

Aging and (Non-HIV-associated) Co-morbidity in HIV-positive Persons: The Swiss HIV Cohort Study (SHCS)

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Background

The population of HIV-positive individuals with access to antiretroviral therapy (ART) is aging (→ Figure 1). Improved survival of HIV infection leads to changing patterns of morbidity and mortality.

Study Aims

We aimed to study the influence of aging on the epidemiology of non-AIDS diseases in our cohort.

Methods

Study population: The Swiss HIV Cohort Study (SHCS) is a prospective observational cohort established in 1988 with continuous enrolment.

SHCS participants with at least one cohort visit between January 1, 2008, and June 30, 2010, were included in the analyses.

An expanded clinical questionnaire was introduced on July 1, 2008, covering non-AIDS endpoints since January 1, 2008.

Statistical analysis: We analyzed the incidence of clinical events per 1000 person-years of follow-up.

Associations with age were analyzed in uni- and multivariable Cox proportional hazards regression models.

Multivariable models were adjusted for latest square-root-transformed CD4 cell counts per μL , latest \log_{10} -transformed HIV-RNA copies/mL, female sex, HIV acquisition via injecting drug use, and time-updated smoking.

We used Stata (Version 11.1, StataCorp, College Station, Texas) for analyses.

Results

Participants: 7746 of 8105 (96%) participants had complete data for analyses and contributed to 20,292 visits; 1990 (26%) individuals were >50 (older) and 378 (5%) >65 yrs (elderly).

Baseline characteristics: Clinical baseline characteristics are shown in → Table 1A, and antiretroviral therapy and non-HIV medication in → Table 1B.

Variables	Total	Age-group			P
		<50	50-64	>65	value
Patients, n (%)	8138 (100)	5558 (68.3)	2148 (26.4)	431 (5.3)	
Female n (%)	2390 (29.4)	1882 (33.9)	435 (20.2)	73 (16.9)	< 0.001
HIV transmission groups, n (%)					< 0.001
MSM	3465 (42.6)	2281 (41.0)	983 (45.7)	201 (46.6)	
Heterosexual	3282 (40.3)	2260 (40.7)	795 (37.0)	227 (52.7)	
IDU	1391 (17.1)	1017 (18.3)	371 (17.3)	3 (0.7)	
Prior clinical AIDS, n (%)	1878 (23.1)	117 (2.1)	822 (38.3)	139 (32.3)	< 0.001
Age at HIV diagnosis, median y (IQR)	32 (27-40)	29 (25-35)	40 (33-47)	58 (52-63)	< 0.001
Years HIV-infected, median (IQR)	10.9 (5.06-17.7)	9.15 (4.15-15.9)	15.0 (8.73-21.1)	12.1 (7.62-17.2)	< 0.001
Nadir CD4 cells/ μL , median (IQR)	350 (180-542)	366 (197-554)	313 (150-527)	285 (125-482)	< 0.001
First CD4 cells/ μL , median (IQR)	190 (84-288)	204 (101-306)	150 (64-245)	157 (65-253)	< 0.001
CD4/ μL at last visit, median (IQR)	523 (370-701)	527 (377-707)	518 (360-697)	487 (340-632)	< 0.001
BMI, kg/m^2 , median (IQR)	23.5 (21.2-26.0)	23.2 (21.1-25.9)	23.8 (21.3-26.5)	24.2 (22.0-26.6)	< 0.001
Comorbidities, n (%)					
Smoking	3629 (44.5)	2663 (47.9)	892 (41.5)	74 (17.2)	< 0.001
Hypertension	4533 (55.7)	2717 (48.9)	1484 (69.1)	332 (77.0)	< 0.001
Diabetes mellitus	331 (4.1)	111 (2.0)	146 (6.9)	72 (16.7)	< 0.001
Hepatitis B virus coinfection	329 (4.0)	246 (4.4)	67 (3.1)	16 (3.7)	< 0.001
Hepatitis C virus coinfection	1854 (22.8)	1299 (23.4)	529 (24.6)	26 (6.0)	0.029
Drug use, n (%)					
Illicit injectables	221 (2.7)	175 (3.2)	46 (2.1)	0 (0)	< 0.001
Illicit non-injectables	1495 (18.4)	1192 (21.4)	293 (13.6)	10 (2.3)	< 0.001
Opiate substitution program	740 (9.1)	554 (10.0)	186 (8.7)	0 (0)	< 0.001

Table 1A: Clinical baseline characteristics of 8138 HIV-seropositive cohort participants, stratified by age

Figure 1: Age distribution among active participants of the Swiss HIV Cohort Study over time.

