

HIV as a risk factor in the initial presentation of a range of cardiovascular, coronary, cerebrovascular, and peripheral arterial diseases: a linked electronic health records study of 8 million adults in the UK

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Background

HIV has been associated with increased risk of myocardial infarction (MI), ischaemic stroke, and heart failure. However, associations with other cardiovascular diseases (CVDs), such as stable angina, abdominal aortic aneurysm, peripheral arterial disease, atrial fibrillation, or mortality from coronary heart disease, remain understudied. This study uses structured, national linked electronic health records (EHRs) from primary care, hospital care, and mortality statistics to examine associations between HIV and the incidence of a range of heterogeneous cardiovascular, cerebrovascular, peripheral diseases, in a large unselected population without pre-existing CVDs.

Aims

(i) To estimate and compare the incidence of 11 fatal or non-fatal CVDs according to time-updated primary care recorded HIV-serostatus, accounting for the risk of incidence of other CVDs or death from other causes.

(ii) To determine whether risk factor associations differ by HIV-serostatus according to age.

(iii) To estimate the hazard ratios for the association of HIV-positive serostatus and the 11 diseases using disease-specific Cox proportional hazards models, accounting for known CVD risk factors.

Methods

Prospective open cohort study using anonymised linked primary care (Clinical Practice Research Datalink), hospital admission (Hospital Episode Statistics), and mortality records (Office of National Statistics) from the CALIBER resource. HIV-positive serostatus was defined as a time-updated record of HIV-related Read codes and/or a record of antiretroviral therapy prescription in the CPRD, while CVDs and risk factors were ascertained using diagnostic codes in individual EHRs (Read codes in CPRD, ICD-10 in HES and ONS). Adults registered with a GP and free from clinically diagnosed CVDs at baseline were followed-up between 1997 and 2016. The primary endpoint was first record of one of 11 CVDs according to time-updated HIV-serostatus. For each CVD presentation, and by time-updated HIV-serostatus, we compared cumulative and excess incidence rates (IR) per 1,000 person-years (PY) and used Cox models to estimate cause-specific hazard ratios for the association of HIV-serostatus and initial presentation of each CVDs

Results

A total of 8,092,909 individuals registered with a GP were included, of which 9,500 (0.1%) were HIV-diagnosed during 110,136 total PY of follow-up (55,260 PY before HIV diagnosis, 54,876 after). Significant differences were observed in socio-demographic and CVD risk factors by HIV-serostatus (Table 1).

Table 1: Socio-demographic factors and cardiovascular risk factors by HIV-serostatus* (N= 8,092,909)

	HIV-diagnosed (N=9,500)		Not HIV-diagnosed (N= 8,083,409)		p-value
Age at entry, years n(%)					
18-29	2,660 (28.0)	1,651,859 (20.4)			
30-39	2,996 (31.5)	1,410,504 (17.4)			
40-49	1,559 (16.4)	1,071,762 (13.3)			
50-59	687 (7.2)	861,012 (10.7)			
≥60	384 (4.0)	1,146,122 (14.2)			<0.001
Women, n (%)	3,493 (36.8)	4,159,670 (51.5)			<0.001
Ethnicity, n (%)					
White	1,859 (34.5)	1,731,511 (54.0)			
Black African	1,541 (28.6)	63,724 (2.0)			
Black Caribbean or other	265 (4.9)	41,144 (1.3)			
Asian or Mixed	349 (6.5)	229,472 (7.2)			<0.001
Smoking status, n (%)					
Non-smoker	719 (51.2)	962,201 (60.3)			
Former smoker	194 (13.8)	210,768 (13.2)			
Current smoker	491 (35.0)	422,883 (26.5)			<0.001
Alcohol use status, n (%)					
Non- or former drinker	512 (52.5)	516,608 (49.8)			
Occasional drinker	279 (28.6)	344,510 (33.2)			
Moderate or heavy drinker	184 (18.9)	175,489 (16.9)			0.007
Mean body mass index, kg/m ² [SD]	25.0 [4.9]	25.3 [5.0]			0.004
Mean high density lipoprotein, mmol/L [SD]	1.4 [0.9]	1.4 [0.6]			0.022

*Data on covariates at different time points: HIV serostatus, body mass index and high density lipoprotein are time-updated; age groups shown at study entry; smoking and alcohol status measured within five years of study entry. Proportion of participants with non-missing covariate values (of N=8,396,971): ethnicity 30.7%, smoking 20.6%, alcohol 13.8%, body mass index 32.3%, lipids 3.6%.

