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ORIGINAL RESEARCH

COVID-19 mortality among people with diagnosed HIV compared to those without during the first wave of the COVID-19 pandemic in England

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Abstract

Objectives: We describe COVID-19 mortality among people with and without HIV during the first wave of the pandemic in England.

Methods: National surveillance data on adults (aged ≥ 15 years) with diagnosed HIV resident in England were linked to national COVID-19 mortality surveillance data (2 March 2020–16 June 2020); HIV clinicians verified linked cases and provided information on the circumstances of death. We present COVID-19 mortality rates by HIV status, using negative binomial regression to assess the association between HIV and mortality, adjusting for gender, age and ethnicity.

Results: Overall, 99 people with HIV, including 61 of black ethnicity, died of/with COVID-19 (107/100 000) compared with 49 483 people without HIV (109/100 000). Compared to people without HIV, higher COVID-19 mortality

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rates were observed in people with HIV of black (188 vs. 122/100 000) and Asian (131 vs. 77.0/100 000) ethnicity, and in both younger (15–59 years: 58.3 vs. 10.2/100 000) and older (≥ 60 years: 434 vs. 355/100 000) people. After adjustment for demographic factors, people with HIV had a higher COVID-19 mortality risk than those without (2.18; 95% CI: 1.76–2.70). Most people with HIV who died of/with COVID-19 had suppressed HIV viraemia (91%) and at least one comorbidity reported to be associated with poor COVID-19 outcomes (87%).

Conclusions: In the first wave of the pandemic in England, COVID-19 mortality among people with HIV was low, but was higher than in those without HIV, after controlling for demographic factors. This supports the strategy of prioritizing COVID-19 vaccination for people with HIV and strongly encouraging its uptake, especially in those of black and Asian ethnicity.

KEYWORDS

adults, COVID-19, England, HIV, mortality

INTRODUCTION

Reliable ascertainment and description of mortality are critical in informing the public health response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which can lead to coronavirus disease (COVID-19). Examining the disparities in outcomes between population subgroups provides critical insight into which are the most severely affected, enabling the development of specific health policies to protect these populations.

In England, an estimated 96 200 people live with HIV, with 6% unaware of their infection [1]. Of those diagnosed, 98% receive antiretroviral treatment (ART) and of those on treatment, 97% are virally suppressed; this is equivalent to at least 89% of all people living with HIV in England having an undetectable viral load [1]. Although ART is effective in restoring immunity and uptake is high [2], persistent immune dysfunction and chronic inflammation may put people with HIV at increased risk of COVID-19 mortality due to a reduced ability to mount a protective immune response. Additionally, in England, people with HIV are more likely to be male and belong to communities known to experience socioeconomic deprivation, both of which are predictors of adverse COVID-19 outcomes [3,4]. Evidence on the risk of death from COVID-19 among people with HIV versus the general population is mixed, with some studies suggesting higher mortality rates [5–8] but others reporting little difference in mortality [9–11].

We use comprehensive national surveillance data to provide an epidemiological description of COVID-19 mortality among all people with diagnosed HIV during the first wave of the COVID-19 pandemic in England and compare the mortality burden to people without HIV.

METHODS

Data sources

People with HIV

As part of the national HIV surveillance programme, clinical and epidemiological information on all adults (aged ≥ 15 years) accessing HIV care in England is submitted to the HIV and AIDS Reporting System (HARS) at Public Health England (PHE) by National Health Service (NHS) specialist outpatient clinics [12]. Individual follow-up begins at diagnosis; data collected for each subsequent attendance for HIV outpatient care include: CD4 count (where indicated), HIV treatment status, HIV viral load and the presence of AIDS-defining illnesses.

Information on deaths among people with HIV (date and cause of death) are reported through routine surveillance, as well as through matching to mortality data from the Office for National Statistics (ONS). In 2019, PHE introduced enhanced surveillance of deaths among people with HIV (Annual National HIV Mortality Review) in collaboration with the British HIV Association (BHIVA) [13]. Briefly, HIV clinicians complete an online modified Causes of Death in HIV [14] reporting form for all deaths among their patients, which captures information on HIV clinical profile, comorbidities, lifestyle risk factors, causes of death and end-of-life care. Data are usually submitted annually and retrospectively. However, to better understand the impact of COVID-19 on people with HIV,

clinicians were contacted through the BHIVA network and asked to submit a mortality review form following each death of/with COVID-19 in a person with HIV.

