

# Insurability of HIV-positive people treated with antiretroviral therapy in Europe: collaborative analysis of HIV cohort studies

Josee Kaulich-Bartz<sup>a</sup>, Wayne Dam<sup>a</sup>, Margaret T. May<sup>b</sup>,  
 Bruno Lederberger<sup>c</sup>, Urs Widmer<sup>a</sup>, Andrew N. Phillips<sup>d</sup>,  
 Sophie Grabar<sup>e,f,g</sup>, Amanda Mocroft<sup>d</sup>, Josep Vilaro<sup>h</sup>,  
 Ard van Sighem<sup>i</sup>, Santiago Moreno<sup>j</sup>, François Dabis<sup>k</sup>,  
 Antonella D'Arminio Monforte<sup>l</sup>, Ramon Teira<sup>m</sup>, Suzanne M. Ingle<sup>b</sup>,  
 Jonathan A.C. Sterne<sup>b</sup>, Writing Committee for the  
 Antiretroviral Therapy Cohort Collaboration

**Objective:** To increase equitable access to life insurance for HIV-positive individuals by identifying subgroups with lower relative mortality.

**Design:** Collaborative analysis of cohort studies.

**Methods:** We estimated relative mortality from 6 months after starting antiretroviral therapy (ART), compared with the insured population in each country, among adult patients from European cohorts participating in the ART Cohort Collaboration (ART-CC) who were not infected via injection drug use, had not tested positive for hepatitis C, and started triple ART between 1996–2008. We used Poisson models for mortality, with the expected number of deaths according to age, sex and country specified as offset.

**Results:** There were 1236 deaths recorded among 34 680 patients followed for 174 906 person-years. Relative mortality was lower in patients with higher CD4 cell count and lower HIV-1 RNA 6 months after starting ART, without prior AIDS, who were older, and who started ART after 2000. Compared with insured HIV-negative lives, estimated relative mortality of patients aged 20–39 from France, Italy, United Kingdom, Spain and Switzerland, who started ART after 2000 had 6-month CD4 cell count at least 350 cells/ $\mu$ l and HIV-1 RNA less than  $10^4$  copies/ml and without prior AIDS was 459%. The proportion of exposure time with relative mortality below 300, 400, 500 and 600% was 28, 43, 61 and 64%, respectively, suggesting that more than 50% of patients (those with lower relative mortality) could be insurable.

<sup>a</sup>Swiss Re Limited, Zurich, Switzerland, <sup>b</sup>School of Social and Community Medicine, University of Bristol, Bristol, UK, <sup>c</sup>Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, <sup>d</sup>Research Department of Infection and Population Health, UCL Medical School, London, UK, <sup>e</sup>Institut National de la Santé et de la Recherche Médicale, <sup>f</sup>Faculte de Medecine, Universite Paris Descartes, <sup>g</sup>AP-HP, Hopital Cochin, Paris, France, <sup>h</sup>Consorci Hospitalari de Vic, Barcelona, Spain, <sup>i</sup>Stichting HIV Monitoring, Amsterdam, the Netherlands, <sup>j</sup>Hospital Ramón y Cajal, Servicio de Enfermedades Infecciosas, Instituto Ramón y Cajal de Investigación Sanitaria, Madrid, Spain, <sup>k</sup>INSERM U.897, ISPED, Université Bordeaux, Bordeaux, France, <sup>l</sup>Clinic of Infectious Diseases and Tropical Medicine, San Paolo Hospital, University of Milan, Milan, Italy, and <sup>m</sup>Hospital Sierrallana, Torrelavega, Spain.

Correspondence to Dr Margaret T. May, Reader in Medical Statistics, School of Social and Community Medicine, University of Bristol, Bristol BS8 2PS, UK.

Tel: +44 117 928 7287; fax: +44 117 928 7325; e-mail: m.t.may@bristol.ac.uk

Received: 4 October 2012; revised: 6 February 2013; accepted: 11 February 2013.

DOI:10.1097/QAD.0b013e3283601199

ISSN 0269-9370 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 3.0 License, where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially.

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

**Conclusion:** The continuing long-term effectiveness of ART implies that life insurance with sufficiently long duration to cover a mortgage is feasible for many HIV-positive people successfully treated with ART for more than 6 months.

© 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins

AIDS 2013, 27:1641–1655

**Keywords:** antiretroviral therapy, cohort study, HIV, insurability, life tables

## Introduction

Since its introduction in 1996, improvements to combination antiretroviral therapy (ART) such as new regimens [1] and one pill per day coformulations [2] have led to improved prognosis and better adherence to treatment [3]. Rates of mortality among HIV-positive people have declined sufficiently dramatically [4,5] to justify the introduction of limited life insurance for HIV-positive applicants who are not coinfected with hepatitis C virus (HCV) [6]. On the basis of estimated standardized mortality ratios for nine countries, a recent study concluded that a significant proportion of HIV-positive individuals experience similar mortality to those with other conditions requiring lifelong treatment, such as diabetes [7]. However, access to life insurance remains limited.

Analyses of data from cohorts of treated HIV-positive people, in which the comparator is the subset of the general population that takes out life insurance rather than the general population [7], can inform the promotion of fair access to underwritten insurance for HIV-positive individuals. By accounting for risk factors that have been established as strongly prognostic for mortality [8], such analyses can identify insurable subgroups and facilitate the calculation of evidence-based ratings for longer term insurance, based on extrapolation of current mortality rates. We identify insurable subgroups of the HIV-positive population in Europe, using data from European cohorts participating in the ART Cohort Collaboration (ART-CC).

## Methods

The ART-CC, described in detail elsewhere [9,10], is an international collaboration of HIV cohort studies that combines data on HIV-positive individuals who were antiretroviral-naïve when they started ART. Here, eligible patients were participants in European cohorts, aged at least 18 years, had presumed mode of transmission that was not via IDU, and initiated ART between 1996 and 2008. All had CD4 cell count and HIV-1 RNA measured in the 3 months before ART initiation, and between 3 and 9 months after initiation. The included cohorts, from six countries, were: the AIDS Therapy Evaluation Project Netherlands (ATHENA); the Agence

Nationale de Recherches sur le SIDA et les hépatites virales (ANRS) CO4 French Hospital Database on HIV (FHDH) and ANRS CO3 Aquitaine Cohort, France; Italian Cohort of Antiretroviral-Naïve Patients (ICONA); Royal Free Hospital Cohort, London United Kingdom; Swiss HIV Cohort Study (SHCS); the Cohorte de la Red de Investigación en Sida (CoRIS), the Proyecto para la Informatización del Seguimiento Clínico-epidemiológico de la Infección por HIV y SIDA (PISCIS) Cohort, VACH, Spain; and the multicenter study, EuroSIDA (restricted to patients from the selected six countries). Data on follow-up for mortality were available to 31 December 2009. Patients not known to have died were considered lost to follow-up 3 months after their last CD4 cell count measurement, except when this was within 6 months of study end. Institutional review boards from each cohort approved analysis of routinely collected data.

Expected numbers of deaths according to age, sex and country were calculated based on so-called 'standard' insured lives (those healthy lives accepted for life insurance using standard premium rates without a health loading). These were based on published insurance tables where available (France, Netherlands, United Kingdom), or on adjustments to population mortality tables (Italy, Spain, Switzerland) commonly used in those markets by pricing actuaries. The specific percentages used for each market (country) were obtained from interviews with Swiss Re (a reinsurance company with headquarters in Zurich, Switzerland) regional pricing actuaries and were based on their knowledge of pricing levels in those markets. Such multiplicative adjustments reflected typical industry pricing levels for individual life insurance in 2004, taking into account the risk assessment (underwriting) practices in 2011 and accounts for insured lives having lower mortality than general population lives. Insurance mortality trends are a combination of the underlying health and accident trends in the insured population and the trends in (or changes in practice of) how underwriters decide which lives belong to the pool of insured persons with standard risk. For France we used 50% of mortality rates in actuarial tables TF00-02 (women) and 40% of TH00-02 (men), respectively ([www.institutdesactuaires.com/docs/2007017232113\\_NOTICETHF0002.pdf](http://www.institutdesactuaires.com/docs/2007017232113_NOTICETHF0002.pdf)). For the Netherlands we used 55% of the respective GBM/V00-5 tables ([www.ag-ai.nl/download/10351-Prognosetafel+2005+-+2050.pdf](http://www.ag-ai.nl/download/10351-Prognosetafel+2005+-+2050.pdf) p66). For the UK we used 70% of TF00 and 60% of TM00,

respectively ([www.actuaries.org.uk/research-and-resources/pages/00-series-mortality-tables-assured-lives-annuitants-and-pensioners](http://www.actuaries.org.uk/research-and-resources/pages/00-series-mortality-tables-assured-lives-annuitants-and-pensioners)). For Italy we used 55% of the respective 2002 population mortality tables for each sex published by the Italian National Institute of Statistics (table SI 2002 [www.istat.it](http://www.istat.it)). For Spain we used 45% of the 2006 population mortality and for Switzerland we used 80% of the 2006 population mortality (Human Mortality Database [www.mortality.org](http://www.mortality.org)).

The United Kingdom and Netherlands tables provided rates by age and duration at policy inception: the effect of duration generally decreases with increasing time since the underwriting date and the rates after which there is no substantial change with increasing duration are termed 'ultimate'. The lives in the HIV study were not screened through the normal insurance processes. It is, thus, consistent to compare them with insurance rates where the effects of such screening have worn off, which correspond to the 'ultimate rates' in the comparator insured population. Therefore, we used the ultimate rates, which depend only on age, from these tables.

We graphed assumed mortality rates for insured lives (using the above-mentioned tables) by age, sex and country, and compared mortality rates for insured lives and the general population by age and sex. The general population reference was based on the human mortality database ([www.mortality.org](http://www.mortality.org)) for 2004, and the rates for each country weighted according to the person-years of observation in the analysis dataset.

Data analyses used generalized linear models (GLM) assuming a Poisson error distribution with log link function [11] and with expected numbers of deaths based on the insured population (person-years at risk multiplied by the rate in the corresponding insured population) according to age, sex and country specified as an offset [12]. As we wished to model duration of ART explicitly, we did not allow for it in the offset. The variables considered for inclusion were country, sex, transmission risk group (MSM, heterosexual contact, blood and other), year of initiation of ART, age at start of ART, AIDS diagnosis prior to ART and CD4 cell count and HIV-1 RNA at start of ART and 6 months later (see Table 1 for categorizations). The 6-month CD4 cell count and HIV-1 RNA used in the analysis were those measured closest to 6 months after start of ART and within a window of 3–9 months. We additionally considered for inclusion in the GLM three variables that varied over time: calendar time (1996–2000, 2001–2008), current age (20–29, 30–39, 40–49, 50–59, ≥60 years) and duration of ART since the 6-month measurement (1–3, 4–6, 7–9, ≥10 years). Note that duration of ART equal to 1–3 corresponds to the first 3 years after the 6-month measurement, and therefore is follow-up time from 0.5 to 3.49 years after starting ART.

