European Journal of Cancer 183 (2023) 162–170

Available online at www.sciencedirect.com

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journal homepage: www.ejcancer.com

Original Research

Uptake of COVID-19 vaccination in people with blood cancer: Population-level cohort study of 12 million patients in England

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Received 31 January 2023; accepted 2 February 2023
Available online 10 February 2023

KEYWORDS
COVID-19 vaccine;
Blood cancer;
Vaccination uptake;
Health inequalities

Abstract ***Background:*** People with blood cancers have increased risk of severe outcomes from COVID-19 and were prioritised for vaccination.
Methods: Individuals in the QResearch database aged 12 years and above on 1st December 2020 were included in the analysis. Kaplan–Meier analysis described time to COVID-19 vaccine uptake in people with blood cancer and other high-risk disorders. Cox regression was used to identify factors associated with vaccine uptake in people with blood cancer.
Results: The analysis included 12,274,948 individuals, of whom 97,707 had a blood cancer diagnosis. 92% of people with blood cancer received at least one dose of vaccine, compared to 80% of the general population, but there was lower uptake of each subsequent vaccine dose (31% for fourth dose). Vaccine uptake decreased with social deprivation (HR 0.72, 95% CI 0.70, 0.74 for most deprived versus most affluent quintile for first vaccine). Compared with White groups, uptake of all vaccine doses was significantly lower in people of Pakistani and Black ethnicity, and more people in these groups remain unvaccinated.
Conclusions: COVID-19 vaccine uptake declines following second dose and there are ethnic and social disparities in uptake in blood cancer populations. Enhanced communication of benefits of vaccination to these groups is needed.

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https://doi.org/10.1016/j.ejca.2023.02.001

1. Introduction

People with haematological malignancies are at increased risk of severe outcomes from COVID-19 including hospitalisation and death [1–3]. Non-cancerous blood disorders, such as sickle cell disease, may also be linked to poor outcomes following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [4,5].

COVID-19 vaccines are safe and effective in the general population [6]. The UK began its COVID-19 vaccination rollout on 8th December 2020, prioritising people with blood cancers. A third vaccine dose was offered to immunocompromised individuals (including those with haematological malignancies) from 14th September 2021, and fourth dose rollout for immunocompromised groups proceeded from January 2022. As of July 2022, over 90% of the general UK population had received at least one vaccine, but uptake of the second and third doses has been lower, especially in younger age groups [7].

Uptake of COVID-19 vaccinations in severely immunocompromised people in England is high for the first three doses of vaccine, with 95.7% having had a first vaccine, 94.5% with two and 86.6% with three vaccines as of March 2022. However, uptake of the fourth vaccine has been lower at 45.5% [8,9]. In the general population, vaccine uptake is lower in some ethnic minority groups, more socioeconomically deprived groups and younger people [10–12].

Currently, there are no reports on vaccine uptake in people with haematological malignancies or whether uptake varies by type of cancer or population characteristics. This study explores the uptake of COVID-19 vaccines in people with blood cancers and other high-risk disorders using QResearch, a multi-million person electronic healthcare record database. This includes uptake in different demographic groups, including age, ethnicity, and socioeconomic status, in view of the inverse equity hypothesis, where disparities become more exaggerated when new interventions are introduced [13]. This work aims to inform policy makers, healthcare professionals, patients and the public on progress of the COVID-19 vaccination campaign and guide strategies for future booster vaccination campaigns.

2. Methods

Individuals aged 12 years and above on 1st December 2020 (immediately prior to start of the UK COVID-19 vaccination programme), who were eligible for vaccination and were registered with a general practice contributing data to the QResearch database, were included in the analysis. The study period was from 1st December 2020 to 11th April 2022, the latest date for which linked data was available at the time of the analysis.

The analyses used the QResearch primary care database, linked to the following datasets.

- Civil registration national data, for mortality with date and causes of death
- Hospital episode statistics (HES)
- National Cancer Registration and Analysis Service data (NCRAS)
- National Immunisation (NIMS) Database of COVID-19 vaccinations, of all vaccinations in England.

2.1. Defining study population

Individuals with a recorded blood cancer diagnosis in primary care or HES record, or in NCRAS before the COVID-19 vaccination programme began were identified. Blood cancers were classified according to World Health Organisation classifications [14,15] and expert opinion (Table A1).

Where individuals in the cohort were coded as having more than one type of haematological malignancy in one or more data sources, NCRAS classification, then HES, were prioritised over primary care data as more reliable sources. Where applicable, the most recent or clinically significant diagnosis, and the most specific diagnosis rather than generic codes were prioritised (e.g. *acute myeloid leukaemia* instead of *acute leukaemia*), so that each individual had a diagnosis of only one blood cancer type.

Those with diagnoses of aplastic anaemia, sickle cell disease or sickle cell trait were identified from primary care and HES records. The immunocompromised group included anyone who received chemotherapy, radiotherapy, was prescribed drugs that affect immune response (specified in BNF chapter 8.2), or received dialysis between 1st June 2020 and 30th November 2020; received a solid organ transplant before 1st December 2020; or a bone marrow transplant between 1st December 2018 and 1st December 2020. Full definitions of code groups are specified in the QCode library (https://www.qresearch.org/data/qcode-group-library/).

