vanhems P, Porter K on behalf of the CASCADE Collaboration. Rates and determinants of virologic and immunologic response to HAART resumption after treatment interruption in HIV-1 clinical practice. *JAIDS*. 2008;49:492-8.
3. Bhaskaran K, Hamouda O, Sannes M, Boufassa F, Johnson A, Lambert P and Porter K on behalf of the CASCADE Collaboration. Changes in the risk of death after HIV seroconversion compared with mortality in the general population. *JAMA* 2008; 2;300:51-9
4. Jarrin I, Geskus R, Bhaskaran K, Prins M, Perez-Hoyos S, Muga R, Hernández-Aguado I, Meyer L, Porter K, del Amo J and CASCADE. Gender differences in HIV progression to AIDS and Death in industrialised countries: Slower disease progression following HIV seroconversion in women. *AJE* 2008; 168:532-40
5. The Collaboration of Observational HIV Epidemiological Research Europe (COHERE) Study. Response to combination antiretroviral therapy (cART): variation by age. *AIDS* 2008;22:1463-73
6. Bhaskaran K, Mussini C, Antinori A, Walker AS, Dorrucci M, Sabin C, Phillips A, Porter K on behalf of CASCADE Collaboration. Changes in the incidence and predictors of HIV-associated dementia in the era of highly active antiretroviral therapy. *Ann Neurol*. 2008;63:213-21

7. Guiguet M, Porter K, Phillips A, Costagliola D, Babiker A on behalf of the CASCADE collaboration. Clinical progression rates by CD4 cell category before and after the initiation of combination antiretroviral therapy (cART). *Open AIDS Journal* 2008;2:3-9
8. Dunn DT, Woodburn P, Duong T, Peto J, Phillips A, Gibb D, Porter K on behalf of HIV Paediatric Prognostic Markers Collaborative Study (HPPMCS) and the CASCADE Collaboration. Current CD4 cell count and the short-term risk of AIDS and death before the availability of effective antiretroviral therapy in HIV-infected children and adults. *J Infect Dis* 2008; 197:398-404.

Conference presentations

1. Pantazis N, Touloumi G, Vanhems P, Gill J, Porter K. The effect of antiretroviral treatment of different durations in primary HIV infection. 15th Conference on Retroviruses and Opportunistic Infections, Boston, February 2008.
2. Porter K, Hamouda O, Sannes M, Boufassa F, Johnson A, Walker S. Changes over time in the risk of death following HIV seroconversion compared with mortality in the general population. 15th Conference on Retroviruses and Opportunistic Infections, Boston, February 2008.

Publications & presentations 2007

Publications

1. Dorrucci M, Rezza G, Porter K, Phillips A and Concerted Action on Seroconversion to AIDS and Death in Europe Collaboration. Temporal trends in post-seroconversion CD4 cell count and HIV load: the Concerted Action on Seroconversion to AIDS and Death in Europe Collaboration, 1985-2002. *J Infect Dis* 2007; 195:525-34.
2. Lampe FC, Porter K, Kaldor J, Law M, Kinloch-de Loes S, Phillips AN on behalf of the CASCADE Collaboration. Effect of transient antiretroviral treatment during acute HIV infection: comparison of the Quest trial results with CASCADE natural history study. *Antivir Ther* 2007; 12:189-93.
3. Fidler S, Fox J, Touloumi G, Pantazis N, Porter K, Babiker A, Weber J and the CASCADE Collaboration. Slower CD4 cell decline following cessation of a 3-month course of HAART in primary HIV infection. *AIDS*. 2007 Jun 19; 21:1283-91.

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1. Marin B, Thiébaud R, Rondeau V, Costagliola D, Dorrucci M, Bucher H, Hamouda O, Walker AS, Bhaskaran K, Chêne G on behalf of the CASCADE Collaboration. Association between CD4 and HIV RNA with non AIDS-related causes of death in the era of combination Antiretroviral Therapy (cART). 4th IAS Conference on HIV Pathogenesis and Treatment, Sydney July 2007 [WEPEB019].
2. Touloumi G, Pantazis N, Stirnadel HA, Walker AS, Boufassa F, Vanhems P, Porter K on behalf of the CASCADE Collaboration. Determinants of immunological response to HAART resumption after treatment interruption in HIV-1 clinical practice. 4th IAS Conference on HIV Pathogenesis and Treatment, Sydney July 2007 [WEPEB072].

3. Porter K, Bhaskaran K on behalf of CASCADE Collaboration. Continuing improvements in survival in the era of HAART. 4th IAS Conference on HIV Pathogenesis and Treatment, Sydney July 2007 [TUPEB093].
4. Brown AE, Gifford RJ, Porter K, Clewley JP, Gill ON, Johnson AM, Pillay D on behalf of the CASCADE Collaboration. A phylogenetic exploration of the role of seroconverters in transmitting HIV drug resistant viruses within Europe. 14th International Workshop on HIV Dynamics & Evolution, Parador De Segovia, Spain April 2007 [53].
5. Dunn D, Woodburn P, Duong T, Phillips A, Gibb D, Porter K on behalf of HIV Paediatric Prognostic Markers Collaborative Study (HPPMCS) and the Concerted Action on SeroConversion to AIDS and Death in Europe (CASCADE Collaboration). A comparison of the rate of clinical disease progression in HIV-infected children and adults allowing for current CD4 cell count. 14th Conference on Retroviruses and Opportunistic Infections, Los Angeles, February 2007 [700].
6. Fidler S, Touloumi G, Fox J, Pantazis N, Porter K, Babiker A, Weber J on behalf of the CASCADE Collaboration. Slower CD4 cell decline following cessation of a 3-month course of HAART in Primary HIV infection. 14th Conference on Retroviruses and Opportunistic Infections, Los Angeles, February 2007 [348].
7. Jarrin I, Del Amo J, Bhaskaran K, Pérez-Hoyos S, Hernández-Aguado I, Meyer L, Prins M, Porter K on behalf of the CASCADE Collaboration. Changes over time in the risk of AIDS by sex: slower progression in women in recent periods. 14th Conference on Retroviruses and Opportunistic Infections, Los Angeles, February 2007 [776].

