People living with HIV in the UK have a higher risk of progression to CNS disorders and other comorbidities than matched counterparts

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Introduction

- As a direct result of treatment effectiveness, the survival rate of people living with HIV (PLHIV) has improved over the previous two decades, resulting in HIV evolving into a chronic disease.[1]
- HIV associated comorbidities are a key concern for patients and healthcare providers as the number of people ageing with HIV increases in the UK.[2]
- Although previous studies have indicated greater risk of comorbidities in PLHIV, there is a need for further UK real-world evidence to understand whether the risk of developing these diseases is related directly to HIV infection or from other influences, such as an ageing population.

Objectives

- To assess the relative risk (RR) of progression to selected comorbidities in PLHIV when compared with matched, HIV-negative controls, using UK specific real-world data.
- More specifically, building on previous observational analyses in the UK, assess the real-world risk of progression to central nervous system (CNS) disorders (defined as anxiety, depression, sleep disorders) and other pre-specified comorbidities (end stage renal disease, osteoporosis, diabetes, cardiovascular disease, hypertension, stroke, cancer, all infections) in people diagnosed with HIV versus matched controls.

Methods

Data Source

- Patients were selected from the Clinical Practice Research Datalink (CPRD) GOLD database, a routine primary care database in the UK comprising of approximately 15 million patients.[3]
- CPRD captures data characterising the care of approximately 10% of the UK general practice records and it is representative of the UK as a whole.
- Approximately 60% of primary care practices participate in a linkage scheme, by which their patient records are linked to hospital episode statistics (HES), providing data on inpatient and outpatient data occurring within the NHS hospitals in England.[4]
- Read codes (primary care) and ICD-10 codes (inpatient/ outpatient records) were used to identify patients with a HIV diagnosis and define events recorded.

Patient Selection

- The study population was selected from permanently registered patients diagnosed with HIV between 1st January 1970 and 31st December 2017 from primary care practices of acceptable research quality, who were eligible for the hospital data linkage scheme.
- The index date for PLHIV was set to the earlier of the patient's documented diagnosis of HIV, or the patient's first positive test result for HIV. For matched HIV-negative controls, their index date was set to the index date of their matched case.
- PLHIV were matched 1:2 with HIV-negative controls according to age, gender, GP practice and HES eligibility status.

Analysis

- Demographic data was presented for both PLHIV and their matched HIV-negative controls.
- Cox proportional hazard models were generated to determine the risk of developing the comorbidity of interest (hazard ratio (HR), 95% CI).
- For HR calculation, people with a comorbidity of interest on or prior to index date were excluded in each relevant analysis, along with their matched equivalent. Thus, the risk estimate was for incident disease.

Results

- Overall there were 2,945 PLHIV cases matched to 5,890 HIV-negative controls eligible for the analysis. Baseline characteristics for the overall cohort are shown in table 1.
- All prior comorbidities in PLHIV were statistically different compared to HIV-negative controls with the exception of osteoporosis, diabetes and hypertension.

Table 1. Baseline Characteristics for overall population

	PLHIV cases	HIV-negative controls	p-value
N	2,945	5,890	
Males, n (%)	1,941 (65.9)	3,882 (65.9)	1
Age, mean (SD)	39.1 (12.7)	39.1 (12.7)	1
BMI, mean (SD)	25.2 (5.4)	27.5 (6.1)	<0.0001
Ethnicity, n (%)			<0.0001
White	1,336 (45.4)	3,177 (53.9)	
Black	770 (26.1)	347 (5.9)	
Asian	74 (2.5)	332 (5.6)	
Mixed	71 (2.4)	53 (0.9)	
Other	60 (2.0)	120 (2.0)	
Missing	634 (21.5)	1,861 (31.6)	
Prior CNS comorbidities, n (%)			
Depression	645 (21.9)	949 (16.1)	<0.0001
Anxiety	287 (9.8)	493 (8.4)	0.0350
Sleep disorders	228 (7.7)	271 (4.6)	<0.0001
Prior other comorbidities, n (%)			
Infection	639 (21.7)	629 (10.7)	<0.0001
Hypertension	219 (7.4)	417 (7.1)	0.5703
Cancer	204 (6.9)	162 (2.8)	<0.0001
Cardiovascular disease	132 (4.5)	129 (2.2)	<0.0001
Diabetes	73 (2.5)	121 (2.1)	0.2277
End stage renal disease	68 (2.3)	68 (1.2)	<0.0001
Stroke	33 (1.1)	26 (0.4)	0.0004
Osteoporosis	10 (0.3)	20 (0.3)	1

