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## ORIGINAL ARTICLE

# Changing co-morbidity and increasing deprivation among people living with HIV: UK population-based cross-sectional study

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## Abstract

**Background:** The great success of HIV treatments means that, increasingly, people living with HIV (PLHIV) are growing old enough to develop age-associated comorbid conditions. We investigated the evolution of comorbid conditions and demographics among PLHIV in England.

**Methods:** In a cross-sectional study linking Clinical Practice Research Data-link (CPRD) primary care, hospitalization, death registry and Index of Multiple Deprivation data, we measured the prevalence of 304 individual health conditions, categorized into 47 condition groups (36 non-communicable, 11 communicable). Using logistic regression, we calculated odds ratios (ORs) for the likelihood of each condition and condition group in 2015 versus 2008, adjusting for age, sex and deprivation.

**Results:** In 2015, there were 964 CPRD-registered PLHIV compared with 1987 in 2008; 62% were male and 38% female in both cohorts. The 2015 cohort was older, with 51.1% aged 45–64 years and 7.2% aged 65–84 years compared with 31.8% and 3.2%, respectively, in 2008. Deprivation was higher in 2015, at 23.9% (quintile 4) and 28.7% (quintile 5) compared with 5.8% and 6.6%, respectively, in 2008.

Of 36 non-communicable condition groups, 14 (39%) occurred in  $\geq 10\%$  of PLHIV in 2015, of which seven were more likely in 2015 than in 2008: renal-chronic-kidney-disease [odds ratio (OR) = 1.96 (95% CI: 1.33–2.90); endocrine-obesity [OR = 1.76 (1.12–2.77)]; rheumatology [OR = 1.64 (1.30–2.07)]; dermatology [OR = 1.55(1.29–1.85)]; genito-urinary-gynaecological [OR = 1.44(1.18–1.76)]; eyes-ears/nose/throat [OR = 1.31(1.08–1.59)]; and gastro-intestinal conditions [OR = 1.28 (1.04–1.58)]. Two condition groups, respiratory-chronic-obstructive-pulmonary-disease [OR = 0.36 (0.19–0.69)] and endocrine-diabetes [OR = 0.49 (0.34–0.70)], were less likely in 2015. Ten out of 11 communicable infectious condition groups were less likely in 2015.

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**Conclusions:** Although infections in PLHIV have fallen, chronic non-communicable comorbidity is increasingly prevalent. Alongside the marked increases in deprivation and ageing, this study suggests that socio-economic measures in addition to healthcare provision are needed to achieve holistic health for PLHIV.

#### KEYWORDS

comorbid conditions, communicable conditions, deprivation, HIV care provision, non-communicable conditions, people living with HIV (PLHIV)

## BACKGROUND

In 2020, for the first time, the UK met the UNAIDS 95-95-95 target; at least 95% of people living with HIV (PLHIV) were diagnosed, 99% of those diagnosed were on treatment, and 97% of those on treatment had an undetectable viral load [1]. It is estimated that 0.15% of the UK population is living with HIV, but mortality in adults with HIV has fallen dramatically since antiretroviral therapy was first introduced [2, 3]. Those who start treatment soon after diagnosis and engage with care now have life expectancy close to that of the general population [4–8].

Alongside this huge advance, though, epidemiological evidence suggests that people living with HIV (PLHIV) have a higher prevalence of some comorbidities compared with people who are not infected; these include cardiovascular, renal, gastrointestinal and mental health disorders as well as some malignancies [8–12]. A US-based study of Medicare patients during 2000–2016 describes increasing numbers of comorbidity–HIV associations over the period examined [12].

There is little information on comorbid conditions afflicting PLHIV in the UK. The 2020 HIV Commission report [13] noted that ‘multi-morbidity is increasingly an important matter’ for PLHIV and that ‘non-clinical complexity including factors such as use of social care, poverty, insecure housing or migrant status can also affect treatment and care needs’. [13] But the report provides no data on the nature of the comorbidities or on factors such as deprivation, even though mortality from cardiometabolic disease, stroke and liver disease is higher among PLHIV than in the general population [8, 9, 13]. Similarly, the King’s Fund report on the future of HIV services in England acknowledged that ‘as people with HIV live into older age, they are likely to develop additional long-term medical problems (comorbidities)’ but included no data on comorbidities or their potential impact upon healthcare provision [14].

With the objective of providing insight into the demographics and prevalence of comorbidity among PLHIV in England, we conducted a cross-sectional population-based study using data from a nationally representative linked primary care database, examining 304 health conditions.

## METHODS

### Study population, data sources and study design

In England, almost all healthcare is coordinated through primary care where general practitioners (GPs) refer patients to specialist secondary care. HIV differs in that PLHIV can access specialist services directly without GP referral, and treatment is coordinated through the specialist centres for the lifetime of the patient. Non-HIV care, including referrals for associated secondary care needs, is still provided via GPs.

In order to examine comorbidities among PLHIV, we interrogated the database of de-identified primary care records maintained by Clinical Practice Research Data-link (CPRD) within the UK Department of Health and Social Services [15]. Data from the CPRD GOLD database include information on diagnoses, symptoms, prescriptions, referrals and tests. Covering some 7% of the UK population, the data are broadly representative of the whole population in terms of age, gender, and ethnicity [16]. General practices contributing data to CPRD GOLD do so voluntarily; practices using the Vision Electronic Health Record system for CPRD GOLD have fallen and the numbers and geographic distribution of contributing practices change over time.

We conducted a cross-sectional analysis of data for adults aged 18 years and over, alive and registered within CPRD GOLD at 30 November 2008 and 30 November 2015 (index dates). All patients were required to be from practices contributing data of research quality and have at least 2 years of observation prior to the index date. Additional data were provided through CPRD-conducted linkage with the UK national disease-specific death registry and Index of Multiple Deprivation (IMD) from the Office of National Statistics (ONS) and with Hospital Episodes Statistics (HES) [15]. The IMD, the official measure of relative deprivation in England, combines information from seven domain indices which measure different dimensions of deprivation (income; employment; education, skills and training; health and disability; crime;

barriers to housing and services; and living environment) to produce an overall relative measure of deprivation at small local area level in England, classified into five quintiles [17]. HES provide information on diagnoses and medical procedures related to all elective and emergency hospital admissions across all National Health Service (NHS) hospitals in England [15].

Study approval was granted by the Independent Scientific Advisory Committee of the Medicines and Healthcare products Regulatory Agency (Protocol 15\_199RA2R).

## Statistical analysis

### HIV cases

People with HIV were defined based on a coded diagnosis or record of a positive HIV test in CPRD GOLD or coded diagnosis in HES at any point during the study period (Tables C1 and C2).

### Comorbid health conditions

We examined the presence of 304 adult physical and mental health conditions previously identified using CPRD data as involving intensive use of healthcare resources and/or distinct pathological pathways [18, 19]. Conditions were measured individually and after grouping related conditions into 47 higher-level 'condition groups' of which 36 were non-communicable and 11 were communicable infectious condition groups. Conditions were defined using either *International Classification of Disease* [tenth revision (ICD-10)] codes recorded in HES or Read codes recorded within primary care (Tables C1 and C2). Algorithms defining these conditions were based on diagnosis or procedural codes recorded at any point prior to the index date.