General population

In England, COVID-19 deaths in the general population are reported to PHE daily through four sources: (1) the COVID-19 Patient Notification System (hospital deaths) [15]; (2) local PHE Health Protection Teams (deaths in non-hospital settings); (3) NHS Demographic Batch Service matching of all laboratory-confirmed COVID-19 cases against records of registered deaths; and (4) ONS death registration records. Data from each source are merged and de-duplicated, creating a single dataset [COVID-19 Specific Mortality Surveillance System (COSMOSS)]. Data are matched to ONS death registrations using NHS number [16] to ascertain cause and place of death, and to Hospital Episode Statistics to identify ethnicity, and linkage to area-level data on socioeconomic status [index of multiple deprivation (IMD)] [17]. In England, COVID-19 was first detected on 30 January 2020, with the first death of/with COVID-19 occurring on 2 March 2020 [18].

Data linkage

The general population COVID-19 mortality dataset (data to 16 June 2020) was linked to the national HIV surveillance dataset using a combination of pseudo-anonymized identifiers [Soundex (scrambled surname) [19], first initial, date of birth, gender and lower super output area of residence] (PHE Caldicott approval: NISCRP552020). Two epidemiologists reviewed all matches independently, with disparities reviewed by an HIV clinician and consensus agreed. For matches deemed to be definite (exact matches for all information) or probable (matches for

TABLE 1 Mortality rates stratified by age group, HIV status and other demographics: England, 2 March to 16 June 2020

	People with HIV								
	All			15–59 years			≥ 60 years		
	Deaths	Population	Crude mortality rate per 100 000	Deaths	Population	Crude mortality rate per 100 000	Deaths	Population	Crude mortality rate per 100 000
Total	99	92 643	107	47	80 669	58.3	52	11 974	434
Gender									
Men	68	63 585	107	29	54 339	53.4	39	9246	422
Women	31	28 978	107	18	26 252	68.6	13	2726	477
Region of residence									
London	60	39 070	154	25	34 224	73.0	35	4846	722
South	12	15 788	76.0	6	13 259	45.3	6	2529	237
Midlands	19	20 166	94.2	11	17 583	62.6	8	2583	310
North	8	17 605	45.4	5	15 589	32.1	3	2016	149
Ethnicity									
White	32	48 526	65.9	13	40 528	32.1	19	7998	238
Black	61	32 490	188	31	29 443	105	30	3047	985
Asian	5	3821	131	2	3437	58.2	3	384	781
Other/mixed	1	5634	17.7	1	5232	19.1	0	402	0.0
Index of multiple deprivation (IMD)									
1 – most deprived	33	30 235	109	16	27 078	59.1	17	3157	538
2	31	24 488	127	15	21 520	69.7	16	2968	539
3	21	14 671	143	8	12 460	64.2	13	2211	588
4	11	9772	113	5	8154	61.3	6	1618	371
5 – least deprived	3	6331	47.4	3	5179	57.9	0	1152	0.0

most information), clinicians were contacted by PHE and asked to confirm that the HIV patient had died and to submit the mortality review form (Figure S1). Where clinical information collected through the mortality review form conflicted with that collected in HARS (e.g. ART start date), the clinician-reported data were prioritized. For the five people with no mortality review form completed, HARS clinical profile data were used, where available.

Definition of COVID-19 mortality

People were considered to have died of/with COVID-19 if their death occurred within 60 days of a positive COVID-19 test [either polymerase chain reaction (PCR) (majority), nucleic acid amplification test (NAAT) or serological], with COVID-19 included on the ONS death registration form (death certificate), or if COVID-19 was reported as a cause of death by the reporting clinician.

Analyses

We present a descriptive analysis of adults with and without HIV resident in England who died of/with COVID-19 between 2 March and 16 June 2020 (3.5 months). There were no deaths reported among children aged < 15 years with HIV over this time period.

Crude mortality rates were calculated as the number of COVID-19 deaths per 100 000 population for those with and without HIV, comparing those aged 15–59 years with those aged ≥ 60. The number of adults living with diagnosed HIV in England at the end of 2019 ($n = 92\,643$) was estimated as the number of people who accessed HIV outpatient care in 2019 ($n = 88\,341$), plus: (1) people last seen for HIV outpatient care in 2018 and not known to have died by the end of 2019 ($n = 3580$); and (2) those newly diagnosed with HIV in 2018 and 2019 but not yet seen for outpatient care ($n = 722$). The number of people without HIV was calculated by subtracting the number of people

TABLE 1 (Continued)