2.2. Statistical analysis

The primary outcome was uptake of first, second, third and fourth vaccine doses in people with types of blood cancer, other haematological disorders and those who were immunocompromised. Vaccine uptake was stratified by demographic characteristics. People who died during follow-up were excluded from analyses following death. Time to uptake of each COVID-19 vaccine in the groups was compared in Kaplan Meier curves. Follow-up started on 1st December 2020, 1st March 2021, 14th September 2021 and 1st January 2022 for the first, second, third and fourth doses of vaccine, respectively, and continued until the vaccine dose was received or censoring due to death by any cause or the study end date.

Table 1
Demographic characteristics of whole study population and cohort with blood cancer and other disorders.

	Full population	Blood cancer	Aplastic anaemia	Sickle cell disease	Sickle cell trait
Total (N)	12,274,948	97,707	2583	5087	25,200
Died (any cause) (N)	154,880	8302	434	54	188
Age, years mean (SD)	44.0 (19.9)	65.2 (17.9)	61.7 (20.1)	37.2 (17.1)	41.9 (17.2)
Female sex, %	6,135,259 (50.0)	45,785 (46.9)	1663 (46.3)	2947 (56.4)	16,690 (63.5)
BMI, kg/m^2 mean (SD)$^{++}$	26.6 (5.7)	27.2 (5.6)	27.0 (6.3)	25.3 (5.8)	28.3 (6.2)
BMI category, N (%)					
Underweight (<18.5)	379,281 (3.1)	2551 (2.6)	146 (5.6)	353 (6.8)	674 (2.6)
Normal weight (18.5 − <25)	3,460, 591 (28.2)	28,823 (29.5)	1148 (44.4)	1624 (31.1)	5716 (24.3)
Overweight (25.0 − <30)	2,802,279 (22.8)	29,749 (30.5)	937 (36.2)	1034 (19.8)	6564 (49.3)
Obese (≥30.0)	2,069,954 (16.9)	21,726 (15.1)	781 (30.2)	699 (13.4)	6991 (26.6)
Missing BMI $^{++}$	3,562,835 (29.0)	14,726 (15.1)	588 (22.3)	1516 (29.0)	6352 (24.2)
Townsend quintile of deprivation, n (%)					
Q 1 (most affluent)	2,865,427 (23.3)	30,305 (31.0)	627 (24.3)	340 (6.7)	1372 (5.4)
Q 2	2,605,028 (21.2)	23,879 (24.4)	536 (20.8)	478 (9.4)	2223 (8.8)
Q 3	2,379,336 (19.4)	18,159 (18.6)	476 (18.4)	838 (16.5)	4066 (16.1)
Q 4	2,182,826 (17.8)	13,769 (14.1)	465 (18.0)	1238 (24.3)	6038 (24.0)
Q 5 (most deprived)	2,094,943 (17.1)	10,902 (11.2)	447 (17.3)	2130 (41.9)	11,166 (44.3)
Ethnicity, n (%)					
White	7,725,590 (62.9)	73,183 (74.9)	1782 (69.0)	523 (10.3)	2103 (8.3)
Indian	372,335 (3.0)	1757 (1.8)	52 (2.0)	<100 (1.5)	252 (1.0)
Pakistani	249,501 (2.0)	1193 (1.2)	49 (1.9)	<100 (1.5)	97 (0.4)
Bangladeshi	163,241 (1.3)	616 (0.6)	29 (1.1)	<100 (1.5)	46 (0.2)
Other Asian	247,560 (2.0)	1010 (1.0)	36 (1.4)	<100 (1.5)	163 (0.6)
Black Caribbean	127,309 (1.0)	1550 (1.6)	47 (1.8)	615 (12.1)	4206 (16.7)
Black African	331,438 (2.7)	1526 (1.6)	92 (3.6)	2133 (41.9)	10,077 (40.0)
Chinese	142,119 (1.2)	291 (0.3)	18 (0.7)	<100 (1.5)	11 (0.0)
Other	535,231 (4.4)	2087 (2.1)	84 (3.3)	983 (19.3)	5563 (22.1)
Missing	2,380,624 (19.4)	14,494 (14.8)	394 (15.3)	619 (12.2)	2682 (10.6)

Data are N (%) unless otherwise specified. BMI = body mass index.

Cox regression models were used to identify factors associated with uptake of first, third and fourth vaccines. Secondary analyses used logistic regression and mixed effects models to explore uptake of any vaccine and Poisson regression to include the number of vaccinations within a single model. In the primary analysis, covariates in Table A1 were included. A secondary analysis included type of blood cancer as an additional covariate, using monoclonal gammopathy of undetermined significance (MGUS) as the reference category.

Analyses were performed using Stata 17MP (StataCorp, Tx) statistical software.

3. Results

Cohort characteristics are described in Table 1. The full population in the QResearch dataset meeting the inclusion criteria was 12,274,948 individuals, of whom 97,707 had a blood cancer diagnosis, 5087 had sickle cell disease, 25,200 had sickle cell trait and 2583 had aplastic anaemia. The mean age of the whole cohort was 44 (standard deviation 19.9) years and of the blood cancer group was 65.2 (17.9) years.