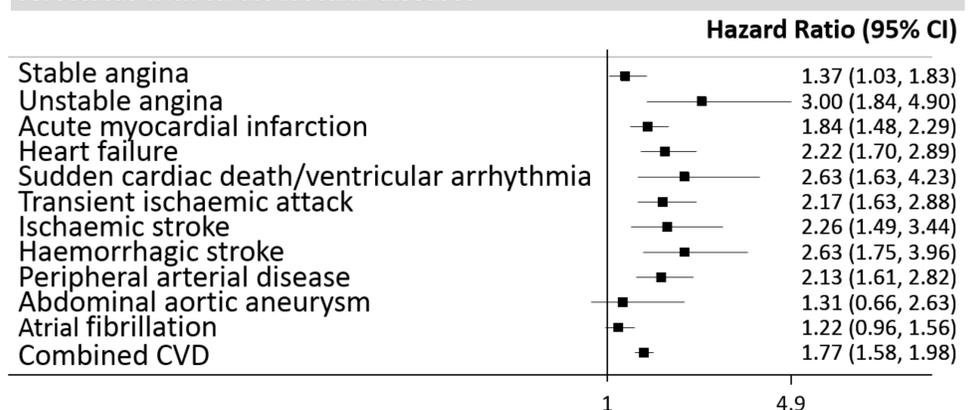
Table 2: Crude incidence rates (IR) of cardiovascular diseases per 1,000 person years at risk (PYR) by HIV-serostatus

Endpoint	HIV-diagnosed (N=9,500)		Not HIV-diagnosed (N=8,083,409)	
	N events	IR/1000 PYR [95%CI]	N events	IR/1000 PYR [95%CI]
Stable angina	81	1.2 [1.0,1.6]	91,003	1.1 [1.1,1.1]
Unstable angina	22	0.3 [0.2,0.5]	12,958	0.1 [0.1,0.2]
Acute myocardial infarction	142	2.3 [1.9,2.7]	95,300	1.1 [1.0,1.1]
Heart failure	87	1.4 [1.1,1.7]	93,340	1.1 [1.1,1.1]
Sudden cardiac death/cardiac arrest/ventricular arrhythmia	17	0.3 [0.2,0.5]	9,894	0.1 [0.1,0.2]
Transient ischaemic attack	70	1.2 [0.9,1.5]	73,768	0.9 [0.8,0.9]
Ischaemic stroke	34	0.5 [0.4,0.8]	25,485	0.3 [0.3,0.3]
Haemorrhagic stroke	35	0.6 [0.4,0.8]	17,770	0.2 [0.2,0.3]
Peripheral arterial disease	73	0.7 [0.5,0.8]	58,370	0.7 [0.7,0.7]
Abdominal aortic aneurysm	11	0.2 [0.1,0.3]	17,122	0.2 [0.2,0.2]
Atrial fibrillation	112	1.8 [1.4,2.2]	158,563	1.9 [1.9,1.9]
Combined CVD endpoint*	756	8.9 [8.2,9.7]	645,767	5.6 [5.5,5.6]

*Includes stable angina, acute myocardial infarction, coronary heart disease NOS, any CVD death, heart failure, transient ischaemic attack, ischaemic and haemorrhagic stroke, stroke NOS, and peripheral arterial disease

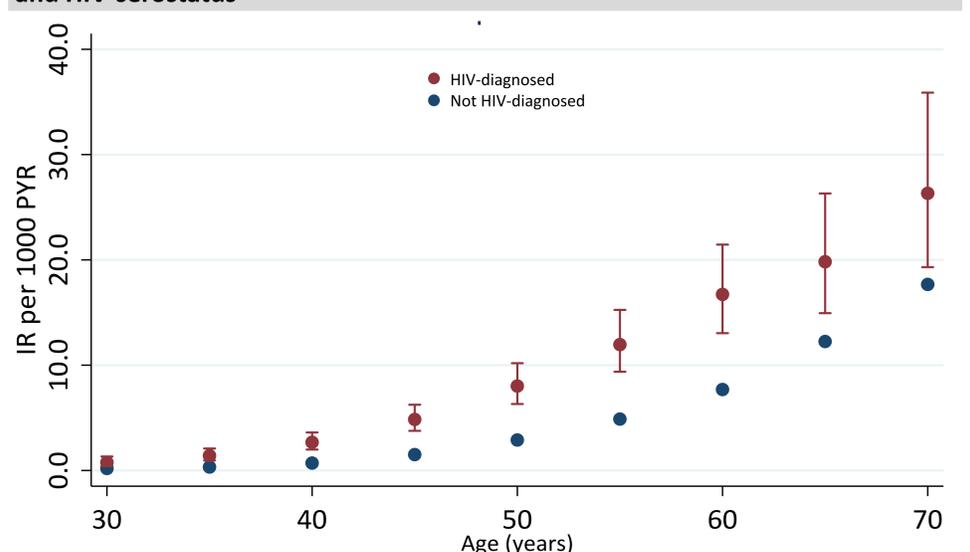
We observed 654,257 first presentations of CVDs during a median follow-up of 10 years [IQR 5-15]. Among HIV-diagnosed people, 684 (7.2%) had a first CVD presentation, the most common being MI, atrial fibrillation, and heart failure (Table 2).

Figure 1: Age and sex-adjusted hazard ratios (95%CI) for the association of HIV-serostatus with cardiovascular diseases



HIV-serostatus was significantly associated with initial presentation of stable and unstable angina, MI, heart failure, sudden cardiac death, stroke subtypes, and peripheral arterial disease (Figure 1). No significant association was observed between abdominal aortic aneurysm or atrial fibrillation and HIV-serostatus.

Figure 2: Crude incidence rates [95%CI] of composite CVD per 1000 PY by age and HIV-serostatus



Conclusion

In this population-based cohort study of a large-scale primary care sample, we observed heterogeneous associations between HIV-serostatus and initial presentation of a range of acute and chronic CVDs. Future work will examine trends in excess risk by calendar time and gender. These results have implications for clinical risk assessment and trial design among HIV-diagnosed individuals.