People without HIV								
All			**15–59 years**			**≥ 60 years**		
Deaths	**Population**	**Crude mortality rate per 100 000**	**Deaths**	**Population**	**Crude mortality rate per 100 000**	**Deaths**	**Population**	**Crude mortality rate per 100 000**
49 483	45 565 024	109	3288	32 548 652	10.1	46 195	13 016 372	355
27 204	22 539 107	121	2115	16 284 914	13.0	25 089	6 254 193	401
22 279	23 025 997	96.8	1173	16 263 816	7.21	21 106	6 762 181	312
8644	7 176 318	120	992	5 708 575	17.4	7652	1 467 743	521
9984	12 194 322	81.9	491	8 288 873	5.92	9493	3 905 449	243
15 035	13 897 941	108	921	9 658 375	9.54	14 114	4 239 566	333
15 440	12 733 662	121	834	8 892 843	9.38	14 606	3 840 819	380
42 790	39 188 964	109	2141	26 812 333	7.99	40 649	12 376 631	328
1882	1 559 535	121	381	1 359 679	28.0	1501	199 855	751
2780	3 613 726	76.9	431	3 103 265	13.9	2349	510 461	460
1175	1 379 770	85.2	190	1 254 921	15.1	985	124 849	789
11 228	8 769 575	128	979	6 731 433	14.5	10 249	2 038 142	503
10 577	9 427 316	112	867	7 017 999	12.4	9710	2 409 317	403
9535	9 484 187	101	575	6 637 473	8.66	8960	2 846 714	315
9313	9 282 606	100	468	6 234 391	7.51	8845	3 048 215	290
8441	9 045 691	93.3	347	5 933 634	5.85	8094	3 112 057	260

with HIV from the number of people in the general population (ONS) [20]. Latest available mid-year ONS population estimates were used: 2019 for IMD and region of residence and 2017 for ethnicity. Data were available by gender, age at death (5-year age bands) and ethnicity, region or IMD.

Multivariable negative binomial regression was used to assess the association between HIV and death of/with COVID-19, adjusting firstly for age at death and subsequently for gender, age at death and ethnicity. Interaction terms were added to assess effect modification by age and ethnicity. Separate models were built to describe associations between mortality and region of residence and IMD, adjusting for gender, age at death and HIV status.

We also describe the clinical profile of people with HIV who died of/with COVID-19 overall and by gender, age and ethnicity. Comorbidities reported to increase the risk of COVID-19 death include: cardiovascular disease (CVD) (including hypertension), diabetes mellitus, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), obesity and dementia/cognitive impairment [21]. Detailed information on comorbidities was available for those people with a completed mortality review form ($n = 94$); for the remainder, information on comorbidities was taken from the death certificate. Viral suppression was defined as a viral load of < 200 copies/mL. HIV viral load and CD4 count measurements were considered to be 'at death' if within a year of death.

All analyses were carried out using Stata v.15.0 (Stata Corp, College Station, TX, USA).

RESULTS

Mortality among people with and without HIV

As of 16 June 2020, there were 99 COVID-19 deaths reported among the 92 643 adults with diagnosed HIV in England, equivalent to a crude mortality rate of 107/100 000 population (Table 1). In comparison, there were 49 483 COVID-19 deaths reported among the 45 565 024 people without HIV over the same period, equivalent to a crude rate of 109/100 000.

Overall, the median age of death among people with HIV who died of/with COVID-19 was 60 years [interquartile range (IQR): 51–72], with 53% (52/99) aged ≥ 60. By comparison, median age of death among people without HIV who died with/of COVID-19 was 83 years (IQR: 74–89), with 93% (46 195/49 483) aged ≥ 60. Sixty-nine percent ($n = 68$) of all COVID-19 deaths in people with HIV were among men, compared with 55% ($n = 27\ 204$) of those among people without HIV (Table 1). These differences largely reflect variation in the structure of the populations, whereby 13% (11 974/92 643) of all people with HIV were aged ≥ 60 and 69% ($n = 63\ 585$) were men compared with 29% (13 016 372/45 565 024) and 49% ($n = 22\ 539\ 107$) of those without HIV, respectively. Figure S2 shows the age and sex structure of both populations compared with the age and sex structure of those who died of/with COVID-19 and of any cause.

Higher crude mortality rates were observed among people aged ≥ 60 than among younger individuals (434 vs. 58.3/100 000 among people with HIV and 355 vs. 10.1/100 000 among those without) (Table 1). Crude mortality rates among people with HIV of black and Asian ethnicity were higher than those among people of equivalent ethnicity without HIV, and lower in the most deprived residential areas.