A higher proportion of people with blood cancer received at least one dose of vaccine compared to the general population (92% vs 79.8%) (Table 2). Similar numbers of people received the BNT162b2 and ChAdOx1 vaccine for their first and second doses, whereas the majority of third and fourth doses were BNT162b2, with smaller numbers of mRNA-1273. Numbers receiving Janssen or Valneva vaccines were negligible for all groups (not shown).

Time to uptake of the first and fourth COVID-19 vaccines in all age groups and people aged 60 years and over are shown in Fig. 1. The time to uptake of the first vaccine in people with blood cancer was similar to other immunocompromised populations. These patterns were similar for the fourth vaccine, although overall uptake of the fourth vaccine was lower. In people aged 60 or over, uptake of the first vaccine was similar between blood cancer and immunocompromised groups and slightly lower in those with aplastic anaemia and the general population. Uptake in those with sickle cell disease and sickle cell trait was lower than any of the other groups for both first and fourth vaccine. Pattern of uptake of the second and third vaccines were similar (Figure A1).

Characteristics of people with blood cancer who received zero, one to two, three or four doses of vaccine are shown in Table A2, with the majority (53.7%) receiving three doses. Uptake of each dose of vaccine stratified by demographic characteristics is shown in Figures A2–A4. Cox regression shows that uptake of

Table 2
Uptake of first, second, third and fourth dose of COVID-19 vaccine by vaccine type in people with blood cancer and other disorders.

	Full population	Blood cancer	Aplastic anaemia	Sickle cell disease	Sickle cell trait
Total (N)	12,274,948	97,707	2583	5087	25,200
Vaccine Dose 1					
Received at least 1 dose of vaccine	9,794,885 (79.8)	90,059 (92.2)	2269 (87.8)	3371 (66.3)	16,474 (65.4)
unvaccinated	2,480,063 (20.2)	7648 (7.8)	314 (12.2)	1716 (33.7)	8726 (34.6)
ChAdOx1	4,488,704 (36.6)	46,905 (48.0)	1327 (51.4)	1561 (30.7)	7796 (30.9)
BNT162b2	4,935,864 (40.2)	42,890 (43.9)	917 (35.5)	1757 (34.5)	8174 (32.4)
mRNA-1273	368,647 (3.0)	264 (0.3)	19 (0.7)	53 (1.0)	504 (2.0)
Vaccine Dose 2					
Received 2 doses of vaccine	9,245,967 (75.3)	87,603 (90.9)	129 (4.99)	3054 (60.0)	15,021 (59.6)
Unvaccinated	3,027,609 (24.7)	8732 (9.1)	454 (17.6)	2033 (40.0)	10,179 (40.4)
ChAdOx1	4,370,200 (35.6)	45,562 (47.3)	1238 (47.9)	1471 (28.9)	7441 (29.5)
BNT162b2	4,538,372 (37.0)	41,793 (43.4)	874 (33.8)	1544 (30.4)	7169 (28.4)
mRNA-1273	336,282 (2.7)	246 (0.3)	12 (0.5)	39 (0.8)	411 (1.6)
Vaccine Dose 3					
Received 3 doses of vaccine	7,123,089 (58.0)	78,289 (82.3)	1745 (67.6)	1919 (37.7)	9083 (36.0)
Unvaccinated	5,149,310 (42.0)	16,869 (17.7)	838 (32.4)	3168 (62.3)	16,117 (64.0)
ChAdOx1	17,392 (0.1)	412 (0.4)	15 (0.6)	8 (0.2)	37 (0.1)
BNT162b2	5,545,366 (45.2)	72,044 (75.7)	1578 (61.1)	1669 (32.8)	7332 (29.1)
mRNA-1273	1,560,211 (12.7)	5831 (6.1)	147 (5.7)	242 (4.8)	1714 (6.8)
Vaccine Dose 4					
Received 4 doses of vaccine	418,246 (3.4)	28,829 (31.3)	635 (24.6)	79 (1.6)	191 (0.8)
Unvaccinated	11,851,120 (96.6)	63,296 (68.7)	1948 (75.4)	5008 (98.4)	25,009 (99.2)
ChAdOx1	473 (0.0)	34 (0.0)	0 (0.0)	0 (0.0)	
BNT162b2	265,651 (2.2)	22,404 (24.3)	507 (19.6)	67 (1.3)	146 (0.6)
mRNA-1273	152,111 (1.2)	6391 (6.9)	123 (4.8)	12 (0.2)	44 (0.2)

Data are N (% of column total) unless otherwise specified.

the first dose increased with age (adjusted HR 1.02, 95% CI 1.02–1.02 per 1 year increase) and was lower in men compared to women (0.96, 0.95–0.97). These patterns were the same for the third and fourth vaccines, but uptake in men was no longer significantly lower for the fourth vaccine (Table 3).