Starting with a model including all variables, we removed variables to find a model containing only variables with clear associations ( $P < 0.05$ ) with mortality and where the residuals were not overly overdispersed or underdispersed. The dispersion parameter measures both underdispersion and overdispersion and should be close to one for a well fitting Poisson model. We combined categories where this improved model fit, and tested two-way, but not higher-order, interactions. We chose the final model based on dispersion parameter within 5% of 1, lower Akaike Information Criterion (AIC) [13] and normality of the distribution of Anscombe residuals [11]. In sensitivity analyses we used  $P$  value less than 0.1 as the threshold for variable selection and considered models with a negative binomial distribution.

The final GLM was used to estimate the relative mortality of the group with reference values of all included variables, compared with insured lives within the same age and country group. The relative mortality of other groups was derived by multiplying baseline relative mortality by mortality rate ratios from the GLM. Potential insurability is determined by the actual/expected claims ratio (relative mortality multiplied by 100%). A claims ratio of 100% represents no excess mortality, whereas 500%, or equivalently relative mortality 5, represents 400% excess mortality. Bounds for insurability are not fixed, and therefore we illustrated the extent of excess mortality by drawing plots of actual/expected claims ratios with contours at 100, 250, 500, 750, 1000, 2000 and 3000% relative mortality, according to 6-month CD4 cell count, ART duration, age and calendar period of ART initiation, among people with lower risk values of other variables. Stata<sup>TM</sup> version 12 and Microsoft Excel 2007 were used to perform analyses.

## Results

Among 34 680 patients followed for 174 906 person-years there were 1236 deaths (overall mortality rate 0.71 [95% confidence interval (CI) 0.67–0.75] per 100 person-years). The majority of the data were from France and the Netherlands (Table 1) and 70% of patients were men. Crude mortality rates increased with age and were higher for men and those with an AIDS diagnosis prior to baseline. The association of lower CD4 cell count and higher HIV-1 RNA with mortality was greater for 6-month measurements than those at initiation of ART. Crude mortality rates varied between countries and were lower for the United Kingdom and Italian cohorts, which may reflect true lower mortality or might be due to sampling variability or incomplete death ascertainment.

Figure 1 (upper panel) shows mortality rates in the insured population according to sex, age and country. Differences in mortality rates between countries were

**Table 1.** Characteristics of 34 680 HIV-positive patients included in the analyses.

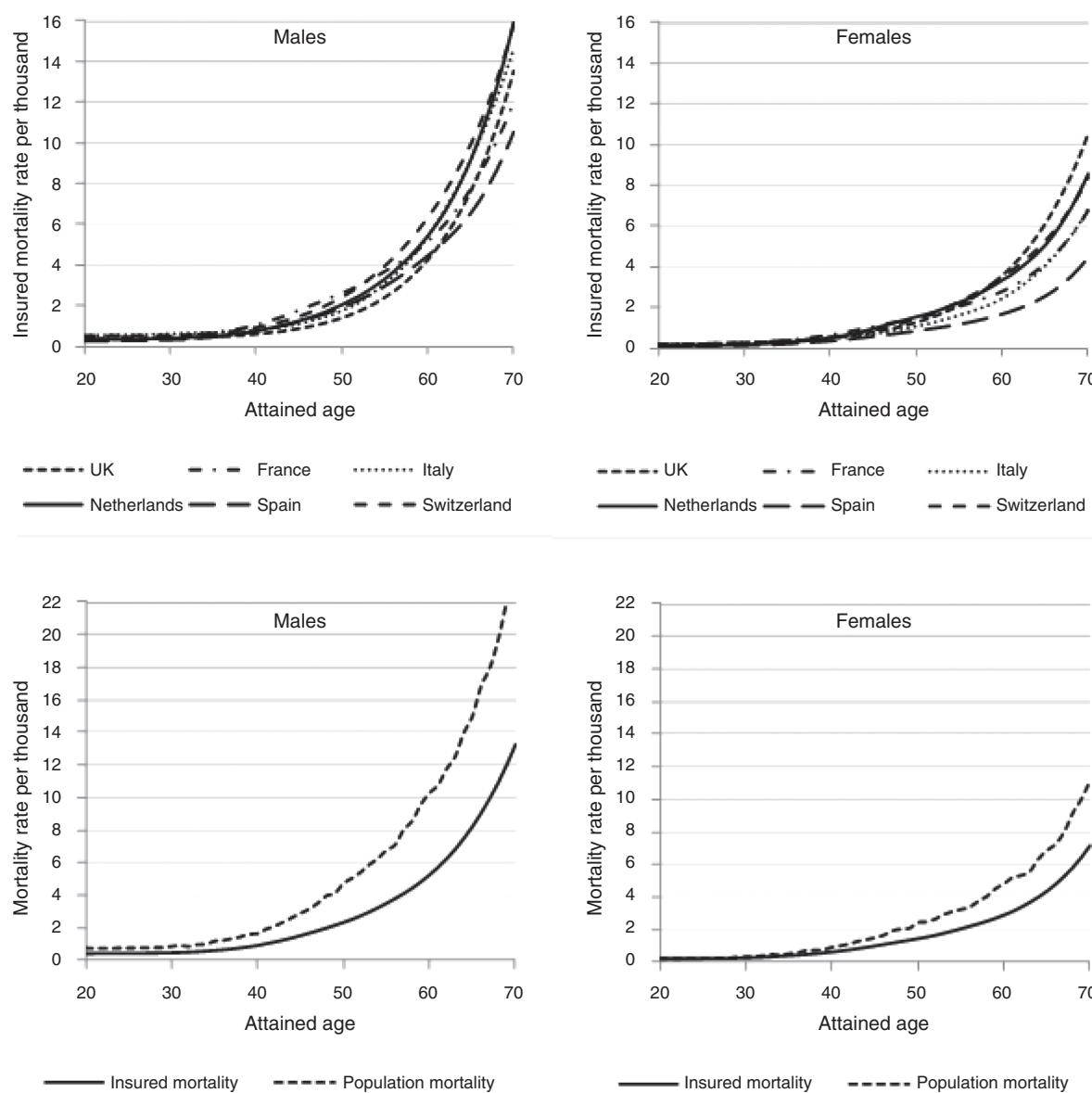
Characteristic	Category	Number of patients (%)	No. of deaths (%)	Crude mortality rate per 100 person-years (95% CI)
Total		34 680 (100)	1236 (100)	0.71 (0.67–0.75)
Country	France	19 503 (56)	684 (55)	0.71 (0.66–0.76)
	Italy	1683 (5)	38 (3)	0.43 (0.29–0.58)
	Netherlands	5718 (16)	250 (20)	0.78 (0.69–0.89)
	Spain	3379 (10)	85 (7)	0.61 (0.48–0.75)
	Switzerland	3209 (9)	147 (12)	0.82 (0.69–0.96)
	UK	1188 (3)	32 (3)	0.53 (0.36–0.74)
Sex	Female	10 504 (30)	216 (17)	0.44 (0.38–0.50)
	Male	24 176 (70)	1020 (83)	0.81 (0.76–0.86)
Age at initiation of ART (years)	15–29	6891 (20)	118 (10)	0.34 (0.28–0.41)
	30–49	22 437 (65)	685 (55)	0.59 (0.55–0.64)
	≥50	5352 (15)	433 (35)	1.71 (1.54–1.87)
Year of ART initiation	1996–2000	13 005 (38)	765 (62)	0.76 (0.71–0.81)
	2001–2004	12 807 (37)	375 (30)	0.64 (0.57–0.71)
	2005–2008	8868 (26)	96 (8)	0.62 (0.50–0.75)
Transmission risk group	MSM	13 845 (40)	497 (40)	0.66 (0.60–0.72)
	Heterosexual	17 948 (52)	580 (47)	0.67 (0.62–0.73)
	Blood	335 (1)	24 (2)	1.29 (0.83–1.93)
	Other	2552 (7)	135 (11)	1.15 (0.96–1.35)
Baseline CD4 cell count (cells/µl)	≥350	8200 (24)	186 (15)	0.40 (0.34–0.46)
	200 to 349	10 669 (31)	266 (22)	0.54 (0.47–0.60)
	100 to 199	7020 (20)	263 (21)	0.79 (0.69–0.89)
	50 to 99	3404 (10)	175 (14)	1.00 (0.85–1.16)
	<50	5387 (16)	346 (28)	1.24 (1.11–1.38)
Six-month CD4 cell count (cells/µl)	≥350	17 001 (49)	349 (28)	0.40 (0.36–0.44)
	200 to 349	9425 (27)	312 (25)	0.68 (0.61–0.76)
	100 to 199	5689 (16)	275 (22)	0.95 (0.83–1.06)
	50 to 99	1788 (5)	147 (12)	1.57 (1.32–1.84)
	<50	777 (2)	153 (12)	4.61 (3.88–5.37)
Baseline HIV-1 RNA (copies/ml)	<500	2683 (8)	63 (5)	0.57 (0.43–0.72)
	≥500 to $1 \times 10^4$	5053 (15)	148 (12)	0.58 (0.49–0.68)
	$\geq 1 \times 10^4$ to $1 \times 10^5$	12 265 (35)	376 (30)	0.59 (0.53–0.66)
	≥1 × 10 <sup>5</sup>	14 679 (42)	649 (53)	0.86 (0.80–0.93)
Six-month HIV-1 RNA (copies/ml)	<500	24 725 (71)	685 (55)	0.60 (0.56–0.65)
	≥500 to $1 \times 10^4$	7298 (21)	313 (25)	0.65 (0.58–0.72)
	$\geq 1 \times 10^4$ to $1 \times 10^5$	1788 (5)	117 (9)	1.33 (1.09–1.58)
	≥1 × 10 <sup>5</sup>	869 (3)	121 (10)	3.01 (2.47–3.57)
Clinical CDC stage at baseline	A/B	27 067 (78)	749 (61)	0.55 (0.51–0.59)
	C	7613 (22)	487 (39)	1.25 (1.14–1.36)

ART, antiretroviral therapy; CDC, Centers for Disease Control.

relatively small, UK men and women had the highest mortality rates at most ages, whereas Spanish women had the lowest mortality. Figure 1 (lower panel) shows the lower mortality in the insured population compared with the whole population, in both men and women.