Risk factors for dying of/with COVID-19

After adjustment, the risk of COVID-19 death was 2.18 [95% confidence interval (CI): 1.76–2.70] times higher in people with HIV than in those without (Table 2). Regardless of HIV status, risk of death increased with increasing age [adjusted risk ratio (aRR) per increasing 5-year age band = 1.79, 95% CI: 1.77–1.81] and was higher in those of black (3.44, 95% CI: 3.06–3.87), Asian (2.24, 95% CI: 2.00–2.52) and other/mixed (3.23, 95% CI: 2.86–3.65) ethnicity, compared with those of white ethnicity. Women were less likely to die than were men (0.55, 95% CI: 0.51–0.60). There was no statistical evidence of interaction between HIV status and age or ethnicity. Separate models describing the association between region of residence and IMD on mortality can be found in Table S1.

Clinical characteristics of people with HIV who died of/with COVID-19

Table 3 shows the demographic and clinical characteristics of the 99 people with HIV who died of/with COVID-19; comparable data from the 96 243 people living with diagnosed HIV can be found in Table S2. Overall, 80% ($n = 79$) of people had a positive COVID-19 test prior to death, of whom 99% ($n = 78$) died within a month (28 days) of their positive test. This compares with 77% ($n = 38\ 056$) and 72% ($n = 35\ 481$) for deaths among those without HIV, respectively. Most people with HIV died in hospital [85% (84/99) vs. 64% (29 544/46 176) among those without HIV], while fewer died in a nursing home [9% ($n = 9$) vs. 30% ($n = 13\ 664$)].

The median time between HIV diagnosis and COVID-19-related death was 15 years (IQR: 10–19); three people

TABLE 2 Risk factors associated with dying of/with COVID-19: England, 2 March to 16 June 2020

Explanatory variables	Number of deaths	Adjusted risk ratio[b]			Adjusted risk ratio[c]		
		aRR	95% CI	*p*-value[d]	aRR	95% CI	*p*-value[d]
Gender							
Men	27 272	1.00	–	–	1.00	–	–
Women	22 310	0.56	0.45–0.69	< 0.001	0.55	0.51–0.60	< 0.001
Age at death[a] (years)							
15–19	13	1.80	1.75–1.85	< 0.001	1.79	1.77–1.81	< 0.001
20–29	80						
30–39	226						
40–49	726						
50–59	2290						
60–69	4840						
70–79	11 120						
80–89	19 542						
≥ 90	10 745						
Ethnicity							
White	42 822	1.00	–	–	1.00	–	–
Black	1943	3.89	3.14–4.78		3.44	3.06–3.87	
Asian	2785	2.25	1.82–2.77		2.24	2.00–2.52	
Other/mixed	1176	2.84	2.29–3.52	< 0.001	3.23	2.86–3.65	< 0.001
Unknown	856	–	–	–	–	–	–
HIV status							
Without HIV	49 483	1.00	–	–	1.00	–	–
With HIV	99	2.21	1.64–2.97	< 0.001	2.18	1.76–2.70	< 0.001

Abbreviations: aRR, adjusted risk ratio; CI, confidence interval.

[a]Age at death modelled as a continuous variable (increasing 5-year age bands).

[b]Adjusted for age at death and each explanatory variable (gender, HIV status or ethnicity).

[c]Adjusted for all explanatory variables (gender, age at death, HIV status and ethnicity).

[d]Likelihood ratio test.

died within 3 months of their HIV diagnosis and five within 1 year (Table 3). Access to outpatient specialist HIV care was high, with 95% ($n = 94$) attending at least once since their HIV diagnosis. Among those who accessed HIV care, 94% ($n = 88$) were last seen between 2018 and 2020, 5% ($n = 5$) were last seen between 2016 and 2017 and one person was last seen in 2002. The coverage of ART was 99% ($n = 98$) overall, with 94% (89/95) documented as receiving ART at death or in the preceding year [median time since ART initiation: 14 years (IQR: 9–18)]. Of the 69 people with a CD4 count reported in the year prior to death, 1.4% ($n = 1$), 16% ($n = 11$) and 42% ($n = 29$) had a CD4 count < 50, < 200 and < 350 cells/μL, respectively. Of those with a CD4 < 350 cells/ μL, all were aged ≥ 40 years, 83% ($n = 24$) were ≥ 50 years old and 62% ($n = 18$) were ≥ 60. Of the 92 people with any CD4 count available, 14% ($n = 13$), 53% ($n = 49$) and 86% ($n = 79$) had a CD4 nadir < 50, < 200 and < 350 cells/μL, respectively. Overall, 91% (83/91) of people were virally suppressed. There were no significant differences by gender or ethnicity with regard to HIV clinical markers and ART uptake.