The proportion receiving each vaccine dose varied by type of blood cancer (Table A3). Between 3.9% and 14.1% of people across all blood cancer types did not receive any vaccines, including over 9% of people with acute lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML), and Hodgkin lymphoma. The

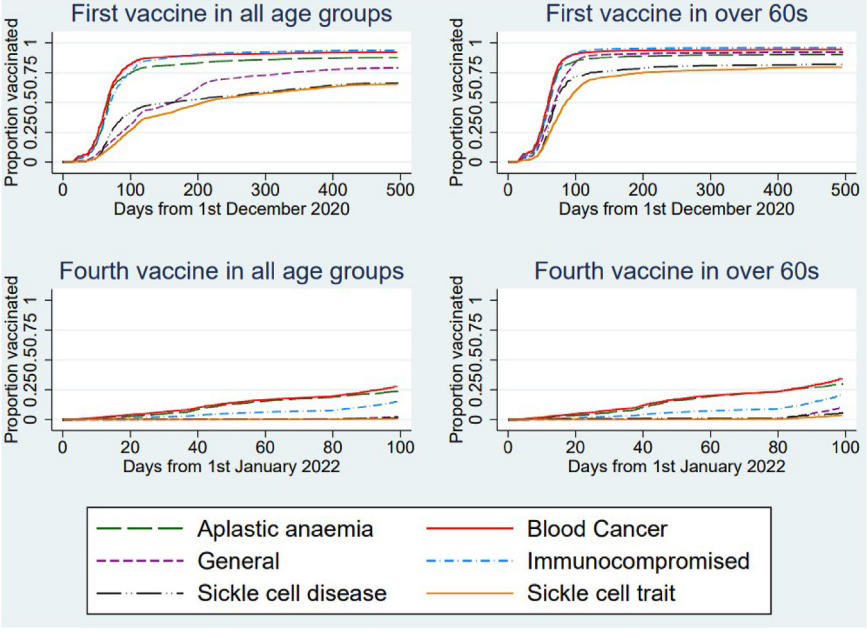

Fig. 1. Kaplan–Meier analyses of first and fourth COVID-19 vaccine uptake in people with blood cancer and other disorders, immunocompromise, and the general population, in all age groups and those 60 years and over only.

Table 3
Multivariable Cox regression analyses of first, third and fourth COVID-19 vaccine uptake in people with blood cancer.

	First vaccine		Third vaccine		Fourth vaccine	
	HR (95%CI)	p value	HR (95%CI)	p value	HR (95%CI)	p value
Age (per year)	1.02 (1.02, 1.02)	<0.001	1.01 (1.01, 1.01)	<0.001	1.00 (1.00, 1.01)	<0.001
Sex (male vs female)	0.96 (0.95, 0.97)	<0.001	0.97 (0.95, 0.98)	<0.001	1.01 (1.00, 1.02)	0.121
BMI category						
Normal weight	1		1		1	
Underweight	0.91 (0.88, 0.95)	<0.001	0.77 (0.74, 0.80)	<0.001	0.90 (0.86, 0.94)	<0.001
Overweight	1.03 (1.02, 1.05)	<0.001	1.11 (1.09, 1.12)	<0.001	1.02 (1.01, 1.04)	0.009
Obese	0.99 (0.97, 1.00)	0.122	1.07 (1.05, 1.09)	<0.001	0.97 (0.96, 0.99)	0.004
Missing	0.95 (0.93, 0.97)	<0.001	0.92 (0.90, 0.94)	<0.001	0.94 (0.93, 0.96)	<0.001
Region of England						
London	1		1		1	
East Midlands	0.99 (0.94, 1.04)	0.683	0.95 (0.91, 1.00)	0.052	0.97 (0.92, 1.02)	0.226
East of England	0.95 (0.92, 0.99)	0.006	0.93 (0.90, 0.97)	<0.001	1.00 (0.97, 1.03)	0.976
North East	1.04 (0.99, 1.08)	0.118	1.00 (0.95, 1.04)	0.830	0.95 (0.91, 1.00)	0.042
North West	1.02 (1.00, 1.04)	0.102	0.97 (0.95, 0.99)	0.002	0.99 (0.97, 1.01)	0.271
South Central	1.01 (0.98, 1.03)	0.657	1.00 (0.98, 1.03)	0.817	1.02 (1.00, 1.05)	0.094
South East	0.93 (0.91, 0.96)	<0.001	0.92 (0.90, 0.94)	<0.001	0.97 (0.95, 0.99)	0.011
South West	1.01 (0.99, 1.04)	0.316	1.05 (1.02, 1.07)	<0.001	1.11 (1.08, 1.14)	<0.001
West Midlands	1.00 (0.97, 1.02)	0.883	0.98 (0.96, 1.00)	0.110	1.00 (0.98, 1.03)	0.943
Yorkshire & Humber	1.05 (1.01, 1.09)	0.009	1.03 (0.99, 1.07)	0.110	0.97 (0.93, 1.01)	0.128
Townsend quintile						
1 (least deprived)	1		1		1	
2	0.95 (0.93, 0.96)	<0.001	0.92 (0.91, 0.94)	<0.001	0.95 (0.93, 0.96)	<0.001
3	0.89 (0.87, 0.90)	<0.001	0.83 (0.81, 0.84)	<0.001	0.90 (0.88, 0.92)	<0.001
4	0.81 (0.79, 0.82)	<0.001	0.74 (0.73, 0.76)	<0.001	0.86 (0.85, 0.88)	<0.001
5 (most deprived)	0.72 (0.70, 0.74)	<0.001	0.68 (0.66, 0.69)	<0.001	0.84 (0.82, 0.86)	<0.001
Ethnicity						
White	1		1		1	
Indian	1.00 (0.95, 1.04)	0.847	0.99 (0.94, 1.04)	0.586	0.93 (0.88, 0.97)	0.002
Pakistani	0.80 (0.75, 0.84)	<0.001	0.67 (0.63, 0.71)	<0.001	0.85 (0.80, 0.90)	<0.001
Bangladeshi	0.92 (0.85, 0.99)	0.034	0.79 (0.72, 0.85)	<0.001	0.89 (0.82, 0.97)	0.006
Other Asian	0.92 (0.86, 0.98)	0.006	0.92 (0.86, 0.98)	0.007	0.91 (0.85, 0.97)	0.002
Black Caribbean	0.53 (0.50, 0.56)	<0.001	0.61 (0.58, 0.64)	<0.001	0.83 (0.79, 0.87)	<0.001
Black African	0.71 (0.67, 0.75)	<0.001	0.71 (0.67, 0.75)	<0.001	0.87 (0.83, 0.92)	<0.001
Chinese	0.87 (0.77, 0.98)	0.020	0.96 (0.85, 1.08)	0.476	0.94 (0.84, 1.06)	0.328
Other	0.79 (0.76, 0.83)	<0.001	0.77 (0.74, 0.81)	<0.001	0.90 (0.87, 0.95)	<0.001
Missing	0.88 (0.87, 0.90)	<0.001	0.88 (0.86, 0.89)	<0.001	0.95 (0.93, 0.97)	<0.001