Chronic kidney disease (CKD) was additionally defined by the inclusion of blood test values, when available, calculated as having an estimated glomerular filtration rate of less than 60 mL/min/1.73m<sup>2</sup> and using the most recent blood test value prior to index date.

For the condition group of lipid disorders, the prevalence for each cohort was based on having a CPRD record of lipid disorder. In the statistical analyses, we included only individuals with blood test values available, using the most recent prior to index date. The following cut-offs were used to define abnormal lipids: total cholesterol (TC) > 5 mmol/L; low-density lipoprotein cholesterol (LDL-C) > 3 mmol/L; triglycerides (TG) > 2.3 mmol/L; and high-density lipoprotein cholesterol (HDL-C) < 1 mmol/L.

## Analyses and reporting

We determined the prevalence of each health condition, or condition group, among the 2015 and 2008 cross-sections of PLHIV. For the analyses, we used logistic regression performed using the generalized linear model (GLM) function in the statistical package, R [20, 21]. We calculated crude and adjusted odds ratios (OR) for the likelihood of each health condition, or condition group, in 2015 compared with 2008, adjusting for age, gender and index of multiple deprivation.

In reporting this work, we have adhered to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for cross-sectional studies [22].

## RESULTS

### Demographics

In the 2008 cross-section cohort, 1987 patients registered in the CPRD dataset had a diagnosis of HIV (mean per practice = 6.5); in 2015, there were 964 patients (mean per practice = 6.8). Male and female proportions were the same in both cohorts: 62% male, 38% female (Table 1). Older ( $\geq 45$  years) versus younger ( $< 45$  years) demographic patterns changed substantially. In 2008, 3.7% of the cohort were aged 18–24 years and 61.2% were aged 25–44 years, compared with 2% and 39.7%, respectively, in 2015 [% difference:  $-1.7$ , (95% confidence interval, 95% CI:  $-3.2$  to  $0.2$ ) and  $-21.5$  ( $-26.7$  to  $-16.2$ ), respectively].

Among older patients, in 2008, 31.8% were aged 45–64 years and 3.2% were aged 65–84 years. By 2015, 51.1% were aged 45–64 years and 7.2% were aged 65–84 years [% difference:  $19.3$  (95% CI:  $14.2$ – $24.5$ ) and  $4.0$  (95% CI:  $1.6$ – $6.5$ ) respectively].

Levels of deprivation increased markedly (Table 1). In 2008, 5.8% of the cohort were in IMD quintile 4 and 6.6% were in quintile 5, as compared with 23.9% and 28.7%, respectively in 2015 [% difference: quintile 4,  $18.1$  (95% CI:  $14.4$ – $21.9$ ); quintile 5,  $22.1$  (95% CI:  $18.2$ – $26.1$ )].

### Condition groups

Among the 47 higher-level condition groups, 36 were non-communicable conditions and 11 were communicable infectious conditions.

Following adjustment for age, sex and deprivation, seven (19%) of the 36 non-communicable condition groups were significantly more likely among PLHIV in 2015 compared with 2008, two (6%) were significantly less likely, and 27 (75%) had similar likelihood in both cohorts (Table 2). Prevalence exceeded 10% of the 2015

**TABLE 1** Cohort demographics describing sex, age group, and index of multiple deprivation quintiles of the 2008 and 2015 people living with HIV (PLHIV) cohorts

Category	PLHIV in 2008 [ <i>n</i> (%)] ( <i>N</i> = 1987)	PLHIV in 2015, [ <i>n</i> (%)] ( <i>N</i> = 964)	Percentage difference (95% CI)
Sex			
Male	1225 (61.7)	595 (61.7)	0.0 (−5.2 to 5.2)
Female	762 (38.3)	369 (38.3)	0.0 (−5.2 to 5.2)
Age group (years)			
18–24	73 (3.7)	19 (2)	−1.7 (−3.3 to 0.2)
25–44	1217 (61.2)	383 (39.7)	−21.5 (−26.7 to −16.2)
45–64	631 (31.8)	493 (51.1)	19.3 (14.2 to 24.5)
65–84	64 (3.2)	69 (7.2)	4.0 (1.6 to 6.5)
85 and over	2 (0.1)	0 (0)	−0.1 (−0.4 to 0.4)
Deprivation (quintiles)			
Q1 (least deprived)	389 (19.6)	143 (14.8)	−4.8 (−8.7 to −0.7)
Q2	775 (39)	137 (14.2)	−24.8 (−29.0 to −20.3)
Q3	577 (29)	177 (18.4)	−10.6 (−15.1 to −6.2)
Q4	115 (5.8)	230 (23.9)	18.1 (14.4 to 21.9)
Q5 (most deprived)	131 (6.6)	277 (28.7)	22.1 (18.2 to 26.1)

Abbreviations: CI, confidence interval; Q, quintile.

cohort for 12 (33%) of the condition groups (Figure 1). Tables S1–S9 and Figures S1–S9 show the individual conditions included in each higher-level condition group.

### Non-communicable condition groups with higher likelihood in 2015

The non-communicable condition groups with higher likelihood in 2015 compared with 2008 were gastrointestinal (GI) conditions [OR = 1.28 (95% CI: 1.04–1.58)], eyes/ears/nose/throat (ENT) conditions [OR = 1.31 (1.08–1.59)], genito-urinary-gynaecological (GU) conditions [OR = 1.44 (1.18–1.76)], dermatology conditions [OR = 1.55 (1.29–1.85)], rheumatology conditions [OR = 1.64 (1.30–2.07)], endocrine-obesity [OR = 1.75 (1.12–2.77)] and renal-CKD (chronic kidney disease) [OR = 1.96 (1.33–2.90)] (Table 2; Figure 2).

Five of these condition groups were highly prevalent. Rheumatology conditions affected 22.1% of PLHIV in 2015 compared with 11.9% in 2008; for GU conditions the figures were 30.4% versus 19.5%; for ENT conditions, 30% versus 22.1%; and for dermatological conditions, 39% versus 29.5% (Figure 1; Table 2). Renal-CKD and endocrine-obesity conditions were less prevalent, affecting 9.4% and 5% of the 2015 cohort, respectively.

### Non-communicable condition groups with lower likelihood in 2015

Two condition groups were less likely in 2015 than in 2008: endocrine-diabetes [OR = 0.49 (0.34–0.70)] (Table 2; Figure 2) and respiratory-chronic obstructive airways disease (COPD) [OR = 0.36 (0.19–0.69)]. In both cases, prevalence in 2015 was < 10% (Figure 1).

### Non-communicable condition groups with similar likelihood

For the remaining 27 condition groups, their likelihood was no different among the 2015 cohort compared with 2008 (Figure 2). For eight groups (30%), their prevalence exceeded 10% of PLHIV in 2015 (Table 2; Figure 1).