Ninety per cent (89/99) of people with HIV who died had at least one reported comorbidity; 87% ($n = 82$) had at least one documented comorbidity known to be associated with higher risk of poor COVID-19 outcomes (65% at least two) [21]. The prevalence of specific comorbidities was as follows: CVD (including hypertension), 69% (57/83); diabetes mellitus, 48% (40/83); CKD, 41% (32/78); COPD, 10% (8/77); and dementia/cognitive impairment, 17% (9/51). Among those with height and weight available ($n = 70$), 49% ($n = 34$) had a body mass index (BMI) of >30 kg/m^2 indicating obesity, and a further 26% ($n = 18$) were overweight (BMI 25–30 kg/m^2). While diabetes mellitus was more common in men, obesity and dementia/cognitive impairment were more common in women. Diabetes mellitus, CVD, CKD and obesity were more common among

TABLE 3 Characteristics of people with HIV who died of/with COVID-19 by gender and ethnicity: England, 2 March to 16 June 2020

	All		Gender				Ethnicity					
			Men		Women		White		Black		Other[f]	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Total	99		68		31		32		61		6	
Age of death (years) [median (IQR)]	60 (51–72)		61 (53–74)		55 (46–69)		66 (50–77)		59 (52–66)		64 (40–73)	
Year diagnosed with HIV												
2020	3	3.0%	3	4.4%	0	0%	2	6.3%	1	1.6%	0	0%
2018–2019	6	6.1%	4	5.9%	2	6.5%	1	3.1%	5	8.2%	0	0%
2006–2017	37	37%	25	37%	12	39%	11	34%	22	36%	4	67%
< 2006	53	54%	36	53%	17	55%	18	56%	33	54%	2	33%
Time living with diagnosed HIV (years) [median (IQR)]	15 (10–19)		15 (9–21)		15 (11–18)		15 (10–25)		15 (10–18)		13 (10–16)	
Death within 3 months of HIV diagnosis	3	3.0%	3	4.4%	0	0%	2	6.3%	1	1.6%	0	0%
Death within 1 year of HIV diagnosis	5	5.1%	4	5.9%	1	3.2%	2	6.3%	3	4.9%	0	0%
Death within 1 month of COVID−19 diagnosis[a]	78	99%	57	100%	21	95%	25	96%	48	100%	5	100%
Not linked to HIV outpatient care before death	5	5.1%	4	5.9%	1	3.2%	2	6.3%	3	4.9%	0	0%
Year last attended for HIV outpatient care prior to death if linked												
2020[b]	28	30%	17	27%	11	35%	11	37%	16	28%	1	17%
2018–2019	60	64%	40	63%	20	65%	15	50%	41	71%	4	67%
2016–2017	5	5.3%	5	7.9%	0	0%	3	10%	1	1.7%	1	17%
< 2016	1	1.1%	1	1.6%	0	0%	1	3.3%	0	0%	0	0%
Ever on HIV treatment	98	99%	67	99%	31	100%	31	97%	61	100%	6	100%
Time since HIV treatment initiation (years) [median (IQR)]	14 (9–18)		14 (9–19)		14 (10–17)		14 (9–22)		14 (9–18)		12 (10–16)	
HIV treatment at death	89	94%	59	91%	30	100%	26	87%	58	97%	5	100%
CD4 nadir (cells/μL)												
< 50	13	14%	6	10%	7	23%	2	6.9%	11	19%	0	0%
50–199	36	39%	21	34%	15	48%	10	34%	23	40%	3	50%
200–349	30	33%	24	39%	6	19%	10	34%	17	30%	3	50%
350–499	7	7.6%	5	8.2%	2	6.5%	3	10%	4	7.0%	0	0%
≥ 500	6	6.5%	5	8.2%	1	3.2%	4	14%	2	3.5%	0	0%

(Continues)

TABLE 3 (Continued)

	All		Gender				Ethnicity					
			Men		Women		White		Black		Other[f]	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
CD4 count at death (cells/μL)[c]												
< 50	1	1.4%	1	2.2%	0	0%	1	4.8%	0	0.0%	0	0%
50–199	10	14%	9	20%	1	4.3%	4	19%	6	13%	0	0%
200–349	18	26%	10	22%	8	35%	7	33%	9	20%	2	67%
350–499	18	26%	14	30%	4	17%	4	19%	13	29%	1	33%
≥ 500	22	32%	12	26%	10	43%	5	24%	17	38%	0	0%
Viral load measurement at death (copies/mL)[c]												
< 50	74	81%	49	80%	25	83%	22	79%	48	83%	4	80%
50–199	9	10%	6	9.7%	3	10%	2	7.1%	6	10%	1	20%
200–1499	1	1.1%	1	1.6%	0	0%	0	0.0%	1	1.7%	0	0%
≥ 1500	7	7.7%	5	7.8%	2	6.7%	4	14%	3	5.2%	0	0%
Comorbidities[d]												
Any comorbidity	89	90%	62	91%	27	87%	27	84%	56	92%	6	100%
Any COVID−19 comorbidity[e]	82	87%	56	82%	26	84%	22	69%	55	90%	5	83%
CVD (including hypertension)	57	69%	42	70%	15	65%	14	56%	38	72%	5	100%
Hypertension	32	39%	24	40%	8	35%	5	20%	26	49%	1	20%
Diabetes mellitus	40	48%	31	52%	9	39%	8	33%	28	52%	4	80%
COPD	8	10%	5	9.3%	3	13%	5	22%	3	6.0%	0	0%
CKD	32	41%	22	40%	10	43%	6	25%	22	44%	4	100%
Obesity	34	49%	19	42%	15	60%	6	29%	27	42%	1	60%
Dementia/cognitive impairment	9	18%	5	15%	4	22%	4	27%	5	15%	0	0%