HR = hazard ratio. BMI = body mass index.

proportion who received four doses of vaccine was highest in people with myeloma and chronic lymphoid leukaemia (CLL) and lowest in those with ALL, Hodgkin lymphoma and histiocytic or mast cell neoplasms.

Cox regression by blood cancer type shows higher vaccine uptake for all doses of vaccine in people with indolent B-cell non-Hodgkin lymphoma (first vaccine HR 1.06, 95% CI 1.04–1.09) and CLL (first vaccine HR 1.07, 95% CI 1.05–1.10) compared to those with MGUS. There was significantly lower uptake for all doses of vaccine in some blood cancers, inlcuding Hodgkin lymphoma (first vaccine HR 0.96, 95% CI 0.93–0.99), and myeloproliferative neoplasms (first vaccine HR 0.89, 95% CI 0.87–0.91) (Table 4).

There was a trend of lower uptake with each subsequent vaccine dose across people with blood cancer, and differences became more apparent with each increasing quintile of deprivation (Figure A2). In the most deprived quintile, 16.5% did not receive any vaccine doses and 15.3% received four doses compared to 3.2% and 40.4%, respectively, in the most affluent quintile (Table A2). The trend remained after adjustment for other covariates, with uptake of the first vaccine dose significantly lower in all quintiles of deprivation compared with the most affluent quintile (adjusted HR 0.72, 95% CI 0.70–0.74 for most deprived quintile) (Table 3). This pattern remained with the third and fourth vaccines, but effect sizes were smaller for the fourth vaccine.

In people with blood cancer, a higher proportion of people from Pakistani, Bangladeshi, Black Caribbean, Black African and Other ethnic groups did not receive any doses of vaccine (13.8%, 13.6%, 28.1%, 19.5% and 19.1%, respectively) and fewer received four vaccines (6.7%, 6.2%, 9.8%, 7.1% and 13.1%, respectively) compared to all other ethnic groups (Table A2, Figure A3). Compared with people of White ethnicity, uptake of the first vaccine dose was lower in Pakistani (adjusted HR 0.80, 95% CI 0.75–0.84), other Asian (0.92, 0.86–0.98) Black Caribbean (0.53, 0.50–0.56) and Black African (0.71, 0.67–0.75) ethnicities in multivariable regression

Table 4
Multivariable Cox regression of first, third and fourth COVID-19 vaccine uptake by type of blood cancer.