### Individual non-communicable health conditions

#### Cardiovascular and lipid disorder groups

The cardiovascular-ischaemic (CVS-ischaemic) condition group [OR = 1.33 (0.94–1.87)] included atrial fibrillation, heart failure, myocardial infarction, stroke, transient

**TABLE 2** Prevalence and odds ratios (ORs) for non-communicable condition groups among people living with HIV (PLHIV) in 2015 compared with 2008. The orange shading shows the seven condition groups with higher likelihood among the 2015 cohort compared with the 2008 cohort in ascending order according to the point estimate of the adjusted OR. The green shading shows the two condition groups that were less likely in 2015. Twenty-seven non-communicable condition groups that did not differ in likelihood across the cohorts are presented in ascending order according to the point estimate of the adjusted OR. Details of the individual conditions included in each condition group and their 2015 versus 2008 comparisons are shown in Tables S1–S9

<b>Health condition group: Non-communicable conditions</b>	<b>PLHIV in 2008, [n (%)] (N = 1987)</b>	<b>PLHIV in 2015, [n (%)] (N = 964)</b>	<b>OR, unadjusted (95% CI)</b>	<b>OR, adjusted for age, gender and IMD (95% CI)</b>
Gastrointestinal	360 (18.1)	234 (24.3)	1.45 (1.20–1.74)	1.28 (1.04–1.58)
Eye-ENT	440 (22.1)	289 (30)	1.51 (1.26–1.79)	1.31 (1.08–1.59)
GU-gynaecological	388 (19.5)	293 (30.4)	1.80 (1.51–2.15)	1.44 (1.18–1.76)
Dermatology	586 (29.5)	376 (39)	1.53 (1.30–1.80)	1.55 (1.29–1.85)
Rheumatology	236 (11.9)	213 (22.1)	2.10 (1.72–2.58)	1.64 (1.30–2.07)
Endocrine-obesity	48 (2.4)	48 (5)	2.12 (1.41–3.19)	1.76 (1.12–2.77)
Renal-CKD	59 (3)	91 (9.4)	3.41 (2.44–4.79)	1.96 (1.33–2.90)
Respiratory-COPD	39 (2)	18 (1.9)	0.95 (0.53–1.65)	0.36 (0.19–0.69)
Endocrine-diabetes	147 (7.4)	58 (6)	0.80 (0.58–1.09)	0.49 (0.34–0.70)
CNS-haemorrhage	12 (0.6)	<5 (<0.5)	0.51 (0.12–1.62)	0.33 (0.07–1.21)
Malignancy-other	69 (3.5)	30 (3.1)	0.89 (0.57–1.37)	0.62 (0.38–1.01)
Immune (immunodeficiency/ gammopathy)	24 (1.2)	12 (1.2)	1.03 (0.50–2.03)	0.67 (0.30–1.44)
Cardiovascular-VTE	61 (3.1)	33 (3.4)	1.12 (0.72–1.71)	0.78 (0.48–1.26)
Malignancy-breast	8 (0.4)	< 5 (< 0.5)	1.29 (0.39–3.88)	0.79 (0.21–2.85)
Lipid <sup>a</sup>	363 (18.3)	399 (41.4)	0.81 (0.62–1.06) <sup>a</sup>	0.80 (0.60–1.07) <sup>a</sup>
CNS-peripheral	134 (6.7)	66 (6.8)	1.02 (0.75–1.37)	0.82 (0.58–1.14)
Respiratory-asthma	250 (12.6)	104 (10.8)	0.84 (0.66–1.07)	0.83 (0.63–1.08)
Haematology-acquired	326 (16.4)	157 (16.3)	0.99 (0.80–1.22)	0.83 (0.66–1.05)
Respiratory-other	97 (4.9)	47 (4.9)	1.00 (0.69–1.42)	0.88 (0.58–1.30)
Renal-other	47 (2.4)	28 (2.9)	1.23 (0.76–1.97)	0.94 (0.55–1.59)
Cardiovascular-other	40 (2)	30 (3.1)	1.56 (0.96–2.52)	1.01 (0.58–1.74)
CNS-psychiatry	668 (33.6)	357 (37)	1.16 (0.99–1.36)	1.06 (0.88–1.27)
Malignancy-haematology	44 (2.2)	28 (2.9)	1.32 (0.81–2.12)	1.08 (0.62–1.85)
Haematology-inherited	43 (2.2)	24 (2.5)	1.15 (0.69–1.90)	1.11 (0.62–1.94)
CNS-other	165 (8.3)	99 (10.3)	1.26 (0.97–1.64)	1.11 (0.82–1.48)
Bone-joint	137 (6.9)	100 (10.4)	1.56 (1.19–2.05)	1.15 (0.84–1.57)
Cardiovascular- hypertension	214 (10.8)	184 (19.1)	1.95 (1.58–2.42)	1.15 (0.90–1.48)
CNS-neurological	136 (6.8)	80 (8.3)	1.23 (0.92–1.64)	1.19 (0.86–1.64)
Endocrine-other	57 (2.9)	38 (3.9)	1.39 (0.91–2.10)	1.24 (0.78–1.95)
Benign neoplasms	137 (6.9)	91 (9.4)	1.41 (1.06–1.85)	1.27 (0.92–1.75)
Gastrointestinal-surgical	236 (11.9)	146 (15.1)	1.32 (1.06–1.65)	1.27 (0.99–1.63)
Cardiovascular- ischaemic	97 (4.9)	96 (10)	2.15 (1.61–2.89)	1.33 (0.94–1.87)
Malignancy-respiratory	< 5 (< 0.5)	< 5 (< 0.5)	2.07 (0.49–8.75)	1.34 (0.27–6.48)
Liver	39 (2)	26 (2.7)	1.38 (0.83–2.28)	1.34 (0.76–2.31)
Malignancy-GI	15 (0.8)	16 (1.7)	2.22 (1.09–4.55)	1.51 (0.67–3.41)