The final model did not include sex: the model offset effectively adjusted for sex as mortality rates were lower in women in the insured population. CD4 cell count and HIV-1 RNA at initiation of ART were not sufficiently prognostic for inclusion in the final model, after adjustment for 6-month values of those variables. Age at initiation was not prognostic after adjustment for current age. There was little difference between mortality from 7–9 and at least 10 years duration of ART and so these categories were combined. Similarly, categories for starting ART in 2001–2004 and 2005–2008 were combined, and HIV-1 RNA was dichotomized at  $10^4$  copies/ml. The dispersion parameter was lowest in models that included all countries separately, and

therefore groupings of countries were examined. Comparing the two countries contributing most person-years, Dutch lives experienced higher adjusted relative mortality than French lives, partly because of the lower standard mortality of the Dutch insured HIV-negative population. We found little evidence that relative mortality in the other included countries differed from that of either France or the Netherlands, but that the best-fitting model was obtained by grouping other countries with France. After choosing prognostic variables and their groupings and restricting to models with dispersion parameter within 5% of 1, two models with similar AIC and Anscombe residual distribution remained. We chose the model that did not include transmission risk category, as differential pricing of insurance based on slightly higher mortality rates in individuals with transmission via blood transfusion would be difficult to justify. The final model did not include any interactions. Sensitivity analyses indicated that variables selected for inclusion in the final model were the same when the *P* value threshold was



**Fig. 1. Mortality rates according to age and country of insurance population (upper panels) and weighted European mortality comparing insurance population and general population (lower panels).**

raised from 0.05 to 0.1 and that the selected Poisson model fitted the data better than a negative binomial model.

Mortality rate ratios for the variables included in the final model are displayed in Table 2, which shows that CD4 cell count and viral load at 6 months were the most strongly prognostic variables. Mortality rate ratios decreased with age ( $P < 0.005$ ) because increases in mortality with age in HIV-positive people were less marked than in comparator populations. Mortality rate ratios decreased with ART duration and were higher for those who initiated ART before 2001 ( $P < 0.005$ ) or who had an AIDS diagnosis prior to starting ART ( $P < 0.005$ ).

The baseline group for comparison of mortality ratios was patients aged 20–39 from France, Italy, United Kingdom, Spain and Switzerland, who started ART after 2000, had 6-month CD4 cell count at least 350 cells/ $\mu$ l, 6-month HIV-1 RNA  $< 10^4$  copies/ml and no AIDS before ART initiation, during the first 3 years of ART. The relative mortality of this group compared with insured HIV-negative lives in the same age group was 459% (95% CI 391–539). The relative mortality of other groups is derived by multiplying by the corresponding mortality rate ratios in Table 2. For example, patients aged 40–49 years with 6-month CD4 cell count 200–349 cells/ $\mu$ l, who started ART before 2001 and otherwise the same characteristics as the baseline group had relative mortality  $459\% \times 0.53 \times 1.44 \times 1.33 = 466\%$  during the

**Table 2.** Crude (univariable) and adjusted (multivariable) mortality rate ratios among 34 680 HIV-positive people included in analyses, based on the final generalized linear model.

Characteristic	Category	Mortality rate ratio Crude (univariable)	(95% CI) Adjusted (multivariable)
6 month CD4 cell count (cells/ $\mu$ l)	0–49	10.75 (8.89–13.01)	6.84 (5.54–8.45)
	50–99	3.17 (2.61–3.85)	2.71 (2.21–3.32)
	100–199	1.87 (1.59–2.19)	1.76 (1.49–2.08)
	200–349	1.44 (1.23–1.67)	1.44 (1.24–1.69)
	350+ (*)	1.00	1.00
6 month HIV-1 RNA (copies/ml)	$0–1 \times 10^4$ (*)	1.00	1.00
	$\geq 10^4$	3.68 (3.19–4.24)	2.42 (2.08–2.82)
Region	Countries excl. NL (*)(**)	1.00	1.00
	Netherlands	1.25 (1.09–1.44)	1.48 (1.28–1.70)
Current age	20–39 (*)	1.00	1.00
	40–49	0.53 (0.46–0.61)	0.53 (0.46–0.62)
	50–59	0.40 (0.34–0.47)	0.41 (0.35–0.48)
	60+	0.26 (0.22–0.30)	0.28 (0.24–0.34)
Duration of ART (years)	1–3 (*)	1.00	1.00
	4–6	0.66 (0.58–0.75)	0.69 (0.61–0.79)
	7+	0.48 (0.41–0.56)	0.51 (0.43–0.61)
Clinical CDC stage at baseline	Stage A/B (*)	1.00	1.00
	Stage C	1.85 (1.65–2.08)	1.40 (1.23–1.58)
Year of ART initiation	1996–2000	1.06 (0.94–1.18)	1.33 (1.18–1.50)
	2001–2008 (*)	1.00	1.00

ART, antiretroviral therapy; CDC, Centers for Disease Control. (\*) The baseline, corresponding to the categories (\*) above, is equal to an actual/expected claims ratio of 459%. (\*\*) Countries excl. NL include France, Italy, Spain, Switzerland and the UK.

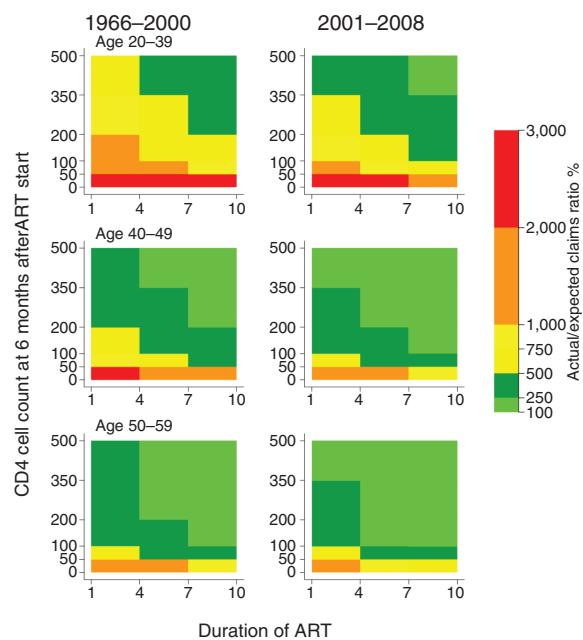
first 3 years,  $466\% \times 0.69 = 321\%$  during years 4–6 and  $466\% \times 0.51 = 238\%$  after 7 or more years on ART.

Figure 2 shows contours of relative mortality according to CD4 cell count and duration of treatment, separately according to age group and calendar period of starting ART, among patients with lower risk values of other variables. Supplementary Table 1, <http://links.lww.com/QAD/A325> shows percentage relative mortality according to risk factors for France, Italy, Spain, Switzerland, and United Kingdom (illustrated in Fig. 2) and supplementary Table 2, <http://links.lww.com/QAD/A325> shows relative mortality for the Netherlands. In our study population (which excluded IDU or those who were hepatitis C positive), the proportion of exposure time with relative mortality below 300, 400, 500 and 600% was 28, 43, 61 and 64%, respectively.

## Discussion

We estimated the relative mortality of HIV-positive lives, compared with insured HIV-negative lives in the same population. Our results apply to HIV-positive individuals who have survived at least 6 months after starting ART in six European countries. Relative mortality was lower for those who started ART after the year 2000 without a prior AIDS diagnosis and who had 6-month CD4 cell count greater than 350 cells/ $\mu$ l and 6-month HIV-1 RNA less than  $10^4$  copies/ml. Relative mortality compared with insured HIV-negative lives declined with increasing duration of ART, and decreased with age despite increases in mortality rates with age, a phenomenon that has been observed in other studies of HIV populations

[14–16]. Because relative mortality varies with age and with time on ART, no single result applies to any particular insurance policy, our results must be used as a



**Fig. 2.** Percentage relative mortality compared with HIV-negative insured lives (actual/expected claims ratio) of HIV-positive people according to CD4 cell count 6 months after start of ART, duration of ART, age group and calendar period of initiation of ART, among individuals without an AIDS diagnosis and with 6-month HIV-1 RNA less than 1000 copies/ml and in countries other than the Netherlands. Typical bounds for insurability range between 400 and 500%.

set. Actuarial methods for converting varying mortality loadings so as to obtain a level of extra premium are beyond the scope of this article. However, our results imply that more than 50% of patients – those with lower relative mortality – in an HIV-positive population with similar risk profile to that analysed in this study could be insurable, based on conventional limits to relative mortality of 500%.

Our study was based on a large HIV-positive study population, we analysed data from over 30 000 patients, with long follow-up during which more than 1000 deaths were recorded. We controlled for underwriting effects by using ‘ultimate rates’, which factor out selection bias (see above for further details). Data were only available to estimate death rates up to 10 years after starting ART, and therefore estimated excess mortality will have to be extrapolated beyond the follow-up time that is currently observable. However, most HIV-related mortality occurs during the first few years of ART [17], and therefore excess mortality rates beyond 7 years duration of ART are likely to be stable. Our estimates are likely to be conservative for patients starting ART today on better tolerated and more effective drug regimens than those for patients included in analyses. A limitation of our study is that there was only limited follow-up of older individuals: 6572 person-years (3.8% of the total follow-up time) among persons aged more than 60 years. Therefore, death rates above age 60 were imprecisely estimated. However, demand for life insurance is mainly for lives under age 60 years. We excluded patients with presumed transmission via IDU, as these are unlikely to be granted insurance even if HIV negative. We did not have data on socioeconomic status. However, bias should be small because we used socioeconomic neutral mortality rates. We did not have data on smoking, this could lead to a bias if, for example, HIV-positive people were on average more likely to smoke than other insured people. The effect of this is likely to be relatively small, for example, a doubling of the proportion of smokers would result in an approximately 25% increase in mortality.

Our dataset included national databases on HIV-positive people from France, the Netherlands and Switzerland; these are likely to be representative of all patients in care in these countries. Data from Spain were contributed by many treatment centres from several regions, whereas those from Italy and Germany were from a limited number of clinics. All clinics provide comprehensive care to HIV-positive people in their locality and are not specialist referral centres. The majority of the data analysed in this study were from France and the Netherlands. We found relative mortality to be somewhat higher in the Netherlands, partly because of relatively lower mortality in Dutch insured HIV-negative lives. We found little evidence that relative mortality in other countries differed from that in France. We found little evidence that effects of variables included in the final

model differed between Dutch lives and those from other countries. Our results may apply to other high-income countries with good access to care but it would be desirable to conduct further analyses of data from European countries not represented here, as insurance policies vary by country. In the USA, part of the HIV epidemic is in socially marginalized populations [18,19], and access to free healthcare is limited, for example, only those with an AIDS diagnosis or with CD4 cell count less than 200 cells/ $\mu$ l are eligible for Medicaid, although provision will be expanded when the Affordable Care Act takes full effect in 2014 [20]. It is, therefore, unclear whether a similar proportion of HIV-positive lives is potentially insurable, and a study based on representative cohorts of HIV-positive people in the USA is highly desirable. Similarly, there is an urgent need for a study of insurability in South Africa, wherein the prevalence of HIV is many times higher than in Europe and there is also a high market penetration of life insurance. Studies are also lacking in Japan, India, China and Brazil – countries with potentially large insurance markets for HIV-positive lives.