Type of blood cancer	First vaccine		Third vaccine		Fourth vaccine	
	HR (95% CI)[a]	p value	HR (95% CI)[a]	p value	HR (95% CI)[a]	p value
MGUS	1		1		1	
Multiple myeloma	0.98 (0.96, 1.01)	0.279	0.94 (0.92, 0.97)	<0.001	1.22 (1.18, 1.25)	<0.001
Plasmacytoma	0.89 (0.79, 1.01)	0.065	0.93 (0.83, 1.05)	0.253	1.01 (0.89, 1.14)	0.911
Hodgkin lymphoma	0.96 (0.93, 0.99)	0.009	0.93 (0.90, 0.96)	<0.001	0.93 (0.91, 0.96)	<0.001
Indolent B-cell non-Hodgkin lymphoma	1.06 (1.04, 1.09)	<0.001	1.07 (1.04, 1.09)	<0.001	1.14 (1.11, 1.17)	<0.001
Aggressive B-cell non-Hodgkin lymphoma	0.99 (0.97, 1.02)	0.558	1.01 (0.98, 1.03)	0.689	1.04 (1.02, 1.07)	0.001
Cutaneous T/NK cell non-Hodgkin lymphoma	0.98 (0.93, 1.03)	0.473	1.00 (0.95, 1.06)	0.911	0.95 (0.90, 1.00)	0.046
Non-cutaneous T/NK cell non-Hodgkin lymphoma	0.94 (0.88, 1.00)	0.036	0.91 (0.86, 0.97)	0.005	1.01 (0.95, 1.07)	0.779
Non-Hodgkin lymphoma (unspecified)	0.89 (0.85, 0.94)	<0.001	0.93 (0.88, 0.98)	0.004	0.92 (0.88, 0.97)	0.002
Acute lymphoblastic leukaemia (ALL)	1.14 (1.09, 1.19)	<0.001	0.89 (0.85, 0.92)	<0.001	0.98 (0.94, 1.03)	0.429
Chronic lymphocytic leukaemia (CLL)	1.07 (1.05, 1.10)	<0.001	1.11 (1.08, 1.13)	<0.001	1.22 (1.19, 1.25)	<0.001
Acute myeloid leukaemia (AML)	0.92 (0.88, 0.95)	<0.001	0.83 (0.80, 0.87)	<0.001	0.99 (0.95, 1.03)	0.557
Acute promyelocytic leukaemia	1.14 (1.02, 1.28)	0.019	1.06 (0.95, 1.19)	0.275	1.01 (0.90, 1.13)	0.874
Chronic myeloid leukaemia	1.05 (1.00, 1.10)	0.040	1.06 (1.01, 1.11)	0.028	1.21 (1.15, 1.27)	<0.001
Unspecified leukaemia	0.86 (0.78, 0.95)	0.002	0.85 (0.77, 0.94)	0.001	0.93 (0.85, 1.03)	0.157
Myeloproliferative neoplasms	0.89 (0.87, 0.91)	<0.001	0.90 (0.88, 0.92)	<0.001	0.91 (0.89, 0.93)	<0.001
Myelodysplastic/myeloproliferative neoplasms	1.08 (0.97, 1.19)	0.153	0.79 (0.71, 0.87)	<0.001	1.02 (0.92, 1.13)	0.690
Myelodysplastic syndrome	0.96 (0.92, 0.99)	0.013	0.82 (0.79, 0.85)	<0.001	0.93 (0.90, 0.97)	<0.001
Histiocytic neoplasms	0.93 (0.87, 0.98)	0.012	0.86 (0.81, 0.91)	<0.001	0.91 (0.86, 0.97)	0.002
Mast cell neoplasms	0.94 (0.87, 1.02)	0.126	0.71 (0.66, 0.77)	<0.001	0.89 (0.82, 0.96)	0.004

[a] Hazard ratios adjusted for age, sex, BMI, deprivation and ethnicity. HR = hazard ratio. MGUS = monoclonal gammopathy of undetermined significance.

(Table 3). Uptake of the third vaccine was also lower in people of Bangladeshi ethnicity and uptake of the fourth vaccine was significantly lower in all ethnic groups (except Chinese) compared to white populations (Table 3).

In each ethnic group, vaccine uptake decreased as deprivation increased. Pakistani and Black Caribbean groups had the lowest uptake of three or more vaccines in the most deprived groups at under 50% (Table A4). Uptake of the first vaccine was significantly lower in those from Pakistani, Black Caribbean and Black African ethnic groups compared to White groups across all quintiles of deprivation (Table 5).

Logistic regression for any vaccine uptake, Poisson regression for number of vaccines received and mixed effects logistic regression to account for clustering within GP practices are presented in Table A5. Results are consistent with the primary analysis showing lower uptake in more deprived groups and in Pakistani, Black Caribbean and Black African populations.

4. Discussion

This is the first study to report uptake of COVID-19 vaccines in people with blood cancers. We used a dataset of over 12 million adults in primary care with linkage to the NHS National Immunisation Management Service. Of these, nearly 98,000 had a code for blood cancer diagnosis.

Compared with the general population, people with haematological malignancies (and particularly B-cell malignancies) are known to have poorer response to COVID-19 vaccination [16–18]. Recent studies have confirmed that booster vaccinations can produce seroconversion and T-cell responses in people with haematological malignancies who are seronegative after the initial course [19]. Thus ensuring uptake of booster doses, particularly in people with conditions associated with poor response, is critical. However, this study shows COVID-19 vaccine uptake in people with haematological malignancies in England declined progressively following the second vaccine, to around 30% uptake of a fourth dose, despite these groups being invited for a fourth dose within the study period. Our results indicate differential patterns of vaccine uptake between blood cancer types, with trend towards higher uptake in people with some types of chronic and low-grade blood cancers compared to acute cancers.

This analysis highlights inequalities in COVID-19 vaccine uptake in an extremely clinically vulnerable population. In the study period, vaccine uptake was over 13% lower in people from the most deprived groups compared to the most affluent, widening to 25% for the fourth vaccine. There were ethnic disparities, and these patterns persisted across all quintiles of deprivation. These findings exemplify the "inverse equity hypothesis", which expounds that when new health interventions are introduced, health inequalities tend to worsen [13]. This phenomenon could have been anticipated in COVID-19 vaccination programmes and measures taken to prevent this. Our results are consistent with UK and international studies, which similarly demonstrate association of lower COVID-19 vaccine uptake with ethnic minority groups, lower socioeconomic status, and younger age, in the general population [11,12,20–22].