Note: Proportions may not add up to 100% due to rounding.

1 month = 28 days; 3 months = 91 days; 1 year = 365 days.

Abbreviations: CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; IQR, interquartile range.

[a]80% ($n = 79$) of people with HIV who died of/with COVID-19 were confirmed (positive SARS-CoV-2 test result).

[b]Data for 2020 not complete – up to mid-June 2020.

[c]Measured within a year of death for people who died of/with COVID-19.

[d]Detailed information available for those people with a mortality review form completed ($n = 94$); for the remainder, information on comorbidities was taken from the death certificate.

[e]Conditions more common in people who died of/with COVID-19 compared with of other causes [21].

[f]Other ethnicity: Asian and other/mixed.

people of black ethnicity than among those of white ethnicity (Table 3).

Table 4 presents the burden of comorbidities known to be associated with poor COVID-19 outcomes among people with diagnosed HIV who died of/with COVID-19 by gender, age at death and ethnicity. Of the 47 people who died aged < 60, 74% had at least one documented comorbidity associated with poor COVID-19 outcomes; 55% had two or more comorbidities and 19% had one. This compares with 96% among the 25 people who died age 60–69 years (80% had two or more comorbidities and 16% had one) and 85% among the 27 people who died aged ≥ 70 (70% had two or more and 15% had one). Among the 12 people aged < 60 years with no documented comorbidities, three were not virally suppressed within a year of death. The prevalence of comorbidities was high for both men and women, and across ethnicities.

DISCUSSION

We describe COVID-19 mortality among people with diagnosed HIV during the first wave of the pandemic in England. The overall mortality rate due to COVID-19 among people with HIV was low, at approximately 0.1%. Whilst this low death rate is reassuring, it is possible that a relatively small proportion of the population (particularly those with HIV) was exposed to the virus during the first 3.5 months of the pandemic [22]. United Kingdom government advice to 'stay at home' and 'socially distance' was released in March and specific groups of the population, identified as clinically extremely vulnerable, were asked to 'shield' by staying home for 3 months and avoid all non-household contacts [23]. People with HIV were initially included in the government's shielding advice; however this was subsequently changed in line with advice issued by BHIVA in late April

TABLE 4 Prevalence of comorbidities among people with HIV who died of/with COVID-19 by gender, age at death and ethnicity: England, 2 March to 16 June 2020

	All				Gender							
					Men				Women			
	Number of people affected		Cumulative categorization		Number of people affected		Cumulative categorization		Number of people affected		Cumulative categorization	
Age and comorbidity profile	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Age at death ≥ 70 years	27	27%	–	–	20	29%	–	–	7	23%	–	–
Two or more documented comorbidities[a,b]	19	70%	19	70%	15	75%	15	75%	4	57%	4	57%
One documented comorbidity[a,b]	4	15%	23	85%	3	15%	18	90%	1	14%	5	71%
Age at death 60–69 years	25	25%	–	–	19	28%	–	–	6	19%	–	–
Two or more documented comorbidities[a,b]	20	80%	20	80%	14	74%	14	74 in%	6	100%	6	100%
One documented comorbidity[a,b]	4	16%	24	96%	4	21%	18	95%	0	0%	6	100%
Age at death < 60 years	47	47%	–	–	29	43%	–	–	18	58%	–	–
Two or more documented comorbidities[a,b]	26	55%	26	55%	17	59%	17	59%	9	50%	9	50%
One documented comorbidity[a,b]	9	19%	35	74%	3	10%	20	69%	6	33%	15	83%

Note: Proportions may not add up to 100% due to rounding.

[a]Cardiovascular disease (including hypertension), diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease, dementia/cognitive impairment, obesity.