People newly diagnosed with HIV can be expected to survive longer than those recruited to cohorts between 1996 and 2010, therefore, studies such as ours necessarily provide trailing indicators of mortality rates. Attempts have been made to allow for this problem in a computer simulation model: estimated life expectancy of MSM aged 30 years who became HIV positive in 2010 with no hepatitis C infection and high CD4 cell count at start of ART in the United Kingdom was 75 years (95% CI 68–77), a loss of only 7 years compared with the male UK population [21], similar to the average loss of life because of smoking.

Theoretically, insurability depends on the financial resources of the person buying insurance as insurance providers discriminate levels of risk, and price products accordingly. However, to prevent fraud and antiselection, insurers commonly apply their own insurability criteria which include limits on insurance ratings. Practices vary with a limit on the percentage extra mortality being the commonest. We have assumed that ratings up to an excess mortality of 400% (relative mortality 500%) are insurable. Insurance ratings beyond these bounds have generally not been accepted by the insurance buying public.

The Dutch Association of Insurers recommended in 2005 that short-term insurance should be made available to successfully treated patients [22] and in 2009 that it should be extended to patients who do not yet need ART [23]. Nevertheless, HIV-positive individuals have routinely been turned down for life insurance, despite advances in ART and evidence its effectiveness [24]. Our study should allow insurance providers to make a fair assessment of risk in order to properly underwrite insurance for HIV-positive people, for longer terms. Assuming that relative mortality does not increase as time on ART increases

beyond the maximum analysed here, our study provides evidence that could allow life insurance up to 20 years term to be offered to lower risk HIV-positive individuals, at affordable premiums. Whole of life insurance at guaranteed rates may become feasible when data on mortality with longer duration of ART become available.

Remaining underwriting challenges include assessment of likely future adherence to ART, the quality of medical care, presence of comorbidities and drug interactions. There are also pricing challenges due to extrapolation of mortality rates beyond the 10 years' follow-up analysed here, and because HIV-positive individuals may apply for insurance at any time prior to or during treatment, but our estimates are based on CD4 cell count and HIV-1 RNA 6 months after ART initiation. Information on CD4 trajectories and viral suppression can be used to map from duration of ART to duration since taking out insurance [25]. Most chronic diseases result in deteriorating health with time on medication, but HIV-positive individuals on ART experience an increasing relative benefit of treatment as their CD4 cell counts increase towards normal levels, which may take more than 5 years [14,26]. Therefore, the lives of people with HIV tend to become more insurable with increasing duration of successful ART. Insurance companies set bounds for insurability for standard lives, including high age at application (which vary considerably between insurers and markets but could be as low as 60 years) as well as restrictions based on prior or current recreational drug use, which would also apply to HIV-positive lives. Our model suggests poorer outcomes for those with AIDS before start of ART. Insurers will have to interpret this with caution as different AIDS-defining conditions have substantially different implications for subsequent mortality [27].

Many people living with HIV and starting ART with currently recommended drugs and in accordance with treatment guidelines will live a near-normal life span [21]. Lack of insurance products is no longer justified, as the excess mortality of those with HIV is comparable to many other groups with morbidities that are insured, such as diabetics or cancer survivors. Our study provides data that will allow the insurance market to open up to people living with HIV. Life insurance could now be extended to 20 years, which would be particularly useful for mortgage cover. We aim to communicate our results directly to insurance providers in order that they can amend their policies, with consequent improvements in the quality of life for HIV-positive people.

## Acknowledgements

We thank all patients, doctors, and study nurses associated with the participating cohort studies.

J.K.B., W.D., U.W., J.S., B.L. and M.M. were responsible for study design. M.M. and S.I. were responsible for data management. J.K.B. did the analyses, assisted by W.D., M.M. and J.S., M.M., J.K.B., W.D., B.L. and J.S. wrote the first draft of the article. All authors contributed to interpreting the results and writing the paper and approved submission of the paper. J.K.B., M.M. and J.S. had full access to the data and take responsibility for the correctness of the analyses.

**Steering group:** Andrew Boulle (IeDEA Southern Africa), Hans-Reinhard Brodt (Frankfurt), Jordi Casabona (PISCIS), Matthias Cavassini (SHCS), Geneviève Chêne (Aquitaine), Dominique Costagliola (FHDH), François Dabis (Aquitaine), Antonella D'Arminio Monforte (ICONA), Julia del Amo (CoRIS-MD), Frank de Wolf (ATHENA), Gerd Fätkenheuer (Koln/Bonn), John Gill (South Alberta Clinic), Jodie Guest (HAVACS), David Hans-Ulrich Haerry (EATG), Robert Hogg (HOMER), Amy Justice (VACS), Amanda Mocroft (EuroSIDA), Mari Kitahata (Washington), Fiona Lampe (Royal Free), Peter Reiss (ATHENA), Michael Saag (Alabama), Tim Sterling (Vanderbilt-Meherry), Matthew Williams (UK-CAB), Robert Zangerle (Austria)

**Co-ordinating team:** J.S. and M.M. (Principal Investigators), S.I. (statistician)

## Collaborating Centres

French Hospital Database on HIV (ANRS CO4 FHDH)

**Scientific committee:** S Abgrall, F Barin, M Bentata, E Billaud, F Boué, C Burty, A Cabié, D Costagliola, L Cotte, P De Truchis, X Duval, C Duvivier, P Enel, L Fredouille-Heripret, J Gasnault, C Gaud, J Gilquin, S Grabar, C Katlama, MA Khuong, JM Lang, AS Lascaux, O Launay, A Mahamat, M Mary-Krause, S Matheron, JL Meynard, J Pavie, G Pialoux, F Pilorgé, I Poizot-Martin, C Pradier, J Reynes, E Rouveix, A Simon, P Tattevin, H Tissot-Dupont, JP Viard, N Vigeat

**DMI2 coordinating center:** French Ministry of Health (Valérie Salomon), Technical Hospitalization Information Agency, ATIH (N Jacquemet).

**Statistical analysis center:** U943 INSERM et UPMC (S Abgrall, D Costagliola, S Grabar, M Guiguet, E Lanoy, L Lièvre, M Mary-Krause, H Selinger-Leneman), INSERM Transfert (JM Lacombe, V Potard)

**COREVIH: Paris area:** Corevh Ile de France Centre (GH Pitié-Salpêtrière: F Bricaire, S Herson, C Katlama, A Simon; Hôpital Saint-Antoine: N Desplanque, PM Girard, JL Meynard, MC Meyohas, O Picard; Hôpital Tenon: J Cadranel, C Mayaud, G Pialoux), Corevh Ile de France Est (Hôpital Saint-Louis: JP Clauvel, JM Decazes, L Gerard, JM Molina; GH Lariboisière-Fernand Widal:

M Diemer, P Sellier; Hôpital Avicenne: M Bentata, P Honoré; Hôpital Jean Verdier: V Jeantils, S Tassi; Hôpital Delafontaine: D Mechali, B Taverne), *Corevih Ile de France Nord* (Hôpital Bichat-Claude Bernard: E Bouvet, B Crickx, JL Ecobichon, S Matheron, C Picard-Dahan, P Yeni), *Corevih Ile de France Ouest* (Hôpital Ambroise Paré: H Berthé, C Dupont; Hôpital Louis Mourier: C Chandemerle, E Mortier; Hôpital Raymond Poincaré: P de Truchis), *Corevih Ile de France Sud* (Hôpital Européen Georges Pompidou: D Tisne-Dessus, L Weiss; GH Tarnier-Cochin: D Salmon; Hôpital Saint-Joseph: I Auperin, J Gilquin; Hôpital Necker adultes: L Roudière, JP Viard; Hôpital Antoine Béclère: F Boué, R Fior; Hôpital de Bicêtre: JF Delfraissy, C Goujard; Hôpital Henri Mondor: C Jung, Ph Lesprit; Hôpital Paul Brousse: D Vittecoq).

**Outside Paris area:** *Corevih Alsace* (CHRU de Strasbourg: P Fraisse, JM Lang, D Rey; CH de Mulhouse: G Beck-Wirth), *Corevih de l'Arc Alpin* (CHU de Grenoble: JP Stahl, P Lecercq), *Corevih Auvergne-Loire* (CHU de Clermont-Ferrand: F Gourdon, H Laurichesse; CHRU de Saint-Etienne: A Fresard, F Lucht); *Corevih Basse-Normandie* (CHRU de Caen: C Bazin, R Verdon), *Corevih Bourgogne* (CHRU de Dijon: P Chavanel), *Corevih Bretagne* (CHU de Rennes: C Arvieux, C Michelet), *Corevih Centre* (CHRU de Tours: P Choutet, A Goudeau, MF Maître), *Corevih Franche-Comté* (CHRU de Besançon: B Hoen; CH de Belfort: P Eglinger, JP Faller); *Corevih Haute-Normandie* (CHRU de Rouen: F Borsa-Lebas, F Caron), *Corevih Languedoc-Roussillon* (CHU de Montpellier: J Reynes; CHG de Nîmes: JP Daures), *Corevih Lorraine* (Nancy Hôpital de Brabois: T May, C Rabaud; CHRU de Reims: JL Berger, G Rémy), *Corevih de Midi-Pyrénées* (Toulouse CHU Purpan: E Arlet-Sauv, L Cuzin, P Massip, MF Thiercelin Legrand; Toulouse Hôpital la Grave: G Pontonnier; Toulouse CHU Rangueil), *Corevih Nord-Pas de Calais* (CH de Tourcoing: N Viget, Y Yasdanpanah), *Corevih PACA Est* (Nice Hôpital Archet 1: P Dellamonica, C Pradier, P Pugliese; CHG Antibes-Juan les Pins: K Aleksandrowicz, D Quinsat), *Corevih PACA Ouest* (Marseille Hôpital de la Conception: I Ravaux, H Tissot-Dupont; Marseille Hôpital Nord: JP Delmont, J Moreau; Marseille Institut Paoli Calmettes: JA Gastaut; Marseille Hôpital Sainte-Marguerite: I Poizot-Martin, F Retornaz, J Soubeyrand; Marseille Centre pénitentiaire des Baumettes: A Galinier, JM Ruiz; CHG d'Aix-En-Provence: T Allegre, PA Blanc; CH d'Arles: D Bonnet-Montchardon; CH d'Avignon: G Lepeu; CH de Digne Les Bains: P Granet-Brunello; CH de Gap: JP Esterni, L Pelissier; CH de Martigues: R Cohen-Valensi, M Nezri; CHI de Toulon: S Chadapaud, A Laffeuillade), *Corevih Pays de la Loire* (CHRU de Nantes: E Billaud, F Raffi), *Corevih de la Vallée du Rhône* (Lyon Hôpital de la Croix-Rousse: A Boibieux, D Peyramond; Lyon Hôpital Edouard Herriot: JM Livrozet, JL Touraine; Lyon Hôtel-Dieu: L Cotte, C Trepo).

**Overseas:** *Corevih Guadeloupe* (CHRU de Pointe-à-Pitre: M Strobel; CH Saint-Martin: F Bissuel), *Corevih Guyane* (CHG de Cayenne: R Pradinaud, M Sobesky), *Corevih Martinique* (CHRU de Fort-de-France: A Cabié), *Corevih de La Réunion* (CHD Félix Guyon: C Gaud, M Contant).