Table 5
Multivariable Cox regression of uptake of first COVID-19 vaccine in people with blood cancer stratified by quintile of deprivation.

	Q1	Q2	Q3	Q4	Q5
	HR (95%CI)[a]	HR (95%CI)[a]	HR (95%CI)[a]	HR (95%CI)[a]	HR (95%CI)[a]
Age	1.03 (1.03, 1.03)	1.03 (1.03, 1.03)	1.03 (1.02, 1.03)	1.02 (1.02, 1.02)	1.02 (1.02, 1.02)
Sex (Male vs female)	0.99 (0.97, 1.02)	0.93 (0.91, 0.96)	0.97 (0.94, 1.00)	0.97 (0.93, 1.00)	0.94 (0.90, 0.98)
Region of England					
London	1	1	1	1	1
East Midlands	0.95 (0.86, 1.04)	0.90 (0.82, 0.99)	1.07 (0.94, 1.22)	0.98 (0.83, 1.16)	1.12 (0.92, 1.35)
East of England	0.88 (0.82, 0.95)	0.90 (0.84, 0.97)	0.93 (0.86, 1.01)	0.93 (0.83, 1.05)	0.87 (0.65, 1.17)
North East	0.97 (0.87, 1.07)	1.11 (1.00, 1.23)	0.92 (0.83, 1.01)	1.07 (0.97, 1.18)	1.08 (0.96, 1.22)
North West	0.97 (0.91, 1.03)	0.99 (0.94, 1.05)	1.00 (0.95, 1.06)	1.00 (0.94, 1.05)	1.06 (1.00, 1.13)
South Central	0.92 (0.87, 0.98)	0.95 (0.90, 1.01)	1.06 (1.00, 1.12)	1.06 (0.99, 1.14)	1.04 (0.91, 1.18)
South East	0.88 (0.82, 0.93)	0.90 (0.85, 0.95)	0.90 (0.85, 0.95)	0.96 (0.90, 1.03)	1.08 (0.98, 1.19)
South West	0.95 (0.89, 1.01)	0.97 (0.92, 1.03)	1.00 (0.94, 1.06)	1.03 (0.96, 1.11)	1.07 (0.97, 1.19)
West Midlands	0.91 (0.86, 0.97)	0.97 (0.92, 1.03)	1.01 (0.95, 1.07)	1.01 (0.95, 1.09)	1.03 (0.94, 1.13)
Yorkshire & Humber	0.94 (0.87, 1.02)	1.03 (0.95, 1.12)	1.12 (1.01, 1.24)	1.06 (0.96, 1.17)	1.18 (1.04, 1.35)
Ethnicity					
White	1	1	1	1	1
Indian	1.06 (0.94, 1.20)	1.04 (0.93, 1.16)	1.02 (0.91, 1.13)	1.05 (0.93, 1.18)	0.93 (0.80, 1.07)
Pakistani	0.66 (0.54, 0.81)	0.76 (0.63, 0.91)	0.74 (0.65, 0.84)	0.83 (0.74, 0.93)	0.81 (0.70, 0.95)
Bangladeshi	0.79 (0.44, 1.42)	1.04 (0.65, 1.68)	0.90 (0.70, 1.16)	0.94 (0.77, 1.15)	0.91 (0.82, 1.01)
Other Asian	0.85 (0.70, 1.04)	0.80 (0.68, 0.96)	1.00 (0.87, 1.15)	0.93 (0.80, 1.07)	0.95 (0.82, 1.11)
Black Caribbean	0.47 (0.35, 0.63)	0.57 (0.46, 0.69)	0.54 (0.47, 0.62)	0.49 (0.44, 0.55)	0.57 (0.53, 0.62)
Black African	0.66 (0.51, 0.86)	0.68 (0.55, 0.83)	0.67 (0.56, 0.79)	0.71 (0.63, 0.81)	0.74 (0.69, 0.81)
Chinese	0.80 (0.59, 1.09)	0.75 (0.56, 1.00)	0.78 (0.58, 1.06)	1.08 (0.81, 1.44)	1.03 (0.81, 1.31)
Other	0.84 (0.73, 0.97)	0.86 (0.75, 0.98)	0.80 (0.71, 0.89)	0.76 (0.69, 0.85)	0.75 (0.69, 0.82)
Missing	0.94 (0.90, 0.97)	0.90 (0.87, 0.94)	0.88 (0.84, 0.92)	0.89 (0.84, 0.94)	0.79 (0.73, 0.86)

[a] Hazard ratios are adjusted for age, sex, BMI and ethnicity.

Some studies show women are less likely to be vaccinated than men, which differs from findings in this blood cancer population [10,23].

Declining booster vaccine uptake in people with compromised immune systems and socioeconomic and ethnic disparities suggest vaccination programmes are not adequately serving all parts of the patient community. These need to be addressed prior to future vaccine booster rollout.

Reasons for COVID-19 vaccine hesitancy may include lack of trust in government/medical authorities, concerns about vaccine safety and effectiveness, and lack of trusted sources of information and accessible communications, particularly for ethnic minority groups [21,24–27]. This study shows that hesitancy by ethnic minority groups also applies to those who are most vulnerable, suggesting targeted measures in clinical settings may be needed.