[b]Information available for those people with a mortality review form completed ($n = 94$) and the two additional people who had relevant comorbidities listed on the death certificate.

[c]Other ethnicity: Asian and other/mixed.

recommending that only individuals with CD4 counts < 50 cells/μL, a recent AIDS diagnosis and/or multiple comorbidities should 'shield' [24]. Consequently, the risk of death among those most clinically vulnerable with HIV may be underestimated in our study.

Although mortality was low overall, COVID-19 mortality among people with HIV in England was more than double that of people without HIV after differences in the population age structure were taken into consideration. This is consistent with other published studies [5–8]. Primary care data from the OpenSAFELY platform showed people living with HIV had higher risk of COVID-19 death (hazard ratio = 2.90, 95% CI: 1.96–4.30) than those without HIV after adjusting for age and sex [5]. The ISARIC study of a subset of patients hospitalized with COVID-19 in the UK found a 63% increased risk of mortality among those with HIV compared with HIV-negative individuals after adjusting for sex, ethnicity, age, baseline date, comorbidities and disease severity at presentation [8]. Similar to these other studies, our findings should be interpreted with caution [25]. Unlike OpenSAFELY and ISARIC, which were restricted to analysis of specific subgroups (e.g. people registered at general practice or in hospital), we utilized comprehensive national HIV surveillance data including all people living with diagnosed HIV and had access to data on all people who died of/with COVID-19 in the general population. Nevertheless, we were limited by a lack of available data on comorbidities for those without HIV to adjust our analyses; this is particularly important as people with HIV are known to have higher levels of comorbidities than the general population [3,26].

Our analyses show that among people with HIV who died of/with COVID-19, the large majority (88%) were either

TABLE 4 (Continued)

Ethnicity											
White				**Black**				**Other**[c]			
Number of people affected		**Cumulative categorization**		**Number of people affected**		**Cumulative categorization**		**Number of people affected**		**Cumulative categorization**	
n	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**
14	44%	–	–	10	16%	–	–	3	50%	–	–
9	64%	9	64%	7	70%	7	70%	3	43%	3	100%
2	14%	11	79%	2	20%	9	90%	0	0%	3	100%
5	16%	–	–	20	33%	–	–	0	0%	–	–
3	60%	3	60%	17	85%	17	85%	0	0%	0	0%
1	20%	4	80%	3	15%	20	100%	0	0%	0	0%
13	41%	–	–	31	51%	–	–	3	50 %	–	–
4	31%	4	31%	20	65%	20	69%	2	67%	2	67%
3	23%	7	54%	6	19%	26	90%	0	0%	2	67%

aged ≥ 60 (53%) or had at least one documented comorbidity known to be a risk factor for COVID-19 death (87%). There were very few deaths among people with diagnosed HIV aged < 60 without a documented comorbidity. The comorbidities commonly reported among people with HIV who died of/with COVID-19 in England included CVD (69%), obesity (49%), diabetes mellitus (48%), CKD (41%) and hypertension (39%). These rates are higher than those reported among all people living with diagnosed HIV (Table S2) [3,26], higher than those documented among people with HIV who died pre-COVID-19 and higher than the general population as a whole [27,28]. These findings are consistent with the literature and highlight the importance of ensuring optimal care of comorbidities alongside HIV care [29–32].

Over two-thirds of the people with HIV who died of/with COVID-19 were from black, Asian or ethnic minority populations; only 35% of people living with diagnosed HIV in England are of these ethnicities. We observed a higher risk of COVID-19 mortality in people of an ethnic minority with HIV, compared with those without, remained after adjustment for age and gender. Higher COVID-19 diagnosis rates have been observed among people of black ethnic groups in England than among other ethnic groups, as well as higher mortality rates [21,33]. This disparity may be partially explained by socioeconomic factors, comorbidities and occupational exposure to COVID-19, with a relatively high proportion of people of black ethnicity employed in health and social care roles [32,34,35]. Our ability to characterize the relationship between ethnicity and mortality was limited by a lack of data on underlying COVID-19 testing and diagnosis rates and an inability to adjust for occupational exposure. Furthermore, despite finding that an increased risk of death was seen among those in London and those living in areas of higher deprivation (Table S1), we could not adjust for ethnicity, IMD and region of residence in the same model, due to a lack of available general population data.

This is the first population-level national study of COVID-19 mortality among people with HIV in the UK, capturing all deaths during the first wave. We linked the national cohort of people diagnosed with HIV to national COVID-19 death data, including people not linked to HIV care and those lost to clinical follow up, groups that may be particularly vulnerable to COVID-19. Additional clinical data were collected on those who died to ascertain the treatment and immunosuppression levels, as well as better understand comorbidities and cause of death. PHE reports to date have focused on people who have died within 28 and 60 days of a positive COVID-19 test or linked to a death registration certificate [36]. We also included deaths where COVID-19 was entered on the death certificate of individuals who were not linkable to a positive COVID-19 test; most of these deaths occurred at the start of the pandemic where testing was not widely available.