### Italian Cohort of Antiretroviral-Naïve Patients (ICONA)

**Governing body:** M. Moroni (Chair), G Angarano, A Antinori, F Castelli, R Cauda, A d'Arminio Monforte, G Di Perri, M Galli, R Iardino, G Ippolito, A Lazzarin, CF Perno, O Armignacco, PL Viale, F Von Schlosser.

**Scientific secretary:** A d'Arminio Monforte

**Steering committee:** A Ammassari, M Andreoni, A Antinori, C Balotta, P Bonfanti, S Bonora, M Borderi, MR Capobianchi, A Castagna, F Ceccherini-Silberstein, P Cinque, A Cozzi-Lepri, A d'Arminio Monforte, A De Luca, M Gargiulo, C Gervasoni, E Girardi, A Gori, G Guaraldi, M Lichtner, S Lo Caputo, G Madeddu, F Maggiolo, G Marchetti, S Marcotullio, L Monno, R Murri, C Mussini, M Puoti, C Torti

**Statistical and monitoring team:** A Cozzi-Lepri, P Cicconi, I Fanti, T Formenti, L Galli, P Lorenzini

**Participating physicians and centers:** Italy A. Giacometti, A Costantini, A. Riva (Ancona); G. Angarano, L Monno, C Carrisa, (Bari); F. Maggiolo, G Lazzari (Bergamo); PL. Viale, M Borderi, G. Verucchi (Bologna); F Castelli, C. Torti, C. Minardi, (Brescia); T. Quirino, C Abeli (Busto Arsizio); P.E. Manconi, P. Piano (Cagliari); J Vecchiet, K Falasca (Chieti); L. Sighinolfi, D. Segala (Ferrara); F Mazzotta, S. Lo Caputo (Firenze); G. Cassola, G Viscoli, A. Alessandrini, R. Pispolo, G Mazzarello (Genova); C. Mastrianni, V. Belvisi (Latina); P. Bonfanti, I. Caramma (Lecco); A. Chiodera, P. Castelli (Macerata); M Galli, A. Lazzarin, G. Rizzardini, M. Puoti, A. d'Arminio Monforte, AL Ridolfo, R Piolini, A Castagna, S Salpietro, A Galli, A Bigoloni, V Spagnuolo, L Carenzi, P Zucchi, M.C. Moioli, R Rossotti, P Cicconi, T Formenti (Milano); C. Mussini, L Bisio (Modena); A Gori, G Lapadula (Monza), N. Abrescia, A. Chiriani, MG Guida, M Gargiulo (Napoli); F Baldelli, B Belfiori (Perugia); G. Parruti, T Ursini (Pescara); G. Magnani, M.A. Ursitti (Reggio Emilia); R. Cauda, M Andreoni, A. Antinori, V Tozzi, V. Vullo, A. De Luca, A. d'Avino, M. Zaccarelli, L Gallo, E. Nicastro, R. Acinapura, M Capozzi, R Libertone, M. Lichtner, G Tebano, (Roma); M.S. Mura, G Madeddu (Sassari); P. Caramello, G. Di Perri, G.C. Orofino, M Sciandra (Torino); G. Pellizzer, V. Manfrin (Vicenza).

### Swiss HIV Cohort Study (SHCS)

Aubert V, Barth J, Battegay M, Bernasconi E, Böni J, Bucher HC, Burton-Jeangros C, Calmy A, Cavassini M,

Egger M, Elzi L, Fehr J, Fellay J, Francioli P, Furrer H (Chairman of the Clinical and Laboratory Committee), Fux CA, Gorgievski M, Günthard H (President of the SHCS), Haerry D (deputy of 'Positive Council'), Hasse B, Hirsch HH, Hirscher B, Hösli I, Kahlert C, Kaiser L, Keiser O, Kind C, Klimkait T, Kovari H, Ledermann B, Martinetti G, Martinez de Tejada B, Metzner K, Müller N, Nadal D, Pantaleo G, Rauch A (Chairman of the Scientific Board), Regenass S, Rickenbach M (Head of Data Center), Rudin C (Chairman of the Mother & Child Substudy), Schmid P, Schultze D, Schöni-Affolter F, Schüpbach J, Speck R, Taffé P, Tarr P, Telenti A, Trkola A, Vernazza P, Weber R, Yerly S.

#### **AIDS Therapy Evaluation project Netherlands (ATHENA)**

L.A. Gras (bio-statistician), A.I. van Sighem (senior researcher), C. Smit (epidemiologist), F. de Wolf (director)

#### **Treating physicians**

(\*Site coordinating physicians) Academisch Medisch Centrum bij de Universiteit van Amsterdam – Amsterdam: Dr J.M. Prins\*, Drs. J.C. Bos, Dr J.K.M. Eeftink-Schattenkerk, Dr S.E. Geerlings, Dr M.H. Godfried, Prof. dr. J.M.A. Lange, Dr J.T.M. van der Meer, Dr F.J.B. Nellen, Drs. D.P. Olszyna, Dr T. van der Poll, Prof. dr. P. Reiss, Drs. S.U.C. Sankatsing, Drs. M. van der Valk, Drs. J.N. Vermeulen, Drs. S.M.E. Vrouenraets, Dr M. van Vugt, Dr F.W.M.N. Wit. Academisch Ziekenhuis Maastricht – Maastricht: Dr G. Schreij\*, Dr S. van der Geest, Dr A. Oude Lashof, Dr S. Lowe, Dr A. Verbon. Catharina Ziekenhuis – Eindhoven: Dr B. Bravenboer\*, Drs. M.J.H. Pronk. Emma Kinderziekenhuis – AMC Amsterdam: Prof. dr. T.W. Kuijpers, Drs. D. Pajkrt, Dr H.J. Scherpelz. Erasmus MC – Rotterdam: Dr M.E. van der Ende\*, Drs. H. Bax, Drs. M. van der Feltz, Dr L.B.S. Gelinck, Drs. Mendoca de Melo, Dr J.L. Nouwen, Dr B.J.A. Rijnders, Dr E.D. de Ruiter, Dr L. Slobbe, Drs. C.A.M. Schurink, Dr T.E.M.S. de Vries. Erasmus MC – Sophia – Rotterdam: Dr G. Driessen, Dr M. van der Flier, Dr N.G. Hartwig. Flevoziekenhuis – Almere: Dr J. Branger. Haga Ziekenhuis, locatie Leyenburg – Den Haag: Dr R.H. Kauffmann\*, Dr E.F. Schippers. Isala Klinieken – Zwolle: Dr P.H.P. Groeneveld\*, Dr M.A. Alleman. Kennemer Gasthuis – Haarlem: Prof. dr. R.W. ten Kate\*, Dr R. Soetekouw. Leids Universitair Medisch Centrum – Leiden: Dr F.P. Kroon\*, Dr S.M. Arend, Drs. M.G.J. de Boer, Prof. dr. P.J. van den Broek, Prof. dr. J.T. van Dissel, Drs. C. van Nieuwkoop. Maasstadziekenhuis – locatie Clara – Rotterdam: Dr J.G. den Hollander\*. Medisch Centrum Alkmaar – Alkmaar: Dr W. Bronsveld\*, Drs. K. Pogány. Medisch Centrum Haaglanden -locatie Westeinde – Den Haag: Dr R. Vriesendorp\*, Dr F.J.F. Jeurissen, Dr E.M.S. Leyten. Medisch Centrum Leeuwarden – Leeuwarden: Dr D. van

Houte\*, Dr M.B. Polée, Dr M. van Vonderen. Medisch Spectrum Twente – Enschede: Dr C.H.H. ten Napel\*, Dr G.J. Kootstra. Onze Lieve Vrouwe Gasthuis – Amsterdam. Prof. dr. K. Brinkman\*, Drs. G.E.L. van den Berk, Dr W.L. Blok, Dr P.H.J. Frissen, Drs. W.E.M. Schouten. St. Medisch Centrum Jan van Goyen – Amsterdam: Dr A. van Eeden\*, Dr D.W.M. Verhagen. Slotervaart Ziekenhuis – Amsterdam: Dr J.W. Mulder\*, Dr E.C.M. van Gorp, Dr A.T.A. Mairuhu Drs. R. Steingrover, Dr J. Wagenaar. St. Elisabeth Ziekenhuis – Tilburg: Dr J.R. Juttmann\*, Dr M.E.E. van Kasteren. St. Lucas Andreas Ziekenhuis – Amsterdam: Dr J. Veenstra\*, Dr W.L.E. Vasmel (until January, 2008). Dr K..D. Lettinga. Universitair Medisch Centrum St. Radboud – Nijmegen: Dr P.P. Koopmans\*, Drs. A.M. Brouwer, Dr A.S.M. Dofferhoff, Prof. dr. R. de Groot, Drs. H.J.M. ter Hofstede, Dr M. Keuter, Dr A.J.A.M. van der Ven. Universitair Medisch Centrum Groningen – Groningen: Dr H.G. Sprenger\*, Dr S. van Assen, Dr C.J. Stek. Universitair Medisch Centrum Groningen – Beatrix Kliniek – Groningen: Dr R. Doedens, Dr E.H. Scholvinck. Universitair Medisch Centrum Utrecht – Utrecht: Prof. dr. I.M. Hoepelman\*, Dr M.M.E. Schneider, Prof. dr. M.J.M. Bonten, Dr P.M. Ellerbroek, Drs. C.A.J.J. Jaspers, Drs. L.J. Maarschalk-Ellerbroek, Dr J.J. Oosterheert, Dr E.J.G. Peters, Dr T. Mudrikova, Drs. M.W.M. Wassenberg, Dr S. Weijer, Drs. M.H. Hoogenwerf, Drs. J.E. Arends, Drs. E. Hoornenborg. Wilhelmina Kinderziekenhuis – UMC Utrecht: Dr S.P.M. Geelen, Dr T.F.W. Wolfs. VU Medisch Centrum – Amsterdam: Prof. dr. S.A. Danner\*, Dr M.A. van Agtmael, Drs. W.F.W. Bierman, Drs. F.A.P. Claessen, Drs. M.E. Hillebrand, Drs. E.V. de Jong, Drs. W. Kortmann, Dr R.M. Perenboom, Drs. E.A. bij de Vaate. Ziekenhuis Rijnstate – Arnhem: Dr C. Richter\*, Drs. J. van der Berg, Dr E.H. Gisolf. Ziekenhuis Walcheren – Vlissingen: Dr A.A. Tanis\*. St. Elisabeth Hospitaal/Stichting Rode Kruis Bloedbank – Willemstad, Curaçao: Dr A.J. Duits, Dr K. Winkel.

