

Response to combination antiretroviral treatment in HIV-positive individuals in Europe: variation by educational level

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Collaboration of Observational HIV Epidemiological Research Europe

Coordination: Copenhagen HIV Programme (CHIP) & Institut de Santé Publique, d'Epidémiologie et de Développement (ISPED)

- Introduction
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- Conclusions

- Socioeconomic status is inversely associated with numerous health outcomes in the general population but less is known on its behaviour among HIV-positive populations in Europe
- Measuring socio-economic position is difficult and, in adults, educational level has been used as a proxy which is stable overtime and easy to measure
- COHERE has recently reported clear differences by educational level in timely HIV diagnosis and antiretroviral treatment (ART) initiation, key cornerstones for successful HIV control at population level

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Objective

- To investigate differences in clinical prognosis and virological and immunological response to ART by maximum attained educational level

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Methods

- COHERE in EuroCoord - Collaboration of Observational HIV Epidemiological Research in Europe
 - ✓ Collaborative group of 35 HIV cohorts across Europe
 - ✓ Analyses included data from 13 cohorts in 6 European countries (Austria, France, Greece, Italy, Spain and Switzerland) collecting data on maximum attained educational level
 - ✓ Data exchange protocol and data quality control procedures
 - ✓ Data from 2011 COHERE merger

Methods

- Patients selection criteria:
 - ✓ Patients who were aged 16 years or older
 - ✓ Recruited after 1st January 1996
 - ✓ Had known educational level information
 - ✓ Had initiated ART and were antiretroviral-naïve at the start of treatment
 - ✓ Had at least one CD4 count and HIV-RNA measurement recorded in both the 6 months before ART and following ART initiation

Methods

- In 2012, EuroCoord defined socio-economic variables to harmonise data collection across cohorts in different European countries
- The definition of *maximum attained level of education* – **main exposure variable** - was based on the UNESCO/ISCED International Standard Classification of Education
 - ✓ uncompleted basic (ISCED 0)
 - ✓ basic (ISCED 1 and 2)
 - ✓ secondary (ISCED 3 and 4)
 - ✓ tertiary (ISCED 5 and 6)

Methods

Study outcomes were:

- ✓ Time from ART initiation to:
 - ✓ Death from any cause
 - ✓ New AIDS event or death from any cause
 - ✓ Virological success (considered to occur at the midpoint between last HIV-RNA \geq 400 and the first HIV-RNA $<$ 400)
- ✓ Rate of CD4 count recovery in the first 6 years of ART

Methods

- Follow-up started at the date of ART initiation and ended at the last date the patient was known to be alive
- Analyses assume that patients remained on ART once initiated and subsequent treatment changes after ART initiation were ignored

Methods - Statistical analyses

- Kaplan-Meier curves and parametric accelerated failure time models were used to explore differences by educational level for each outcome
- Parametric accelerated failure time survival models assume covariates accelerate or decelerate the time to event and provide estimates of time to event ratios, rather than the hazard ratios in Cox models
- Time ratio >1 for a covariate:
 - longer time to the event
 - lower risk of the event
- Time ratio <1 for a covariate:
 - shorter time to the event
 - increased risk of the event

Methods - Statistical analyses

- **Akaike information criterion (AIC)** criterion was used for comparing the goodness of fit of parametric models to our data
 - ✓ Lognormal distribution for death and new AIDS events
 - ✓ Log-logistic distribution for time to virological success
- A shared frailty term with gamma distribution was included to account for heterogeneity by cohort
- Piecewise linear mixed models with change in slope 6 months after ART initiation were used to compare CD4 count trajectories

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| <i>Inclusion criterion</i> | <i>Remaining patients</i> |
|---|---------------------------|
| HIV diagnosis 1996-2011 from cohorts who endorsed the project | 40078 |
| Initiated cART | 31162 |
| ART naive at cART initiation | 29077 |
| CD4 count at cART (-6 month, 1 week) | 24930 |
| HIV RNA at cART (-6 month, 1 week) | 22876 |
| At least 1 CD4 count AND HIV RNA after cART | 21555 |
| Known level of education | 14524 |
| <i>Total included</i> | <i>14524</i> |