In cancer patients, COVID-19 vaccine uptake may be influenced by patient and disease-related factors - not being on current anticancer treatment and disease remission are associated with higher uptake. Key barriers are concerns regarding vaccine side effects and lack of clear medical advice [28,29]. This is reflected in our results. Differences in uptake across blood cancer types may indicate need for targeted messaging on vaccination for specific disease groups. People with conditions involving active/intensive treatments may be less likely to get vaccinated, as vaccination may be perceived to be less efficacious during treatment. However, there is strong expert consensus for recommendation of COVID-19 vaccination in these patients [30]. Further action to increase uptake of COVID-19 vaccines in blood cancer patients is imperative.

Our study has some limitations. Full cancer registry data, the most reliable source of defining populations with cancer, was only available up to December 2018. Hospital and primary care records were used to identify more recent cancer diagnosis, which may have resulted in less accurate classifications. Some people were coded with more than one type of blood cancer in their medical records. This may be due to deficits in recording of cancer remission, relapse and transformation in routine health record data. We assigned the most relevant diagnosis using pre-determined rules (see Methods), guided by expert clinical opinion, but instances of misclassification may still occur. In our analysis, 15% of the cohort with blood cancer had missing ethnicity and 2% were classified as "other" ethnicity, both of which had lower vaccine uptake than white populations. Our analysis did not examine reasons for low uptake; further research is needed to address this.

5. Conclusions

This population-based study shows that there is a reduction in COVID-19 vaccine uptake over time and there are inequalities in uptake affecting those with the greatest clinical need. Current policies, communication on, and delivery of, COVID-19 vaccines to people with

blood cancers should be improved to ensure equitable uptake. To enable confident and accurate communication of benefits/risks of vaccination, further research is needed to understand the effectiveness and safety of vaccination in patients with blood cancer.

Authors' contributions

JHC, CC, MP and EM conceived and designed the study. JHC obtained the funding and oversaw data extraction. EM and JHC designed the code groups for analysis. EM, JAH and EC analysed and interpreted data. MP, JHC and CC supported data analysis. EM, JAH and EC wrote the manuscript and all authors revised the manuscript for intellectual content and approved the final version. All authors had responsibility for the integrity and accuracy of the work and the decision to submit for publication.

Patient and public involvement

Two patient representatives sit on the study steering committee. They have contributed to refinement of the research questions and review of results of analyses to help ensure they are relevant to the patient and clinician community. The patient representatives have helped to develop plans for dissemination of the study findings. A plain English summary of the findings from this study have been shared with the patient representatives.

Ethics approval and consent to participate

The QResearch® ethics approval was provided by the East Midlands-Derby Research Ethics Committee [reference 18/EM/0400] and reviewed by the QResearch science committee [Project OX300]. Consent from participants was not required. The study was performed in accordance with the Declaration of Helsinki.

Data availability

To guarantee the confidentiality of personal and health information only the authors have had access to the data during the study in accordance with the relevant licence agreements. Access to the QResearch data is according to the information on the QResearch website (www.qresearch.org). Code groups are published at https://www.qresearch.org/data/qcode-group-library/

Role of the funding source

The funders of this study had no role in study design, data collection, data analysis, data interpretation, writing of the report, or decision to submit the article for publication.

Conflict of interest statement

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: JHC reports grants from National Institute for Health Research (NIHR) Biomedical Research Centre, Oxford, grants from John Fell Oxford University Press Research Fund, and other research councils, during the conduct of the study. JHC is an unpaid director of QResearch, a not-for-profit organisation which is a partnership between the University of Oxford and EMIS Health who supply the QResearch database used for this work. JHC is a founder and shareholder of ClinRisk ltd and was its medical director until 31st May 2019. ClinRisk Ltd produces open and closed source software to implement clinical risk algorithms (outside this work) into clinical computer systems. JHC was chair of the NERVTAG risk stratification subgroup and is a member of SAGE COVID-19 groups and the NHS group advising on prioritisation of use of monoclonal antibodies in COVID-19 infection. All other authors declare no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

The authors acknowledge Ashley Clift and Allison Hirst for their support in the early part of the project. We wish to thank Jennifer Dziurzynski-Watson and Malcolm Rhodes, our patient representatives, for their contribution to this research. We acknowledge the contribution of EMIS practices who contribute to QResearch® and EMIS Health and the Universities of Nottingham and Oxford for expertise in establishing, developing or supporting the QResearch database. This project involves data derived from patient-level information collected by the NHS, as part of the care and support of cancer patients. The data are collated, maintained and quality assured by the National Cancer Registration and Analysis Service, which is now part NHS Digital. The Hospital Episode Statistics data, SARS-Cov-2 results and civil registration mortality data are used by permission from NHS Digital who retain the copyright in that data. NHS Digital and Public Health England bears no responsibility for the analysis or interpretation of the data.

Funding

This work was funded by Blood Cancer UK, grant number 21019. The researchers are independent from Blood Cancer UK. QResearch is supported by funds from the John Fell Oxford University Press Research Fund, grants from Cancer Research UK (CR-UK) grant

number C5255/A18085, through the Cancer Research UK Oxford Centre during the conduct of the study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejca.2023.02.001.

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