#### **Virologists**

Academisch Medisch Centrum bij de Universiteit van Amsterdam – Amsterdam: Dr N.K.T. Back, Dr M.E.G. Bakker, Dr H.L. Zaaijer. Prof. dr. B. Berkhout, Dr S. Jurriaans. CLB Stichting Sanquin Bloedvoorziening – Amsterdam: Dr Th. Cuijpers. Onze Lieve Vrouwe Gasthuis – Amsterdam: Dr P.J.G.M. Rietra, Dr K.J. Rozendaal. Slotervaart Ziekenhuis – Amsterdam: Drs. W. Pauw, Drs. P.H.M. Smits, Dr A.P. van Zanten. VU Medisch Centrum – Amsterdam: Dr B.M.E. von Blomberg, Dr A. Pettersson, Dr P. Savelkoul. Ziekenhuis Rijnstate – Arnhem: Dr C.M.A. Swanink. HAGA, ziekenhuis, locatie Leyenburg – Den Haag: Dr P.F.H. Franck, Dr A.S. Lampe. Medisch Centrum Haaglanden, locatie Westeinde – Den Haag: Drs. C.L. Jansen. Streeklaboratorium Twente – Enschede: Dr R. Hendriks. Streeklaboratorium Groningen – Groningen:

Dr C.A. Benne. Streeklaboratorium Volksgezondheid Kennemerland – Haarlem: Dr J. Schirm, Dr D. Veenendaal. Laboratorium voor de Volksgezondheid in Friesland – Leeuwarden: Dr H. Storm, Drs. J. Weel, Drs. J.H. van Zeijl. Leids Universitair Medisch Centrum – Leiden: Dr H.C.J. Claas, Prof. dr. A.C.M. Kroes. Academisch Ziekenhuis Maastricht – Maastricht: Prof. dr. C.A.M.V.A. Bruggeman, Drs. V.J. Goossens. Universitair Medisch Centrum St. Radboud – Nijmegen: Prof. dr. J.M.D. Galama, Dr W.J.G. Melchers, Dr Verduyn-Lunel. Erasmus MC – Rotterdam: Dr G.J.J. van Doornum, Dr H.G.M. Nieters, Prof. dr. A.D.M.E. Osterhaus, Dr M. Schutten. St. Elisabeth Ziekenhuis – Tilburg: Dr A.G.M. Buiting. Universitair Medisch Centrum Utrecht – Utrecht: Dr C.A.B. Boucher, Dr E. Boel, Dr R. Schuurman. Catharina Ziekenhuis – Eindhoven: Dr A.F. Jansz, drs. M. Wulf.

### Pharmacologists

Medisch Centrum Alkmaar – Alkmaar: Dr A. Veldkamp. Slotervaart Ziekenhuis – Amsterdam: Prof. dr. J.H. Beijnen, Dr A.D.R. Huitema. Universitair Medisch Centrum St. Radboud – Nijmegen: Dr D.M. Burger. Academisch Medisch Centrum bij de Universiteit van Amsterdam – Amsterdam: Drs. H.J.M. van Kan.

### The EuroSIDA Study Group

#### The multicenter Study Group on EuroSIDA (national coordinators in parentheses)

**Argentina:** (M Losso), M Kundro, Hospital JM Ramos Mejia, Buenos Aires.

**Austria:** (N Vetter), Pulmologisches Zentrum der Stadt Wien, Vienna; R Zangerle, Medical University Innsbruck, Innsbruck.

**Belarus:** (I Karpov), A Vassilenko, Belarus State Medical University, Minsk, VM Mitsura, Gomel State Medical University, Gomel; O Suetnov, Regional AIDS Centre, Svetlogorsk.

**Belgium:** (N Clumeck), S De Wit, M Delforge, Saint-Pierre Hospital, Brussels; R Colebunders, Institute of Tropical Medicine, Antwerp; L Vandekerckhove, University Ziekenhuis Gent, Gent.

**Bosnia-Herzegovina:** (V Hadziosmanovic), Klinicki Centar Univerziteta Sarajevo, Sarajevo.

**Bulgaria:** (K Kostov), Infectious Diseases Hospital, Sofia.

**Croatia:** (J Begovac), University Hospital of Infectious Diseases, Zagreb.

**Czech Republic:** (L Machala), D Jilich, Faculty Hospital Bulovka, Prague; D Sedlacek, Charles University Hospital, Plzen.

**Denmark:** (J Nielsen), G Kronborg, T Benfield, M Larsen, Hvidovre Hospital, Copenhagen; J Gerstoft, T Katzenstein, A-B E Hansen, P Skinhøj, Rigshospitalet, Copenhagen; C Pedersen, Odense University Hospital, Odense; L Ostergaard, Skejby Hospital, Aarhus.

**Estonia:** (K Zilmer), West-Tallinn Central Hospital, Tallinn; Jelena Smidt, Nakkusosakond Siseklinik, Kohtla-Järve.

**Finland:** (M Ristola), Helsinki University Central Hospital, Helsinki.

**France:** (C Katlama), Hôpital de la Pitié-Salpêtrière, Paris; J-P Viard, Hôpital Necker-Enfants Malades, Paris; P-M Girard, Hospital Saint-Antoine, Paris; JM Livrozet, Hôpital Edouard Herriot, Lyon; P Vanhems, University Claude Bernard, Lyon; C Pradier, Hôpital de l'Archet, Nice; F Dabis, D Neau, Unité INSERM, Bordeaux.

**Germany:** (J Rockstroh), Universitäts Klinik Bonn; R Schmidt, Medizinische Hochschule Hannover; J van Lunzen, O Degen, University Medical Center Hamburg-Eppendorf, Infectious Diseases Unit, Hamburg; HJ Stellbrink, IPM Study Center, Hamburg; S Staszewski, JW Goethe University Hospital, Frankfurt; J Bogner, Medizinische Poliklinik, Munich; G. Fätkenheuer, Universität Köln, Cologne.

**Greece:** (J Kosmidis), P Gargalianos, G Xylomenos, J Perdios, Athens General Hospital; G Panos, A Filandras, E Karabatsaki, 1st IKA Hospital; H Sambatakou, Ippokration Genereal Hospital, Athens.

**Hungary:** (D Banhegyi), Szent László Hospital, Budapest.

**Ireland:** (F Mulcahy), St. James's Hospital, Dublin.

**Israel:** (I Yust), D Turner, M Burke, Ichilov Hospital, Tel Aviv; S Pollack, G Hassoun, Rambam Medical Center, Haifa; S Maayan, Hadassah University Hospital, Jerusalem.

**Italy:** (S Vella), Istituto Superiore di Sanità, Rome; R Esposito, I Mazeu, C Mussini, Università Modena, Modena; C Arici, Ospedale Riuniti, Bergamo; R Pristera, Ospedale Generale Regionale, Bolzano; F Mazzotta, A Gabbuti, Ospedale S Maria Annunziata, Firenze; V Vullo, M Lichtner, University di Roma la Sapienza, Rome; A Chiriaci, E Montesarchio, M Gargiulo, Presidio Ospedaliero AD Cotugno, Monaldi Hospital, Napoli; G Antonucci, A Testa, G D'Offizi, C Vlassi, M Zaccarelli, A Antorini, Istituto Nazionale Malattie Infettive Lazzaro Spallanzani, Rome; A Lazzarin,

A Castagna, N Gianotti, Ospedale San Raffaele, Milan; M Galli, A Ridolfo, Osp. L. Sacco, Milan; A d'Arminio Monforte, Istituto Di Clinica Malattie Infettive e Tropicale, Milan.

**Latvia:** (B Rozentale), I Zeltina, Infectology Centre of Latvia, Riga.

**Lithuania:** (S Chaplinskas), Lithuanian AIDS Centre, Vilnius.

**Luxembourg:** (T Staub), R Hemmer, Centre Hospitalier, Luxembourg.

**Netherlands:** (P Reiss), Academisch Medisch Centrum bij de Universiteit van Amsterdam, Amsterdam.

**Norway:** (V Ormaasen), A Maeland, J Bruun, Ullevål Hospital, Oslo.

**Poland:** (B Knysz) J Gasiorowski, Medical University, Wroclaw; A Horban, E Bakowska, Centrum Diagnostyki i Terapii AIDS, Warsaw; A Grzeszczuk, R Flisiak, Medical University, Bialystok; A Boron-Kaczmarska, M Pynka, M Parczewski, Medical University, Szczecin; M Beniowski, E Mularska, Osrodek Diagnostyki i Terapii AIDS, Chorzow; H Trocha, Medical University, Gdansk; E Jablonowska, E Malolepsza, K Wojcik, Wojewodzki Szpital Specjalistyczny, Lodz.

**Portugal:** (F Antunes), M Doroana, L Caldeira, Hospital Santa Maria, Lisbon; K Mansinho, Hospital de Egas Moniz, Lisbon; F Maltez, Hospital Curry Cabral, Lisbon.

**Romania:** (D Duiculescu), Spitalul de Boli Infectioase si Tropicale: Dr Victor Babes, Bucarest.

**Russia:** (A Rakhmanova), Medical Academy Botkin Hospital, St Petersburg; N Zakharova, St Petersburg AIDS Centre, St Peterburg; S Buzunova, Novgorod Centre for AIDS, Novgorod.

**Serbia:** (D Jevtovic), The Institute for Infectious and Tropical Diseases, Belgrade.

**Slovakia:** (M Mokráš), D Staneková, Dérer Hospital, Bratislava.

**Slovenia:** (J Tomazic), University Clinical Centre Ljubljana, Ljubljana.

**Spain:** (J González-Lahoz), V Soriano, P Labarga, J Medrano, Hospital Carlos III, Madrid; S Moreno, J. M. Rodriguez, Hospital Ramon y Cajal, Madrid; B Clotet, A Jou, R Paredes, C Tural, J Puig, I Bravo, Hospital Germans Trias i Pujol, Badalona; JM Gatell, JM Miró, Hospital Clinic i Provincial, Barcelona; P Domingo, M Gutierrez, G Mateo, MA Sambeat, Hospital Sant Pau, Barcelona.

**Sweden:** (A Blaxhult), Venhaelsen-Sodersjukhuset, Stockholm; L Flamholc, Malmö University Hospital, Malmö.

**Switzerland:** (B Ledergerber), R Weber, University Hospital, Zürich; P Francioli, M Cavassini, Centre Hospitalier Universitaire Vaudois, Lausanne; B Hirscher, E Boffi, Hospital Cantonal Universitaire de Geneve, Geneve; H Furrer, Inselspital Bern, Bern; M Battegay, L Elzi, University Hospital Basel.

**Ukraine:** (E Kravchenko), N Chentsova, Kiev Centre for AIDS, Kiev; V Frolov, G Kutsyna, Luhansk State Medical University, Luhansk; S Servitskiy, Odessa Region AIDS Center, Odessa; M Krasnov, Kharkov State Medical University, Kharkov.