Socio-demographic characteristics

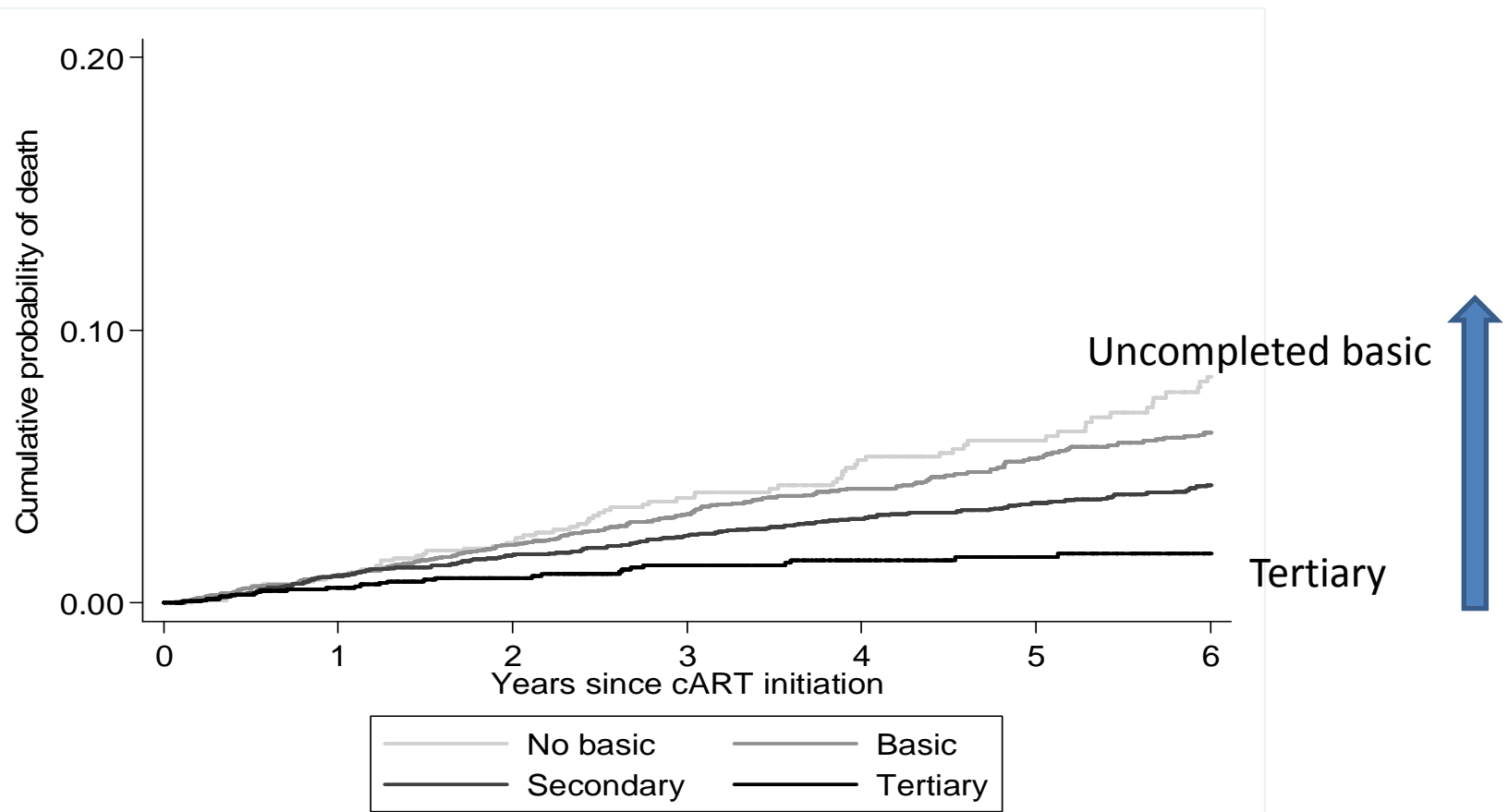
| | Uncompleted basic | Basic | Secondary | Tertiary |
|--------------------------------|-------------------|------------|------------|------------|
| N (%) | 1337 (9%) | 4589 (32%) | 6424 (44%) | 2174 (15%) |
| AIDS before ART | 26% | 22% | 18% | 13% |
| Median CD4 count | 202 | 211 | 239 | 272 |
| Median HIV RNA | 4,9 | 4.9 | 4.9 | 5.0 |
| Sex - Female | 42% | | | |
| Transmission category | | | | |
| Homosexual | 12% | | | |
| Heterosexual | 61% | | | |
| IDU | 19% | 23% | 9% | 2% |
| Other/Unknown | 8% | 6% | 5% | 5% |
| Geographical origin | | | | |
| Europe | 59% | 77% | 83% | 79% |
| Sub-Saharan Africa | 24% | 8% | 6% | 5% |
| Other /unknown | 17% | 15% | 11% | 16% |
| Median year of ART | 2004 | 2004 | 2004 | 2006 |
| Initial ART combination | | | | |
| NNRTI | 38% | 43% | 40% | 48% |
| PI | 58% | 52% | 56% | 49% |