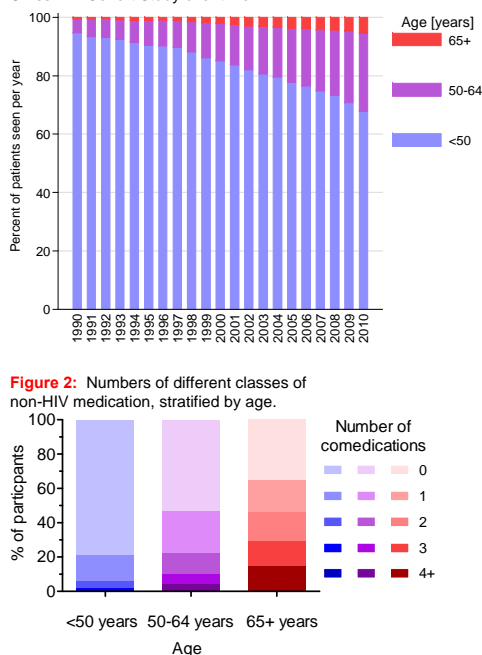
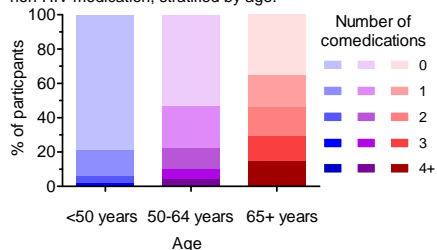


Figure 2: Numbers of different classes of non-HIV medication, stratified by age.



Antiretroviral therapy and non-HIV medication: A total of 6177 of 8138 (76%) participants were taking ART, and 5579 of the 6177 (90%) participants had an undetectable viral load at the last cohort visit in the reference period (→ Table 1B).

2458 of 8138 (30.2%) participants had at least one non-HIV medication. → Figure 2 shows the % of participants with their respective numbers of non-HIV medication stratified by age.

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Table 1B: Antiretroviral therapy and non-HIV medication in 8138 HIV-seropositive cohort participants, stratified by age

¹ Test for trend across age-groups

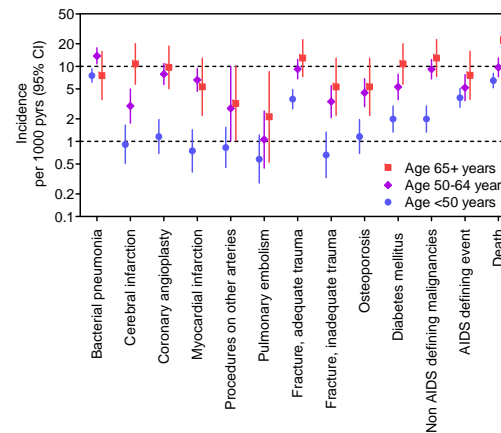
Variables	Total	Age-group			P value ¹
		<50	50-64	>65	
Antiretroviral treatment					
Age at ART start, years, median (IQR)	36 (31-43)	33 (29-37)	44 (39-49)	60 (55-64)	< 0.001
Era of starting ART, n (%)					< 0.001
MonoDual	2173 (26.7)	1193 (21.5)	832 (38.7)	148 (34.3)	
Combination ART	5329 (65.5)	3820 (68.7)	1236 (56.5)	273 (63.3)	
Status at last visit, n (%)					< 0.001
ART naive	636 (7.8)	545 (9.8)	81 (3.8)	10 (2.3)	
ART interrupted	889 (8.5)	534 (9.6)	130 (6.1)	150 (35.8)	
On ART, VL <50 copies/mL	5579 (68.6)	3632 (65.3)	1618 (75.3)	329 (75.3)	
On ART, VL >50 copies/mL	1234 (15.2)	847 (15.2)	320 (14.9)	67 (15.6)	
Time on ART, median (IQR)					< 0.001
Overall years	6.17 (0.740-11.5)	4.55 (0.9-8.5)	9.64 (4.02-13.2)	9.42 (5.09-13.2)	
Years on Mono/ Dual	1.50 (0.504-3.70)	1.19 (0.332-3.25)	2.00 (0.748-4.23)	1.87 (0.671-4.20)	< 0.001
Non-ART medication, n (%)					< 0.001
Anthypertensives (not ACE inhibitors)	785 (9.7)	300 (5.4)	341 (15.9)	144 (33.4)	
Anthypertensives (ACE inhibitors)	874 (10.7)	311 (5.6)	415 (19.3)	148 (34.3)	< 0.001
Lipid-lowering agents	1013 (12.4)	324 (5.8)	511 (23.8)	178 (41.3)	< 0.001
Oral antidiabetics	170 (2.1)	49 (0.9)	82 (3.8)	39 (9.1)	< 0.001
Insulin	110 (1.5)	39 (0.7)	52 (2.4)	27 (6.3)	< 0.001
Antiplatelet drugs	473 (5.8)	110 (2.0)	233 (10.8)	130 (30.2)	< 0.001
Antidepressants	792 (9.7)	514 (9.3)	240 (11.2)	38 (8.8)	0.140