**United Kingdom:** (S Barton), St. Stephen's Clinic, Chelsea and Westminster Hospital, London; AM Johnson, D Mercey, Royal Free and University College London Medical School, London (University College Campus); A Phillips, MA Johnson, A Mocroft, Royal Free and University College Medical School, London (Royal Free Campus); M Murphy, Medical College of Saint Bartholomew's Hospital, London; J Weber, G Scullard, Imperial College School of Medicine at St. Mary's, London; M Fisher, Royal Sussex County Hospital, Brighton; C Leen, Western General Hospital, Edinburgh.

**Steering Committee:** J Gatell, B Gazzard, A Horban, I Karpov, B Ledergerber, M Losso, A D'Arminio Monforte, C Pedersen, A Rakhmanova, M Ristola, J Rockstroh (Chair), S De Wit (Vice-Chair).

**Additional voting members:** J Lundgren, A Phillips, P Reiss.

**Coordinating Centre Staff:** O Kirk, A Mocroft, A Cozzi-Lepri, D Grint, M Sabin, D Podlekareva, J Kjær, L Peters, J Nielsen, J Tverland, A H Fischer.

**EuroSIDA representatives to EuroCoord:** O. Kirk, A. Mocroft, J. Grarup, P. Reiss, A. Cozzi-Lepri, R. Thiebaut, J. Rockstroh, D. Burger, R. Paredes, J. Kjær. L. Peters.

#### ANRS CO3 Aquitaine Cohort, France

**Composition of the Groupe d'Epidémiologie Clinique du Sida en Aquitaine (GECSA):** Coordination: F. Dabis. **Scientific committee:** F. Bonnet, F. Dabis, M. Dupon, G. Chêne, H. Fleury, D. Lacoste, D. Malvy, P. Mercié, I. Pellegrin, P. Morlat, D. Neau, JL. Pellegrin, R. Thiébaut, K. Titier. **Epidemiology and Methodology:** M. Bruyand, G. Chêne, F. Dabis, S. Lawson-Ayayi, R. Thiébaut, L. Wittkop. **Infectious Diseases and Internal Medicine:** F. Bonnal, F. Bonnet,

N. Bernard, L. Caunègre, C. Cazanave, J. Ceccaldi, D. Chambon, I. Chossat, K. Courtaud, FA. Dauchy, S. De Witte, M. Dupon, A. Dupont, P. Duffau, H. Dutronc, S. Farbos, V. Gaboriau, MC. Gemain, Y. Gerard, C. Greib, M. Hessamfar, D. Lacoste, P. Lataste, S. Lafarie-Castet, E. Lazaro, M. Longy-Boursier, D. Malvy, JP. Meraud, P. Mercié, E. Monlun, P. Morlat, D. Neau, A. Ochoa, JL. Pellegrin, T. Pistone, JM. Ragnaud, MC. Receveur, J. Roger-Schmeltz, S. Tchamgoué, P. Thibaut, MA. Vandenhende, JF. Viallard. **Immunology:** JF. Moreau, I. Pellegrin. **Virology:** H. Fleury, ME. Lafon, B. Masquelier, P. Trimoulet. **Pharmacology:** D. Breilh, K. Titier. **Drug monitoring:** F. Haramburu, G. Miremont-Salamé. **Data collection and processing:** MJ. Blaizeau, M. Decoin, J. Delaune, S. Delveaux, C. D'Ivernois, C. Hanappier, O. Leleux, B. Uwamaliya-Nziyumvira, X. Sicard. Computing and **Statistical analysis:** S. Geffard, J. Leray, G. Palmer, D. Touchard.

#### Royal Free Hospital Cohort, London UK

**Clinical:** S Bhagani, A Carroll, I Cropley, Z Cuthbertson, T Drinkwater, A Dunleavy, T Fernandez, AM Geretti, N Marshall, G Murphy, D Nair, D Ivens, M Johnson, S Kinloch-de Loes, M Lipman, S Madge, T Mahungu, B Prinz, L Swaden, A Rodger, M Tyrer, M Youle.

**Data management:** C Chaloner, J Holloway, J Puradiredja, S Scott, R Tsintas.

**Biostatistics/Epidemiology:** V Cambiano, E Harris, F Lampe, R Lodwick, A Phillips, C Smith.

**Laboratory:** E Amoah, C. Booth, G Clewley, A Garcia Diaz, B Gregory, W Labbett, J Libaste, F Tahami, M Thomas, Y Zhong

#### PISCIS, Catalonia and Balearic islands, Spain

**Coordinators:** J. Casabona (Centre d'Estudis Epidemiològics sobre les Infeccions de Transmissió Sexual i Sida de Catalunya: CEEISCAT), Jose M. Miró (Hospital Clínic-Idibaps, Universitat de Barcelona).

**Field coordinator:** A. Gallois (CEEISCAT)

**Steering committee:** J. Casabona, A. Esteve, A. Gallois (CEEISCAT), Jose M. Miró (Hospital Clínic-Idibaps, Universitat de Barcelona), D. Podzamczer (Hospital Universitari de Bellvitge-IDIBELL), J. Murillas (Hospital Son Espases de Mallorca).

**Scientific committee:** JM Gatell, C. Manzardo (Hospital Clínic-Idibaps, Universitat de Barcelona), C. Tural, B. Clotet (Fundació Lluita contra la Sida, Fundacio Irsicaixa, Hospital Universitari Germans Trias i Pujol, Universitat Autònoma de Barcelona), E. Ferrer, A. Imaz

(Hospital Universitari de Bellvitge-IDIBELL), M. Riera (Hospital Son Espases de Mallorca), F. Segura, G. Navarro (Corporació Sanitària i Universitària Parc Taulí, Universitat Autònoma de Barcelona), L. Force (Hospital de Mataró, Consorci Sanitario del Maresme), J. Vilaró (Hospital General de Vic), A. Masabeu (Hospital de Palamós), I. García (Hospital General d'Hospitalat), M. Guadarrama (Hospital Comarcal de l'Alt Penedès), C. Cifuentes, F Homar (Hospital Son Llàtzer), D. Dalmau, À. Jaen (Hospital Universitari Mútua de Terrassa), P. Domingo (Hospital de la Santa Creu i Sant Pau), V. Falcó, A. Curran (Hospital Universitari Vall d'Hebron), C. Campbell, C. Agustí (CEEISCAT).

**Informatics support:** F. Sánchez (CEEISCAT), F. Gargoulas, (Hospital Son Espases and Hospital Son Llàtzer), A. Gómez (Hospital Comarcal de l'Alt Penedès), JC Rubia (Hospital General d'Hospitalat)

**Data Management and statistical analysis:** A. Esteve, A. Montoliu (CEEISCAT), I. Pérez (Hospital Clínic-Idibaps, Universitat de Barcelona), Jordi Curto (Hospital Universitari de Bellvitge-IDIBELL)

**Technical support:** I. Pérez (Hospital Clínic-Idibaps, Universitat de Barcelona), Freyra Gargoulas (Hospital Son Espases and Hospital Son Llàtzer)

**Clinicians involved:** L. Zamora, J.L. Blanco, F. García-Alcaide, E. Martínez, J. Mallolas, (Hospital Clínic-Idibaps, Universitat de Barcelona), JM. Llibre, G. Sirera, J. Romeu, A. Jou, E. Negredo, (Fundació Lluita contra la Sida, Hospital Universitari Germans Trias i Pujol, Universitat Autònoma de Barcelona), M. Saumoy, JM. Tiraboschi, F. Bolao, C. Cabellos, C. Peña, S. DiYacovo (Hospital Universitari de Bellvitge-IDIBELL), M. Sala, M. Cervantes, M.J. Amengual, M. Navarro, V. Segura (Corporació Sanitària i Universitària Parc Taulí, Universitat Autònoma de Barcelona), P. Barrufet, (Hospital de Mataró, Consorci Sanitario del Maresme), J. Molina, M. Alvaro, J. Mercadal (Hospital Alt Penedès de Vilafranca), T. Payeras (Hospital Son Llàtzer).

**Civil society representatives:** Juanse Fernández (Comitè 1er de Desembre), Jesús E. Ospina (RedVIH)

#### CoRIS, Spain

**Steering committee:** Juan Berenguer, Julia del Amo, Federico García, Félix Gutiérrez, Pablo Labarga, Santiago Moreno, María Ángeles Muñoz. **Field work, data management and statistical analyses:** Paz Sobrino, Victoria Hernando, Belén Alejos, Débora Álvarez, Susana Monge, Inmaculada Jarrín. **BioBank:** María Ángeles Muñoz, Isabel García Pilar Martínez. **Hospitals:**

Juan Luis Gómez Sirvent, Patricia Rodríguez Fortúnez, María Remedios Alemán Valls, María del Mar Alonso Socas, Ana María López Lirola, María Inmaculada

Hernández Hernández, Felicitas Díaz-Flores Hospital Universitario de Canarias (Santa Cruz de Tenerife). Vicente Soriano, Pablo Labarga, Pablo Barreiro, Carol Castañares, Pablo Rivas, Andrés Ruiz, Francisco Blanco, Pilar García, Mercedes de Diego Hospital Carlos III (Madrid). Rafael Rubio, Federico Pulido, Silvana Fiorante, Jara Llenas, Violeta Rodríguez, Mariano Matarranz Hospital Doce de Octubre (Madrid). José Antonio Iribarren, Julio Arrizabalaga, María José Aramburu, Xabier Camino, Francisco Rodríguez-Arondo, Miguel Ángel von Wichmann, Lidia Pascual Tomé, Miguel Ángel Goenaga, Ma Jesús Bustinduy, Harkaitz Azkune Galparsoro Hospital Donostia (San Sebastián). Félix Gutiérrez, Mar Masiá, José Manuel Ramos, Sergio Padilla, Andrés Navarro, Fernando Montolio, Yolanda Peral, Catalina Robledano García Hospital General Universitario de Elche (Elche). Juan Berenguer, Juan Carlos López Bernaldo de Quirós, Pilar Miralles, Jaime Cosín Ochaita, Matilde Sánchez Conde, Isabel Gutiérrez Cuellar, Margarita Ramírez Schacke, Belén Padilla Ortega, Paloma Gijón Vidaurreta Hospital Gregorio Marañón (Madrid). Francesc Vidal, Joaquín Peraire, Consuelo Viladés, Sergio Veloso, Montserrat Vargas, Miguel López-Dupla, Montserrat Olona, Alba Aguilar, Joan Joseph Sirvent, Antoni Soriano, Rami AA. Qaneta Hospital Universitari de Tarragona Joan XXIII, IISPV, Universitat Rovira i Virgili (Tarragona). Ignacio de los Santos, Jesús Sanz Sanz, Johana Rodríguez, Ana Salas Aparicio, Cristina Sarriá Cepeda Hospital de la Princesa (Madrid). José Antonio Oteo, José Ramón Blanco, Valvanera Ibarra, Luis Metola, Mercedes Sanz, Laura Pérez-Martínez Hospital San Pedro-CIBIR (Logroño). Julio Sola Boneta, Javier Uriz, Jesús Castielo, Jesús Reparaz, María Jesús Arraiza, Carmen Irigoyen, David Mozas Hospital de Navarra (Pamplona). Santiago Moreno, José Luis Casado, Fernando Dronda, Ana Moreno, María Jesús Pérez Elías, Dolores López, Carolina Gutiérrez, Beatriz Hernández, María Pumares, Paloma Martí Hospital Ramón y Cajal (Madrid). Federico García García, José Hernández Quero, Alejandro Peña Monje, Leopoldo Muñoz Medina, Jorge Parra Ruiz Hospital San Cecilio (Granada).