Higher proportion of AIDS diagnosis before ART and lower CD4 cell counts with decreasing educational level

Socio-demographic characteristics

| | Uncompleted basic | Basic | Secondary | Tertiary |
|--------------------------------|-------------------|------------|------------|------------|
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| AIDS before ART | 26% | 22% | 18% | 13% |
| Median CD4 count | 202 | 211 | 239 | 272 |
| Median HIV RNA | 4.9 | 4.9 | 4.9 | 5.0 |
| Sex - Female | 42% | 33% | 22% | 10% |
| Transmission category | | | | |
| Homosexual | 12% | 20% | 48% | 70% |
| Heterosexual | 61% | 51% | 38% | 23% |
| IDU | 19% | 23% | 9% | 2% |
| Other/Unknown | 8% | 6% | 5% | 5% |
| Geographical origin | | | | |
| Europe | 59% | 77% | 83% | 79% |
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Time to death from all-causes by Educational level

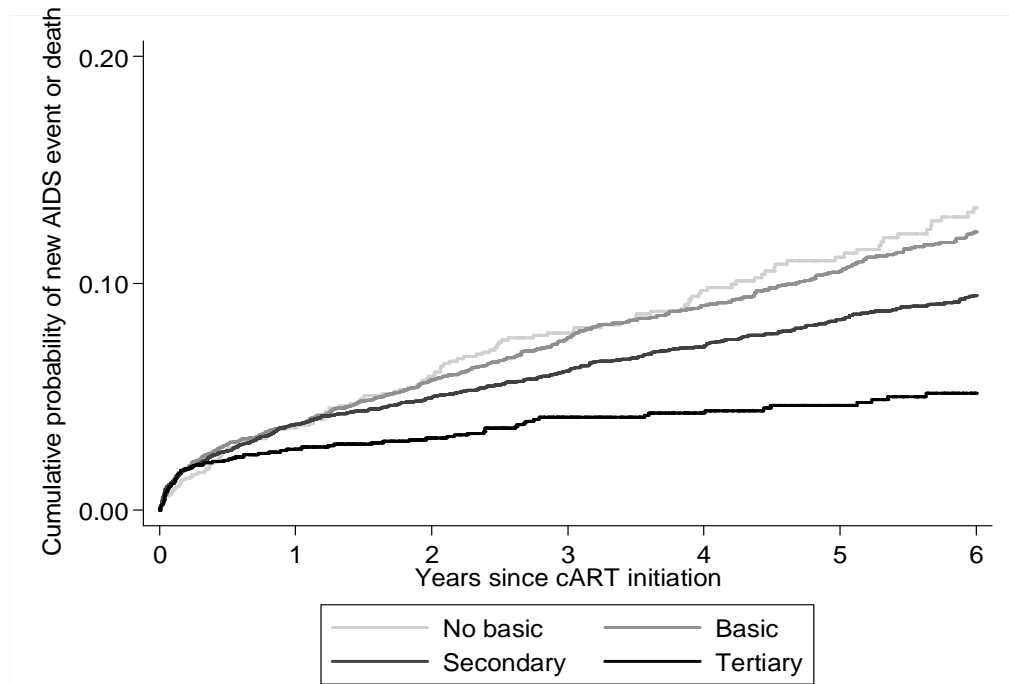