Table 2: Uni- and multivariable hazard ratios for clinical events, hospitalizations, and death, from January 1, 2008, until June 30, 2010, stratified by age

Events	Univariable analyses			Multivariable analyses		
	50-64 HR (95% CI) ^a	>65 HR (95% CI) ^a	P value	50-64 HR (95% CI) ^b	>65 HR (95% CI) ^b	P value
Clinical events						
Bacterial pneumonia	1.82 (1.32-2.51)	1.00 (0.463-2.16)	0.001	2.00 (1.44-2.78)	1.61 (0.729-3.53)	< 0.001
Cerebral infarction	3.27 (1.46-7.19)	11.8 (5.33-27.9)	< 0.001	3.56 (1.59-7.94)	20.5 (7.85-53.4)	< 0.001
Coronary angioplasty	6.78 (3.67-12.5)	8.35 (3.61-19.3)	< 0.001	6.11 (3.28-11.4)	8.65 (3.62-20.7)	< 0.001
Myocardial infarction	8.85 (4.21-18.6)	7.15 (2.40-21.3)	< 0.001	7.73 (3.65-16.4)	7.30 (2.37-22.5)	< 0.001
Procedure on other arteries	3.31 (1.45-7.55)	3.88 (1.07-14.1)	0.289	3.45 (1.49-7.97)	5.46 (1.42-21.0)	0.005
Pulmonary embolism	1.81 (0.576-5.72)	3.67 (0.763-17.7)	0.277	1.69 (0.524-5.45)	4.01 (0.776-21.2)	0.289
Fracture, adequate trauma	2.50 (1.64-3.90)	3.51 (1.85-6.65)	< 0.001	2.36 (1.54-3.62)	4.67 (2.37-9.17)	< 0.001
Fracture, inadequate trauma	5.12 (2.19-11.9)	8.03 (2.63-24.5)	< 0.001	5.37 (2.26-12.8)	13.8 (4.10-46.5)	< 0.001
Osteoporosis	3.82 (1.94-7.51)	4.59 (1.65-12.7)	< 0.001	4.14 (2.08-8.23)	6.79 (2.30-20.0)	< 0.001
Diabetes mellitus	2.66 (1.52-4.67)	5.43 (2.60-11.4)	< 0.001	2.61 (1.48-4.63)	5.21 (2.42-11.2)	< 0.001
Non-AIDS malignancy	4.58 (2.78-7.55)	6.48 (3.24-13.0)	< 0.001	4.21 (2.53-7.00)	6.24 (3.03-12.6)	< 0.001
AIDS-defining event	1.36 (0.831-2.24)	2.00 (0.901-4.43)	0.185	1.74 (1.05-2.90)	2.85 (1.25-6.52)	0.019
Hospitalizations						
Somatic disease	1.47 (1.30-1.66)	2.18 (1.79-2.66)	< 0.001	1.58 (1.40-1.80)	2.75 (2.24-3.37)	< 0.001
Injury	1.27 (0.810-2.00)	3.70 (2.12-6.46)	< 0.001	1.30 (0.819-2.06)	5.11 (2.81-9.30)	< 0.001
Psychiatric disease	0.727 (0.520-1.02)	0.496 (0.219-1.12)	0.040	0.788 (0.561-1.11)	0.937 (0.407-2.15)	< 0.001
Death	1.49 (1.04-2.15)	3.39 (2.10-5.49)	< 0.001	1.55 (1.01-2.24)	5.97 (3.52-10.1)	< 0.001

Figure 3: Incidence of clinical events between January 1, 2008, and June 30, 2010, stratified by age.

Abbreviations: CI, confidence interval; pyrs, person-years



Non-AIDS events: We observed 512 new clinical events in the reference period, including 121 bacterial pneumonias, 29 myocardial infarctions, 20 strokes, 34 incident diabetes mellitus, 67 trauma-associated fractures, 23 fractures without adequate trauma, and 45 non-AIDS malignancies.

→ Figure 3 depicts the incidence/1000 pyrs of new clinical events and deaths during the observation period. Incidence rates for AIDS, death, and most non-AIDS diseases were elevated for persons aged 50-64 and 65+ years (compared with <50).

Associations between endpoints and age are shown in adjusted multivariable analyses in → Table 2.

Conclusions

Non-HIV co-morbidities, particularly diabetes mellitus, cardiovascular disease, non-AIDS malignancies, and osteoporosis, become increasingly important in HIV care, and most of these "non-HIV" events are frequently age-related.

Acknowledgments

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