However, our study has several additional limitations. Mortality rates among people with HIV presented here exclude deaths among the 5900 people estimated to have undiagnosed infection in England; however, this is a relatively low proportion (6%) among all people with HIV in the country [1]. We are not yet able to calculate excess mortality as surveillance of deaths among people with HIV in 2020 is still under way. We cannot calculate case fatality or account for any differences in exposure to COVID-19 comparing HIV and those without [37]. Despite HIV surveillance being comprehensive and of high quality, there were some missing data which may have affected our findings. Notably, CD4 counts in the year preceding death were only available for 70% of people who died of/with COVID-19; this reflects current UK monitoring guidelines which do not require annual CD4 testing for those with well-controlled HIV [38]. COVID-19 is known to dysregulate the immune system and lower CD4 cell counts [39]; in our analysis we included at least 17 people with a CD4 measured within 2 weeks of or after their COVID-19 diagnosis. However, this should have minimal impact as the distribution of these counts was equitable across CD4 strata (Table 3). Where clinical information collected through the mortality review form conflicted with that collected in HARS, clinician-reported data were prioritized. However, clinicians may not have been aware of previous clinical history if patients died in hospitals where they did not receive HIV outpatient care. Our analysis includes data until June 2020. In England, COVID-19 deaths remained at low sustained levels through the summer months of 2020 before rising again in late September [18]. Over 65 000 additional COVID-19 deaths in the general population were reported to PHE as of 15 February 2021. However, the age, sex and ethnic profile of people who died has not changed substantially over this period and thus we believe the results presented remain representative and relevant across the pre-vaccination era [18].

CONCLUSIONS

In England, where 94% of people with HIV are diagnosed and on suppressive ART, the rate of COVID-19 mortality in the first wave of the COVID-19 pandemic among people with HIV was low but higher than among those without HIV after controlling for age. Few people with HIV who died of/with COVID-19 were aged < 60 and did not have a documented comorbidity associated with worse outcomes. Most people with HIV who died of/with COVID-19 had risk factors similar to those identified in the general population; male, older age, non-white ethnicity, comorbid conditions and residential deprivation are important risk factors for COVID-19 mortality regardless of HIV status. People with HIV in the UK are currently

being prioritized for COVID-19 vaccination [40]. Our findings highlight that uptake of vaccination in people with HIV of all ages should be strongly encouraged.

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CONFLICT OF INTEREST

SEC, AEB, SN, MK, AKS, PK, JK, VD and SC have no conflicts of interest to declare. DB reports grants from ViiV Healthcare and Gilead Sciences outside the submitted work. LW reports speaker/advisory fees from Gilead Sciences, Viiv Healthcare, Merck Sharp & Dohme (MSD), Janssen-Cilag, Cipla, Mylan and Theratechnologies and funding for clinical trials from Gilead Sciences and Janssen-Cilag outside the submitted work. FAP reports grants and personal fees from Gilead Sciences, Viiv Healthcare, Janssen-Cilag and MSD outside the submitted work. RFM reports personal fees from Gilead Sciences for conference attendance and non-promotional talks outside the submitted work. CS reports funding from Gilead Sciences and Janssen-Cilag for participation in advisory panels and for the preparation of educational materials outside the submitted work. DRC reports funding from Gilead Sciences and ViiV Healthcare for the preparation of educational materials and research grants outside the submitted work. RH reports educational consultancies from Gilead Sciences and ViiV Healthcare outside the submitted work. DA reports advisory fees from Gilead Sciences and Viiv Healthcare outside the submitted work.

AUTHOR CONTRIBUTIONS

VD, DB, AEB, AKS and SEC conceived this research study. AEB extracted data on COVID-19 deaths in the general population. JK and SN extracted the HIV data and JK performed the data linkage. SEC and AEB reviewed all matches; AKS reviewed all discrepancies. SEC and AKS coordinated mortality review form follow-up. FAP, RFM and SEC reviewed all causes of death. SEC and AEB carried out the majority of analyses and drafted and finalized the paper; SN carried out the descriptive analysis of people with HIV. CS and PK provided input into the research methods as well as statistical support. MK, DB, CS, RFM, FAP, RH, SC, LW, DA, DRC, VD and AKS provided important intellectual content to the discussion and conclusions. All authors critically appraised the manuscript and approved its submission.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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