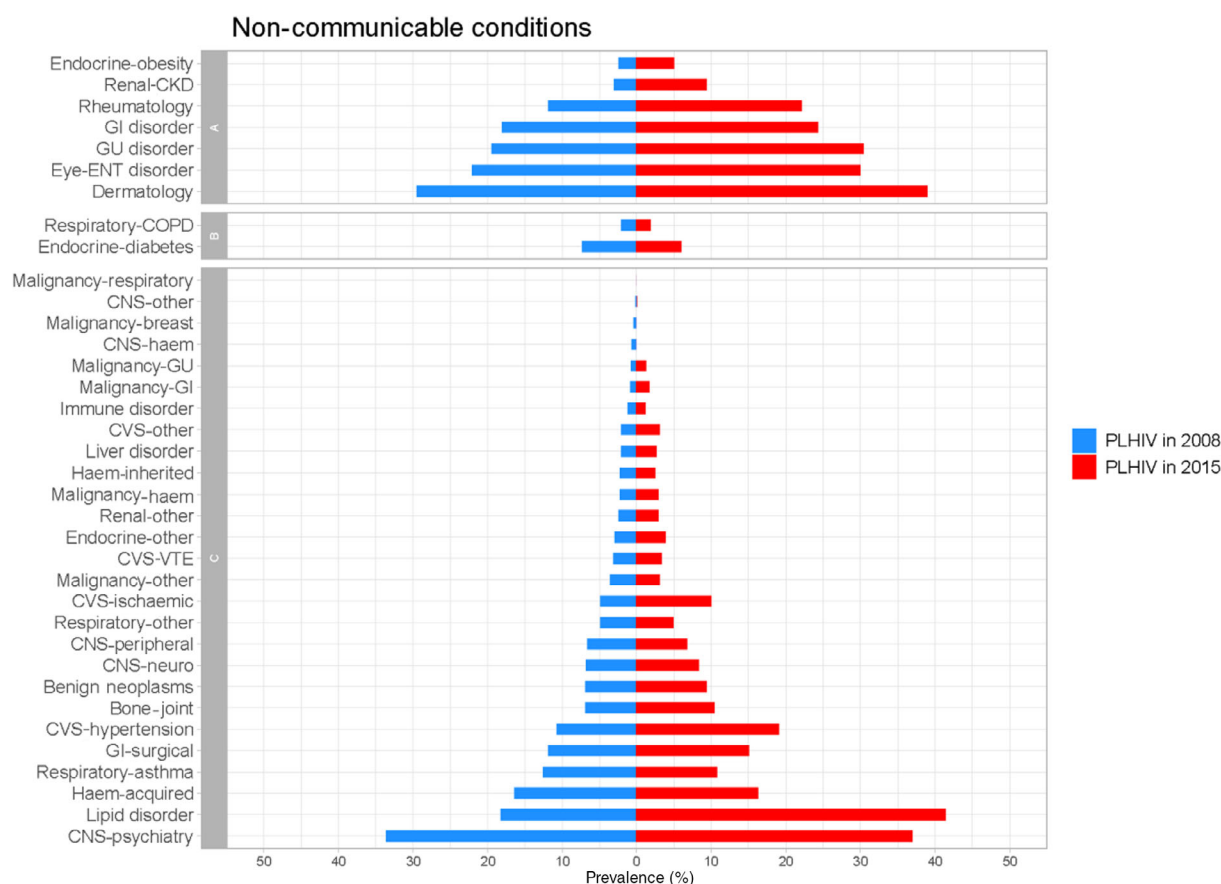
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TABLE 2 (Continued)

Health condition group: Non-communicable conditions	PLHIV in 2008, [n (%)] (N = 1987)	PLHIV in 2015, [n (%)] (N = 964)	OR, unadjusted (95% CI)	OR, adjusted for age, gender and IMD (95% CI)
Malignancy-GU	13 (0.7)	13 (1.3)	2.08 (0.95–4.54)	2.15 (0.85–5.45)

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; ENT, ears, nose and throat; GI, gastro-intestinal; GU, genito-urinary; IMD, Index of Multiple Deprivation; VTE, venous thromboembolism.

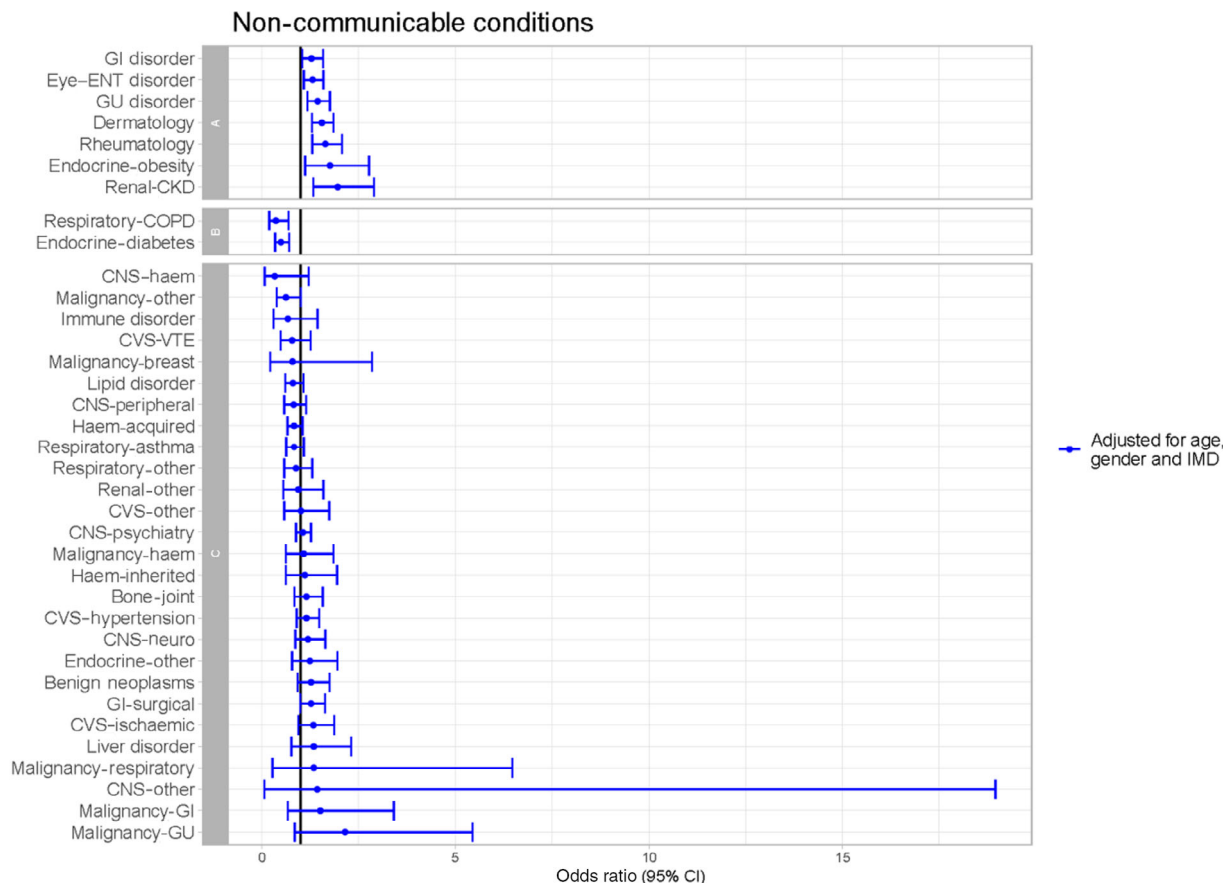
<sup>a</sup>Lipid disorder: prevalence was based on having a Clinical Practice Research Datalink (CPRD) record of a lipid disorder; the OR calculation was based on lipid blood test values, where available, using the most recent test value prior to index date.



**FIGURE 1** Prevalence of non-communicable condition groups among people living with HIV (PLHIV) in 2015 compared with 2008. The top panel illustrates prevalence of the seven condition groups with higher likelihood in 2015; the middle panel illustrates the two conditions with lower likelihood; the bottom panel illustrates the 27 conditions with no difference in likelihood. CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CNS, central nervous system; CVS, cardiovascular system; ENT, ears, nose and throat; GI, gastro-intestinal; GU, genitourinary-gynaecological; VTE, venous thromboembolism; 95% CI, 95% confidence interval

ischaeamic attack, peripheral arterial disease and coronary heart disease not-otherwise-specified (Table S1; Figure S1). Among these conditions, only peripheral arterial disease was more likely in 2015 than in 2008 [OR = 4.02 (1.54–11.91); prevalence, 1.8% vs. 0.3%]. Hypertension was common and prevalence increased, affecting 19.1% of the 2015 cohort compared with 10.8% in 2008; following adjustment for age, sex and deprivation, however, there was no between-cohort difference in likelihood [OR = 1.15 (0.90–1.48)].