Multivariate analyses of the effect of educational level on all-cause mortality

| | Time ratio | 95% CI | P value |
|--------------------------|------------|----------------|---------|
| Educational level | | | |
| Uncompleted basic | 0.38 | (0.23 to 0.61) | <0.001 |
| Basic | 0.48 | (0.31 to 0.72) | |
| Secondary | 0.67 | (0.45 to 1.00) | |
| Tertiary | 1 | | |

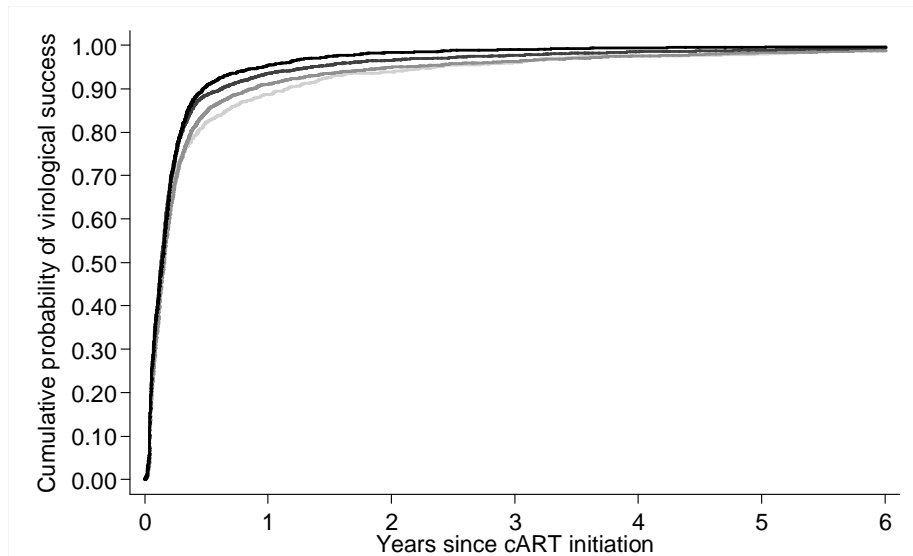
Adjusted by sex, age, transmission category, calendar period, geographical origin, CD4 cell count at ART, previous AIDS, PI-based regime vs NNRTI

Time to death or new AIDS event by educational level



| | Time ratio | 95% confidence interval | P value |
|--------------------------|------------|-------------------------|---------|
| Educational level | | | |
| Non-completed basic | 0.36 | (0.21, 0.63) | |
| Basic | 0.43 | (0.27, 0.69) | |
| Secondary | 0.57 | (0.37, 0.88) | |
| Tertiary | 1 | | 0.001 |