- The risk of presenting with sleep disorders and depression (CNS disorders) was significantly higher for PLHIV than HIV-negative controls, with a HR of 1.7 (95% CI: 1.3 – 2.1) and 1.5 (95% CI: 1.3 – 1.8) respectively, as shown in table 2.
- The risk of presentation with anxiety, another CNS disorder, was not statistically significant.
- Significantly higher HR's were observed for osteoporosis (2.6; 95% CI: 1.6 – 4.2), stroke (1.9; 95% CI: 1.3 – 2.9), cancer (1.9; 95% CI: 1.6 – 2.3), and infection (1.5; 95% CI: 1.3 – 1.8).
- No statistical difference was observed for renal disease, diabetes, hypertension and cardiovascular disease.

Table 2. Cox regression models for progression to comorbidity

		N	N with event	HR (95%CI)	P-value
CNS comorbidites					
Sleep disorders	HIV-negative	4,972	207	Reference	1
	PLHIV	2,486	158	1.71 (1.39 - 2.10)	<0.0001
Depression	HIV-negative	3,340	366	Reference	1
	PLHIV	1,670	255	1.54 (1.32 - 1.81)	<0.0001
Anxiety	HIV-negative	4,508	264	Reference	1
	PLHIV	2,254	127	1.04 (0.84 - 1.28)	0.7400
Other comorbidities					
Osteoporosis	HIV-negative	5,830	31	Reference	1
	PLHIV	2,915	36	2.62 (1.62 - 4.23)	<0.0001
Stroke	HIV-negative	5,774	48	Reference	1
	PLHIV	2,887	41	1.92 (1.26 - 2.91)	0.0022
Cancer	HIV-negative	5,214	216	Reference	1
	PLHIV	2,607	186	1.91 (1.57 - 2.33)	<0.0001
Infection	HIV-negative	3,712	436	Reference	1
	PLHIV	1,856	289	1.55 (1.34 - 1.80)	<0.0001
Hypertension	HIV-negative	4,850	369	Reference	1
	PLHIV	2,425	185	1.12 (0.94 - 1.34)	0.2027
Diabetes	HIV-negative	5,528	179	Reference	1
	PLHIV	2,764	88	1.10 (0.85 - 1.42)	0.4652
Renal disease	HIV-negative	5,640	305	Reference	1
	PLHIV	2,820	149	1.07 (0.88 - 1.30)	0.4948
Cardiovascular disease	HIV-negative	5,422	215	Reference	1
	PLHIV	2,711	95	0.99 (0.78 - 1.26)	0.9110

Conclusions

- **There was an increased risk of presenting with sleep disorders, depression, osteoporosis, stroke, cancer and infection, in PLHIV compared to matched HIV-negative controls.**
- **Earlier diagnosis, improved treatment of comorbidities and tailored antiretroviral treatment associated with a lower risk of developing the comorbidities identified may improve quality of life for PLHIV.**
- **Our findings on CNS disorders are consistent with previous studies in PLHIV compared to the general population.[5]**
- **Mental health is a key focus of the NHS ten-year plan. These findings suggest that PLHIV may warrant greater attention to support this long-term objective.**

Limitations

- Coding of HIV is likely to be under represented in the CPRD & HES population due to many HIV patients being diagnosed and treated in another setting such as STI/GUM clinics.
- Some patients with HIV may not have provided consent for their GP to be informed, therefore these patients may not be identified as HIV patients in the data. Whilst this may impact estimates of absolute risk, this is thought not to impact relative risk estimates in any notable way.

References

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