Lipid disorders were also common, recorded for 41.4% of PLHIV in 2015 and 18.3% in 2008. For the statistical analyses, which were based only on laboratory results, where these were available, and the stated parameters, there was no between-cohort likelihood difference [OR = 0.80 (0.60–1.07)]. Among the individual lipid components though, both low HDL and raised triglycerides were less likely in 2015 than in 2008 [OR = 0.61 (0.45–0.84) and 0.57 (0.41–0.81), respectively] (Table S1; Figure S1).



**FIGURE 2** Odds ratios (ORs) of non-communicable condition groups among people living with HIV (PLHIV) in 2015 compared with 2008. The top panel illustrates ORs of the seven condition groups with higher likelihood in 2015; the middle panel illustrates the two conditions with lower likelihood; the bottom panel illustrates the 27 conditions with no difference in likelihood. CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CNS, central nervous system; CVS, cardiovascular system; ENT, ears, nose and throat; GI, gastro-intestinal; GU, genito-urinary-gynaecological; IMD, index of multiple deprivation; VTE, venous thromboembolism; 95% CI, 95% confidence interval. The lipid disorder OR calculation was based on lipid blood test values, where available, using the most recent test value prior to index date

## Rheumatological and bone-joint groups

Within the rheumatology condition group, the commonest condition, ‘enthesopathies and synovial disorders’, affected 15.1% of PLHIV in 2015 compared with 7.5% in 2008 [OR = 1.75 (1.33–2.31)], followed by carpal tunnel syndrome (2.8% vs. 1.3%) [OR = 1.64 (0.87–3.09)] and gout (2.6% vs. 1%) [OR = 2.01 (1.05–3.89)] (Table S2; Figure S2).

Among six conditions in the bone-joint group, only osteoporosis was more likely in 2015 than in 2008 [OR = 2.04 (1.00–4.21); prevalence 2.6% vs. 0.9%]; osteoarthritis affected 4.4% in the 2015 cohort compared with 2.4% in 2008 [OR = 0.98 (0.60–1.57)].

## Respiratory, renal and endocrine groups

Among respiratory condition groups, asthma was common, diagnosed in 10.8% of the 2015 cohort compared

with 12.6% in 2008 [OR = 0.83 (0.63–1.08)] (Table S3; Figure S3). Chronic obstructive pulmonary disease (COPD) was uncommon, affecting 1.9% in 2015 and, adjusted for age, sex and deprivation, was less likely compared with 2008 [OR = 0.36 (0.19–0.69)].

In the renal-other group, acute kidney injury was the most prevalent condition, reported in 1.6% (2015) and 1.3% (2008) [OR = 0.96 (0.46–1.94)]. In the endocrine-diabetes group, type 2 diabetes (T2DM) was the commonest condition and prevalence was lower in 2015 than in 2008 [5.2% vs. 6.2%; OR = 0.48 (0.32–0.69)] (Table S3; Figure S3).

## GI, liver, GU and gynaecological conditions

Among GI conditions, overall more likely among PLHIV in 2015 than in 2008, the most prevalent were gastro-oesophageal reflux disease [8.3% vs. 5.4%; OR = 1.32



(0.94–1.85)], irritable bowel syndrome [5.1% vs. 3.6%; OR = 1.30 (0.86–1.97)] and oesophagitis/oesophageal ulceration [8.4% vs. 4.5%; OR = 1.63 (1.14–2.32)] (Table S4; Figure S4). Gastritis/duodenitis was less likely in the 2015 cohort [6.3% vs. 7.4%, OR = 0.70 (0.49–0.98)].

Gastrointestinal-surgical conditions afflicted 11.9% of the 2015 cohort and 15.1% in 2008 [OR = 1.27 (0.99–1.63)]. Appendicitis was the commonest condition [7% in 2015 vs. 6.2% in 2008; OR = 1.05 (0.75–1.48)]. Both anal fissures [3.1% vs. 5.4%; OR = 1.98 (1.30–3.02)] and anorectal fistulae [1.4% vs. 2.8%; OR = 2.02 (1.13–3.61)] had higher likelihood in 2015.

Liver disorders were stable across the study period (Table 2; Figure 2); the commonest condition was ‘liver fibrosis, sclerosis and cirrhosis’, affecting 1.6% in 2015 and 1.1% in 2008 [OR = 1.13 (0.54–2.33)] (Table S4; Figure S4).

Genito-urinary-gynaecological conditions increased substantially, prevalence reaching 30.4% in 2015 compared with 19.5% in 2008 [OR = 1.44 (1.18–1.76)] (Table 2; Figure 2). The commonest conditions were erectile dysfunction [11.2% in 2015 vs. 6.8% in 2008; OR = 1.98 (1.59–2.46)] and menorrhagia/poly-menorrhoea [7.7% vs. 5.1%; OR = 1.56 (1.08–2.25)]. Infertility increased (3% in 2015) with higher likelihood among males in 2015 versus 2008 [OR = 2.34 (1.27–4.36)] but not among females [OR = 1.60 (0.89–2.85)] (Table S4; Figure S4).

## Ear, nose and throat (ENT) and dermatology conditions

Both ENT and dermatology condition groups more likely among PLHIV in 2015. The commonest ENT condition was ‘allergic and chronic rhinitis’ which affected 15.9% of the 2015 cohort [OR = 1.33 (1.03–1.70)] followed by hearing loss [4.9%; OR = 1.03 (0.68–1.56)] and chronic sinusitis [4.6%; OR = 1.06 (0.68–1.62)] (Table S5; Figure S5).

In the dermatology condition group, dermatitis [23.9% in 2015 vs. 16.8% in 2008; OR = 1.53 (1.24–1.90)] and acne [9.2% vs. 7.4%; OR = 1.61 (1.17–2.20)] dominated.

## Central nervous system (CNS)-related conditions

The CNS-neurological condition group included autoimmune disorders, epilepsy, migraine and Parkinson's disease; only migraine was more likely in 2015 [6.2% vs. 4% in 2008; OR = 1.77 (1.20–2.60)] (Table S6; Figure S6).

Central nervous system-psychiatric conditions were common, affecting over one-third of both cohorts. The commonest individual conditions were depression [27.1% in 2015 vs. 24.8% in 2008; OR = 1.03 (0.85–1.25)], anxiety disorders [15.7% vs. 12.1%; OR = 1.19 (0.93–1.52)] and alcohol problems [4% vs. 5.3%; OR = 1.27 (0.90–1.80)].

## Benign neoplasm and malignancy groups

Among benign neoplasms, categorized in CPRD GOLD according to anatomic systems, only ‘benign neoplasms of colon, rectum, anus and anal canal’ were more likely in 2015 [OR = 2.45 (1.33–4.54)], diagnosed in 3.2% of PLHIV compared with 1.2% in 2008 (Table S7; Figure S7). Cervical intraepithelial neoplasia affected 3.5% of the 2015 cohort versus 4.5% in 2008 [OR = 0.71 (0.45–1.12)].