Time to virological success by educational level

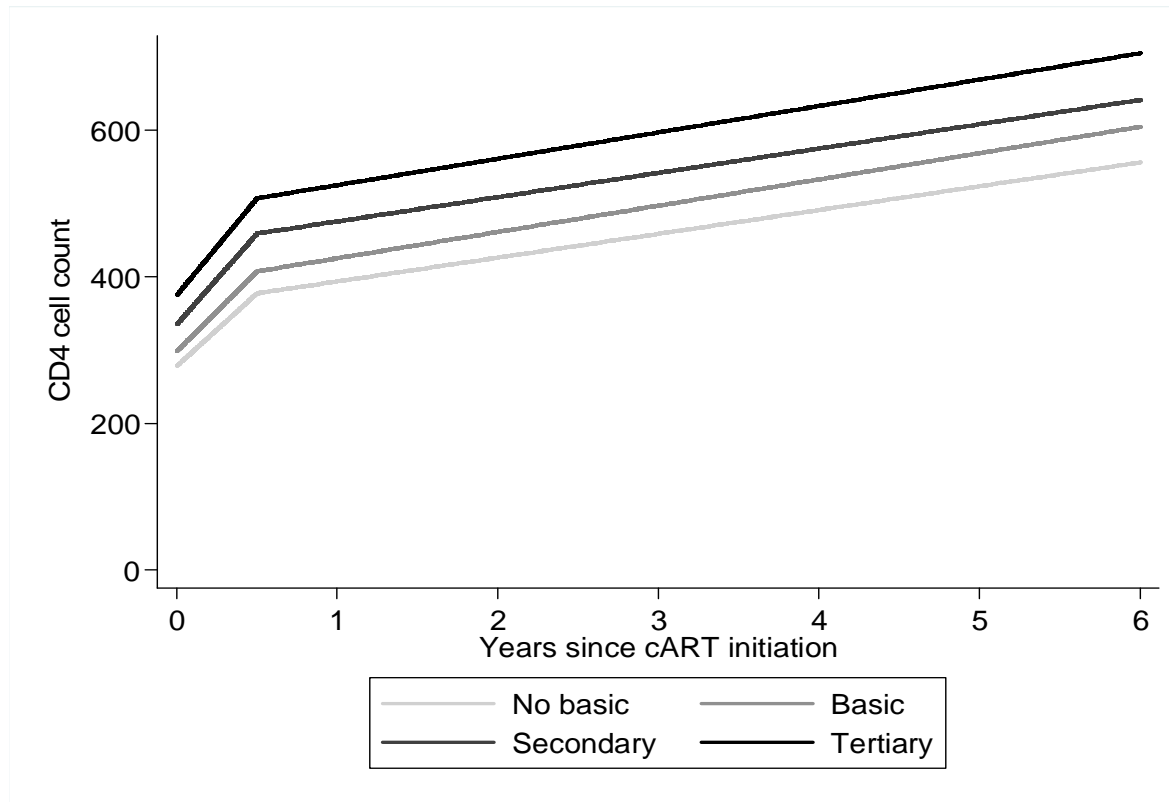


| | |
|-------------|------------|
| — No basic | — Basic |
| — Secondary | — Tertiary |

| | Time ratio | 95% CI | P value |
|--------------------------|------------|----------------|---------|
| <i>Educational level</i> | | | |
| Non -completed basic | 1.06 | (0.99 to 1.11) | 0.001 |
| Basic | 1.08 | (1.02 to 1.15) | |
| Secondary | 1.00 | (0.96 to 1.05) | |
| Tertiary | 1 | | |

Adjusted by sex, age, transmission category, calendar period, geographical origin, CD4 cell count at ART, previous AIDS, PI-based regime vs NNRTI, log10 VL

CD4 response to ART by educational level



Baseline: Male, MSM, European, < 37, AIDS-free at baseline, ART initiation > 2001, NNRTI-based initial ART, median HIV VL

Slide 23

JdAV3

Estoy de acuerdo en quitar la figura y contar el modelo de viva voz. Tengo dudas de si:

¿Has transformado los CD4?

¿Has ajustado por baseline CD4?

Leo que la gente hace una u otra cosa y no entiendo por qué

Julia del Amo Valero; 07-10-2013

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- HIV-positive subjects with lower educational level, a proxy for poorer socio-economic status, have poorer clinical outcomes following ART – higher mortality and rate of new AIDS events and poorer virological and immunological responses - which are seen in crude and in adjusted analyses
- Mechanisms involve both material and psychosocial pathways
- Important to raise awareness on SES inequalities in the ART era and monitor its evolution in Western European countries

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