**Cohort contact person:** Julia del Amo

#### VACH, Spain

Hospital de Cabueñas (Asturias) Luisa García-Alcalde Fernández, Belén de la Fuente García; Hospital Universitario Infanta Cristina (Badajoz) Agustín Muñoz Sanz; Hospital Universitari Vall d'Hebron (Barcelona) Esteban Ribera; Hospital de la Santa Creu i Sant Pau (Barcelona) Pere Domingo; Hospital General de Granollers (Barcelona) Elisabeth Deig Comerma; Hospital de Basurto (Bilbao) Pepa Muñoz Sanchez; Hospital Clínico Universitario (Cádiz) Antonio Vergara Campos; Hospital SAS de Jerez (Cádiz) José Alberto Terrón Pernía; Hospital Virgen del Rosell (Cartagena) Trinitario Sánchez;

Hospital General (Castellón) Bernardino Roca Villa-nueva; Hospital Virgen de la Luz (Cuenca); Paloma Geijo Martínez, Carmen Rosa Herranz; Hospital Infanta Elena (Huelva) Ignacio Suárez Lozano, J Ma Fajardo; Hospital Universitari Arnau de Vilanova (Lleida) Teresa Puig Ganau; Hospital Clínico San Carlos (Madrid) Vicente Estrada, Mónica Fuster, Martín Lagos; Hospital Gregorio Marañón (Madrid) Jaime Cosin Ochaita; Hospital Regional Universitario Carlos Haya (Málaga) Manuel Castaño Carracedo, Juan de Dios Colmenero Castillo; Hospital de Sierrallana (Santander) Ramón Teira Cobo; Hospital Virgen del Rocío (Sevilla) Pompeyo Viciana, Luis López Cortés; Hospital de Valme (Sevilla) Fernando Lozano; Hospital Universitari de Tarragona Joan XXIII (Tarragona) Francisco Vidal Marsal; Hospital Xarxa Sanitaria i Social de Santa Tecla (Tarragona) Enric Pedrol Clotet, Antonio Delegido, Mariona Tasias, Sheila Ruiz; Hospital Clínico (Valencia) José Galindo; Hospital Universitario La Fe (Valencia) José López Aldeguer, Dr Blanes, José Lacruz, Marta Montero, Miguel Salavert, Sandra Cuéllar

**Cohort contact person:** Ramon Teira

#### Conflicts of interest

J.K.B., W.D. and U.W. are employees of SwissRe: this company may benefit financially from increased insurability of HIV-positive lives.

The ART Cohort Collaboration is supported by the UK Medical Research Council (grants G0700820 and MR/J002380/1). Salaries of M.M. and S.I. were funded by MRC grants G0700820 and MR/J002380/1. Sources of funding of individual cohorts include the Agence Nationale de Recherches sur le SIDA et les hépatites virales (ANRS), the Institut National de la Santé et de la Recherche Médicale (INSERM), the French, Italian, Spanish Ministries of Health, the Swiss National Science Foundation (grant 33CS30\_134277), the Stichting HIV Monitoring, the European Commission (EuroCoord grant 260694), the Spanish Network for AIDS Research (RIS; ISCIII-RETIC RD06/006).

**Ethical approval:** Institutional review boards from each cohort approved analysis of routinely collected data to be used for research purposes. The ART Cohort Collaboration does not require ethical approval as all data is anonymised before transfer to ART-CC.

#### References

1. Hogg R, Lima V, Sterne JAC, Grabar S, Battegay M, Bonarek M, et al. **Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies** *1. Lancet* 2008; **372**:293–299.
2. Willig JH, Abrams S, Westfall AO, Routman J, Adusumilli S, Varshney M, et al. **Increased regimen durability in the era of once-daily fixed-dose combination antiretroviral therapy.** *AIDS* 2008; **22**:1951–1960.

3. Hogg RS, Heath KV, Yip B, Craib KJ, O'Shaughnessy MV, Schechter MT, et al. Improved survival among HIV-infected individuals following initiation of antiretroviral therapy. *JAMA* 1998; **279**:450–454.
4. Mocroft A, Vella S, Benfield TL, Chiesi A, Miller V, Gargalianos P, et al. Changing patterns of mortality across Europe in patients infected with HIV-1. EuroSIDA Study Group. *Lancet* 1998; **352**:1725–1730.
5. Mocroft A, Ledergerber B, Katlama C, Kirk O, Reiss P, D'Arminio MA, et al. Decline in the AIDS and death rates in the EuroSIDA study: an observational study. *Lancet* 2003; **362**:22–29.
6. Anglaret X, Toure S, Gourvillec G, Tchey A, Zio L, Zaho M, et al. Impact of vital status investigation procedures on estimates of survival in cohorts of HIV-infected patients from Sub-Saharan Africa. *J Acquir Immune Defic Syndr* 2004; **35**:320–323.
7. Zwahlen M, Harris RJ, Hogg R, Costagliola D, May M, de WF, et al. Mortality of HIV-infected patients starting potent antiretroviral therapy: Comparison with the general population in eight industrialized countries. *Int J Epidemiol* 2009; **38**:1624–1633.
8. Chene G, Sterne JA, May M, Costagliola D, Ledergerber B, Phillips AN, et al. Prognostic importance of initial response in HIV-1 infected patients starting potent antiretroviral therapy: analysis of prospective studies. *Lancet* 2003; **362**:679–686.
9. Egger M, May M, Chene G, Phillips AN, Ledergerber B, Dabis F, et al. Prognosis of HIV-1-infected patients starting highly active antiretroviral therapy: a collaborative analysis of prospective studies. *Lancet* 2002; **360**:119–129.
10. May MT, Ingle SM, Costagliola D, Justice AC, de Wolf F, Cavassini M, et al. Cohort profile: Antiretroviral Therapy Cohort Collaboration (ART-CC). *IJE* 2013 (in press) doi:10.1093/ije/dyt010.
11. McCullagh P, Nelder J. *Generalized linear models*: Chapman and Hall; 1989.
12. Dickman PW, Sloggett A, Hills M, Hakulinen T. Regression models for relative survival. *Stat Med* 2004; **23**:51–64.
13. Akaike H. A new look at the statistical model identification. *IEEE Trans Autom Control AC* 1974; **19**:716–723.
14. Lewden C, Bouteloup V, De Wit S, Sabin C, Mocroft A, Wasimath JC, et al. All-cause mortality in treated HIV-infected adults with CD4 ≥500 cells/mm<sup>3</sup> compared with the general population: evidence from a large European observational cohort collaboration. *Int J Epidemiol* 2012; **41**:433–445.
15. van Sighem Al, Gras LA, Reiss P, Brinkman K, de Wolf F. Life expectancy of recently diagnosed asymptomatic HIV-infected patients approaches that of uninfected individuals. *AIDS* 2010; **24**:1527–1535.
16. Lohse N, Hansen AB, Pedersen G, Kronborg G, Gerstoft J, Sorensen HT, et al. Survival of persons with and without HIV infection in Denmark, 1995–2005. *Ann Intern Med* 2007; **146**:87–95.
17. Gill MJ, May M, Lewden C, Saag M, Mugavero MJ, Reiss P, et al. Causes of death in HIV-1 infected patients treated with antiretroviral therapy 1996–2006: collaborative analysis of 13 HIV cohorts. *Clin Infect Dis* 2010; **50**:1387–1396.
18. Centers for Disease Control and Prevention. *Establishing a Holistic Framework to Reduce Inequities in HIV, Viral Hepatitis, STDs, and Tuberculosis in the United States 2010*. Available from: [www.cdc.gov/socialdeterminants](http://www.cdc.gov/socialdeterminants). [Accessed 16 August 2012].
19. Denning PH, DiNenno EA, Wiegand RE. Characteristics associated with HIV infection among heterosexuals in urban areas with high AIDS prevalence-24 cities, United States, 2006–2007 (Reprinted from MMWR vol 60, p.1045; 2011). *JAMA* 2011; **306**:1320–1322.
20. US Department of Health & Human Services. *How the Affordable Care Act Helps People Living with HIV/AIDS: 2011 and Beyond*. Available from: [http://www.healthcare.gov/news/fact\\_sheets/2011/11/hiv-aids11092011a.html](http://www.healthcare.gov/news/fact_sheets/2011/11/hiv-aids11092011a.html). [Accessed 16 August 2012].
21. Nakagawa F, Lodwick RK, Smith CJ, Smith R, Cambiano V, Lundgren J, et al. Projected life expectancy of people with HIV according to timing of diagnosis. *AIDS* 2012; **26**:335–343.
22. Dutch Association of Insurers. *Insurability of people with HIV: a step closer 2005:28*. Available from: <http://www.verzekeraars.nl/UserFiles/File/download/Hiv-engels.pdf>. [Accessed 16 August 2012].
23. Dutch Association of Insurers. *HIV Insurability Expanded: Report of the HIV Working Group* 2009:38. Available from: [http://www.verzekeraars.nl/UserFiles/File/download/Rapport\\_Verzekerbaarheid\\_hiv%20\\_Engels\\_juni\\_2009.pdf](http://www.verzekeraars.nl/UserFiles/File/download/Rapport_Verzekerbaarheid_hiv%20_Engels_juni_2009.pdf). [Accessed 16 August 2012].
24. AIDS-HILFE SCHWEIZ. *Life insurance policies for people living with HIV: International analysis*. 2008:7. Available from: [http://www.hivnet.org/downloads/pdf/life\\_insurances\\_international\\_analysis.pdf](http://www.hivnet.org/downloads/pdf/life_insurances_international_analysis.pdf). [Accessed 16 August 2012].
25. Hughes RA, Sterne JA, Walsh J, Bansil I, Gilson R, Orkin C, et al. Long-term trends in CD4 cell counts and impact of viral failure in individuals starting antiretroviral therapy: UK Collaborative HIV Cohort (CHIC) study. *HIV Med* 2011; **12**:583–593.
26. Lewden C, Chene G, Morlat P, Raffi F, Dupon M, Dellamonica P, et al. HIV-infected adults with a CD4 cell count greater than 500 cells/mm<sup>3</sup> on long-term combination antiretroviral therapy reach same mortality rates as the general population. *J Acquir Immune Defic Syndr* 2007; **46**:72–77.
27. Mocroft A, Sterne JA, Egger M, May M, Grabar S, Furrer H, et al. Variable impact on mortality of AIDS-defining events diagnosed during combination antiretroviral therapy: not all AIDS-defining conditions are created equal. *Clin Infect Dis* 2009; **48**:1138–1151.