There were no between-cohort differences in the likelihood of malignancy condition groups. Among individual malignant conditions, non-Hodgkin's lymphoma was the most prevalent, diagnosed among 2.3% of PLHIV in 2015 and 1.4% in 2008 [OR = 1.58 (0.83–2.97)].

## Haematological groups

The haematological-acquired condition group included multiple anaemic conditions that were similarly prevalent in both cohorts; iron deficiency anaemia affected 4.1% in 2015 versus 3.4% in 2008 [OR = 1.01 (0.64–1.58)] while other (unspecified) anaemias were less likely in 2015, diagnosed in 6.3% versus 9.5% in 2008 [OR = 0.54 (0.39–0.75)] (Table S8; Figure S8). The haematological-inherited group mainly included individuals with sickle cell trait, which affected 1.5% in PLHIV in 2015 versus 1.7% in 2008 [OR = 0.85 (0.41–1.68)].

## Communicable diseases – infectious condition groups

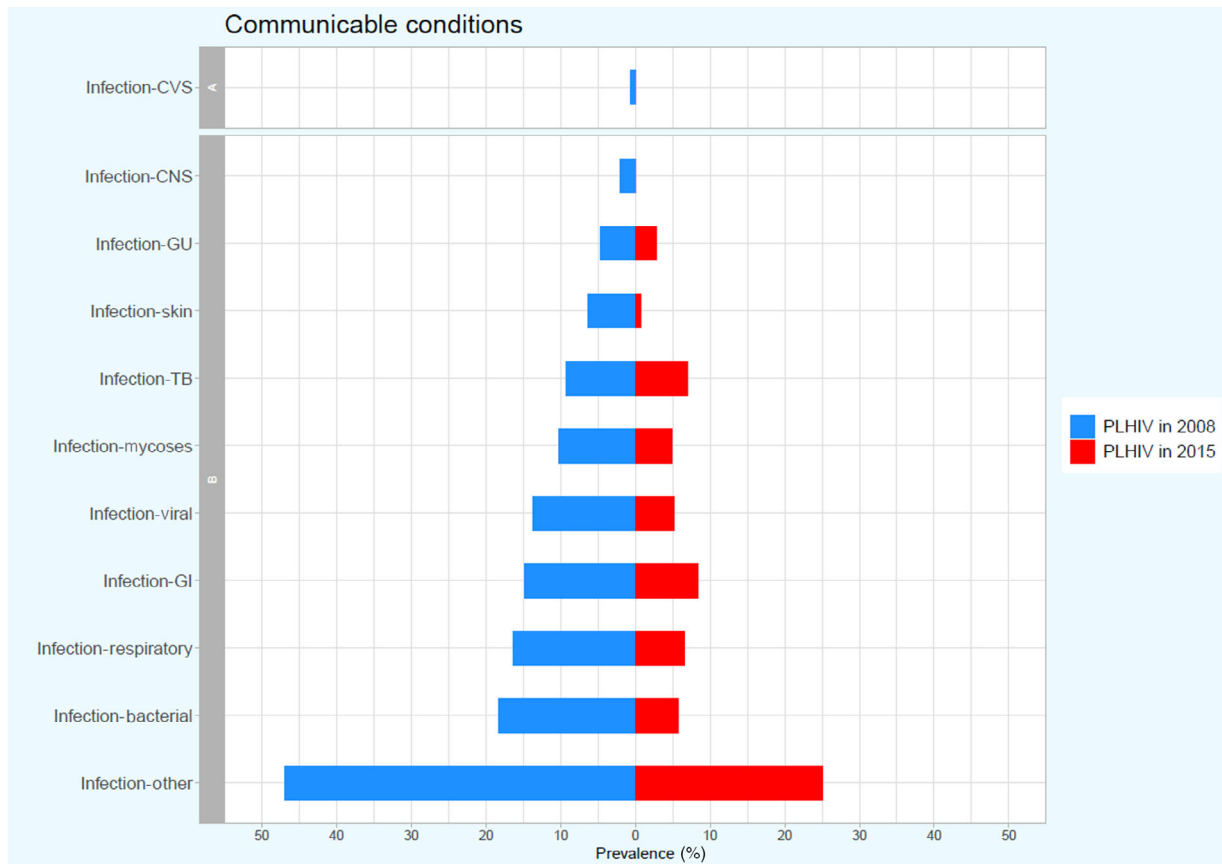
Among 11 communicable infectious condition groups, prevalence and likelihood of 10 (91%) groups were considerably lower in 2015 than in 2008 (Table 3; Figures 3, 4).

Both infections-skin, described in CPRD records as ‘infection of skin and subcutaneous tissues’ [OR = 0.12 (0.05–0.24)] and infections-CNS, which included meningitis and ‘other nervous system infections’ [OR = 0.21 (0.07–0.52)] affected very small proportions of the 2015 cohort (0.8% and < 0.5%, respectively) (Table S9; Figure S9).

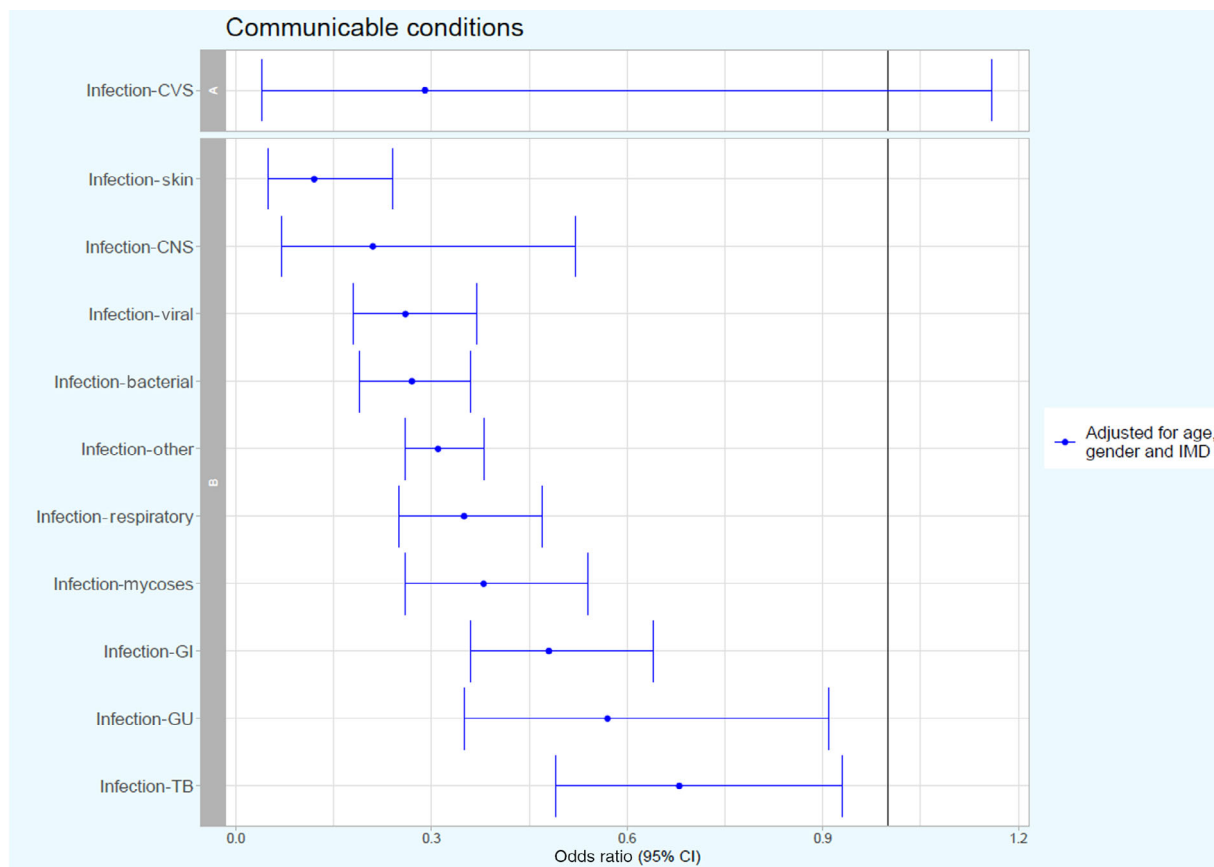
**TABLE 3** Communicable (infectious) condition groups among people living with HIV (PLHIV) in 2015 compared with 2008. The green shading shows infection groups that were less likely among the 2015 cohort than among the 2008 cohort; the grey shading shows the single group with no difference. Details of infections included in each group are shown in the supplementary tables

Health condition group: communicable conditions	PLHIV in 2008 [n (%)] (N = 1987)	PLHIV in 2015 [n (%)] (N = 964)	OR, unadjusted (95% CI)	OR, adjusted for age, gender and IMD (95% CI)
Infection-skin	126 (6.3)	8 (0.8)	0.12 (0.06–0.24)	0.12 (0.05–0.24)
Infection-CNS	42 (2.1)	< 5 individuals	0.24 (0.08–0.56)	0.21 (0.07–0.52)
Infection-viral	272 (13.7)	50 (5.2)	0.34 (0.25–0.47)	0.26 (0.18–0.37)
Infection-bacterial	363 (18.3)	55 (5.7)	0.27 (0.20–0.36)	0.27 (0.19–0.36)
Infection-other	931 (46.9)	241 (25)	0.38 (0.32–0.45)	0.31 (0.26–0.38)
Infection-respiratory	326 (16.4)	64 (6.6)	0.36 (0.27–0.48)	0.35 (0.25–0.47)
Infection-mycoses	205 (10.3)	47 (4.9)	0.45 (0.32–0.61)	0.38 (0.26–0.54)
Infection-gastrointestinal	294 (14.8)	81 (8.4)	0.53 (0.41–0.68)	0.48 (0.36–0.64)
Infection-genitourinary	94 (4.7)	27 (2.8)	0.58 (0.37–0.88)	0.57 (0.35–0.91)
Infection-tuberculosis	184 (9.3)	67 (7)	0.73 (0.54–0.97)	0.68 (0.49–0.93)
Infection-cardiovascular	12 (0.6)	< 5 individuals	0.34 (0.05–1.26)	0.29 (0.04–1.16)

Note: Infection-other refers to infection of bones/joints, parasitic, of unspecified organs, with unspecified organisms, septicaemia. Abbreviations: CI, confidence interval; CNS, central nervous system; IMD, Index of Multiple Deprivation; OR, odds ratio.



**FIGURE 3** Prevalence of communicable condition groups among people living with HIV (PLHIV) in 2015 compared with 2008. The top panel illustrates prevalence of the single condition group with no difference in likelihood between the two cohorts; the lower panel illustrates prevalence of the communicable condition groups with lower likelihood among the 2015 cohort compared with the 2008 cohort. CNS, central nervous system; CVS, cardiovascular system; GI, gastrointestinal; GU, genitourinary-gynaecological; TB, tuberculosis; infection-other, infection of bones/joints, of unspecified organs, with unspecified organisms, parasitic infection, septicaemia



**FIGURE 4** Odds ratios of communicable disease condition groups among people living with HIV (PLHIV) in 2015 compared with 2008. The top panel illustrates the single condition group with no difference in likelihood between the two cohorts; the lower panel illustrates the communicable condition groups with lower likelihood among the 2015 cohort compared with the 2008 cohort. CNS, central nervous system; CVS, cardiovascular system; GI, gastrointestinal; GU, genito-urinary-gynaecological; TB, tuberculosis; Infection-other, infection of bones/joints, of unspecified organs, with unspecified organisms, parasitic infection, septicaemia

'Infections-viral' [OR = 0.26 (0.18–0.37)] excluded chronic hepatitis and affected 5.2% in 2015 compared with 13.7% in 2008. Infections-bacterial [OR = 0.27 (0.19–0.36)] excluded tuberculosis infections; prevalence was 5.7% in 2015 versus 18.3% in 2008. Infections-other were unspecified except for infections of bone and joint [OR = 0.98 (0.21–3.50; affecting < 0.5% in 2015 and 0.5% in 2008], parasitic infections [OR = 0.32 (0.15–0.61; 1.1% vs. 3.2%) and septicaemia [OR = 0.03 (0.00–0.13); < 0.5% vs. 2.8%]. (Table S9; Figure S9).

The infection-respiratory group [OR = 0.35 [0.25–0.47]; 6.6% in 2015 vs. 16.4% in 2008] comprised mainly unspecified infections affecting the lower respiratory tract. In the infection-mycoses group, individual mycoses were not named.

Infection-GI [OR = 0.48 (0.36–0.64)] included chronic viral hepatitis [OR = 0.69 (0.47–0.98); prevalence 4.9% in 2015 vs. 7.6% in 2008] and ano-rectal infections [OR = 0.41 (0.23–0.71); 1.9% vs. 3.5%].

The infection-GU condition group [OR = 0.57 (0.35–0.91); 2.7% in 2015 vs. 4.8% in 2008] included mostly urinary tract infections (Table S9; Figure S9).

Tuberculosis affected 7% of the 2015 cohort compared with 9.3% in 2008 [OR = 0.68 (0.49–0.93)].

## DISCUSSION

This in-depth cross-sectional examination of 304 comorbid conditions among PLHIV in England has findings not previously reported in a UK PLHIV cohort. Firstly, deprivation levels rose markedly between 2008 and 2015. Secondly, in the same period, the age distribution of PLHIV changed, youth dominance giving way to an older majority. Thirdly, comorbid non-communicable conditions became increasingly likely with the passage of time; seven of 36 condition groups were more likely in 2015 than in 2008 but only two were less likely. Together, the findings point to mounting challenges for HIV care provision in England.

A positive finding, confirming HIV care achievements, was that comorbid infectious communicable conditions, including those associated with HIV infection such as chronic viral hepatitis, mycoses and tuberculosis, were significantly less likely in 2015 than in 2008.

The increase in deprivation was remarkable. In 2008, the two highest deprivation quintiles together included 12.4% of the PLHIV cohort; by 2015, they included 52.6%. This extraordinary change in the circumstances of PLHIV in the UK has not been recognized to date, most likely because deprivation information is not reported in annual public health HIV epidemiology data [2]. Although greater levels of deprivation among PLHIV compared with the general population are widely acknowledged [9], we are not aware of studies demonstrating rising deprivation within the PLHIV population. Coupled with the increased age of the 2015 cohort, this raises the possibility that as PLHIV grow older, and age-related non-communicable conditions arise, increase or become more severe, employment opportunities and economic status suffer, reflected in higher deprivation levels across the cohort as a whole. Lending support to this view, PLHIV who died of COVID-19 were more likely than the general population to live in more deprived geographical areas [23]. Moreover, socio-economic disadvantage has been associated with poorer HIV treatment outcomes, and the UNAIDS strategy for 2021–25 has highlighted the necessity for societal enabler programmes in ‘ending AIDS as a public health threat’ [24, 25]. In an examination of data over 16 years, 2004–2019, multimorbidity, comprising two or more chronic conditions, increased with increasing deprivation in the CPRD population as a whole.[26]

In 2008, approximately one-third (35%) of PLHIV were 45 years or older. The proportion climbed to well over half (58.3%) of the cohort by 2015. This may reflect a care achievement, durable long-term control of HIV. Neither CPRD nor public health data categorize according to the numbers of years since HIV diagnosis to help confirm or refute the idea.

Falling proportions of younger PLHIV may signify the success of public health measures such as access to sexual healthcare, vaccination against hepatitis B virus (HBV) infection and risk-awareness campaigns.[2,27] In recent years, the availability of both pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) is likely to have contributed to ongoing reductions in the annual numbers of new diagnoses.

### **Comorbid non-communicable conditions**

Of seven condition groups significantly more likely in 2015 compared with 2008, five groups (rheumatology, dermatology, genito-urinary-gynaecological, eye/ENT and gastro-intestinal conditions) affected one-fifth to one-third of the 2015 cohort, prevalence in each case having increased in absolute terms by 6–10% from 2008. We

were careful when combining individual conditions into higher-level groups not to double-count individuals with more than one condition in a given group; these substantial increases in already prevalent conditions highlight the necessity for future care capacity planning for PLHIV. Furthermore, as HIV is managed at secondary/tertiary care level in England and most of the comorbid conditions in these five groups are managed mainly in community-based primary care, effective communications between care providers are critical, for example, in knowing if new medicines prescribed are likely to interact with HIV drugs. The potential for polypharmacy-associated drug interactions among PLHIV is high, with older patients being at greatest risk [28,29].

The increased prevalence of obesity, affecting 5% of the 2015 cohort, mirrored overall population epidemiology. Unexpectedly, type 2 diabetes was less prevalent, given higher proportions of older people in 2015.

Most non-communicable condition groups examined were similarly prevalent in 2008 and 2015. Several are notable for the substantial proportions of PLHIV affected, thereby having implications for healthcare provision. Over one-third of both cohorts had a CNS psychiatric condition, mainly depression or anxiety disorders; among cardiovascular and related condition groups, hypertension and lipid disorders were commonest, followed by cardiovascular ischaemic diagnoses. As we did not have information on individual accumulation over time of comorbid conditions, progression of conditions or severity, this does not imply that care needs remained stable between 2008 and 2015.

### **Comorbid communicable infectious conditions**

Infections were significantly less likely in 2015 than in 2008 across all but one of the condition groups examined. While the dataset had sparse detail on infections, this finding is of particular interest in relation to infections known to be HIV-associated – chronic viral hepatitis (infection-GI group), mycoses and tuberculosis – three areas for which we felt some interpretation could be made.

Although the data did not distinguish between HBV and hepatitis C virus (HCV) infection, the reduction in chronic viral hepatitis may reflect the availability of HCV treatments. Despite the significant reduction, the absolute proportion of the 2015 cohort with a diagnosis of chronic viral hepatitis nevertheless remained substantial at around 5%.

Tuberculosis was less likely in 2015 than in 2008 but prevalence remained substantial at 7%. The downward trend was also observed in a study among PLHIV in England, Wales and Northern Ireland (combined). [30]

## Limitations and strengths

Data from CPRD, established in 1987 and supported today by the UK's Medicines and Healthcare products Regulatory Agency and the National Institute for Clinical Excellence, are widely held as generalizable population-wide and have supported over 2000 published studies to date, many incorporating HES linkages [31,32]. The CPRD data have been used to study HIV testing rates and, recently, to study PLHIV more broadly. [33–35] Assuming the data are equally representative of HIV diagnoses as they are of other previously studied diagnoses, our findings are likely to be accurate. The numbers of PLHIV in the 2015 cross-section are fewer than in 2008, likely to reflect the changing distribution over time of general practices contributing data to CPRD GOLD. In this regard, 307 linked practices contributed data to PLHIV patients in 2008, which fell to 141 practices in 2015. Despite this, the mean numbers of PLHIV per practice were similar. The CPRD does not share practice distribution information publicly. Notably, HIV prevalence is similar to the estimated UK prevalence of known HIV of 0.14% in 2015 compared with 0.1% in our population, supporting representativeness of the cohort. [35]

One caveat is the possibility that some PLHIV may not disclose their HIV diagnosis to their GP. As HIV care is provided at secondary care level, this is possible. But as we compared two cohorts of CPRD patients with HIV diagnoses, a large between-cohorts difference in disclosures would be needed to distort the comparisons. It is hard to think of a reason why there would be such a difference. Secondary care providers proactively encourage PLHIV to share their diagnosis with GPs in order to facilitate optimal coordinated care. Moreover, suggesting that disclosure is the rule rather than the exception, surveys from PLHIV attending 73 HIV clinics in England and Wales found that 97.5% of respondents were GP-registered, of whom 93.8% had disclosed their HIV diagnosis [34].

A major strength of our study is its examination of over 300 comorbid conditions already identified from CPRD data as requiring intensive use of healthcare resources and/or following distinct pathological pathways. [18,19] Such systematic evaluation of the health of PLHIV in the UK has not been undertaken before now.

## CONCLUSIONS

In this comprehensive cross-sectional study, the marked rise in deprivation levels among PLHIV is a highly concerning new observation on PLHIV in England.

The decreasing proportions observed of younger PLHIV and the marked reduction in HIV-associated communicable infectious conditions suggest that the public

has responded to measures assisting personal infection risk management.

The likelihood of many non-communicable disorders was unchanged over the study period; this does not predict a stable care landscape for PLHIV, especially as seven non-communicable condition groups were more likely in 2015 than in 2008. It is necessary next to gather detailed information on both health and socio-economic trajectories of PLHIV in order to plan and implement effective measures for holistic lifetime support.

## AUTHOR CONTRIBUTIONS

DM-M: data curation, formal analysis, investigation, methodology, resources, software, supervision, validation, visualization, writing, review and editing. DRM: study design, literature search, data collection, data analysis, data interpretation, writing. NM: study design, funding application, comorbidity groupings and assignment to categories, data interpretation, writing, review and editing. PM: study concept and design, funding application, ethics approval, comorbidity groupings and assignment to categories, data interpretation, writing of first draft, review and editing.

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## CONFLICT OF INTEREST

None declared.

## DATA AVAILABILITY STATEMENT

Raw data for the study can be accessed through CPRD's standard terms and conditions (<https://www.cprd.com/>).

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- R General Linear Model <https://www.rdocumentation.org/packages/stats/versions/3.6.2/topics/glm>
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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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