Outcomes of the SARS-CoV-2 omicron (B.1.1.529) variant outbreak among vaccinated and unvaccinated patients with cancer in Europe: results from the retrospective, multicentre, OnCovid registry study

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Summary

Background The omicron (B.1.1.529) variant of SARS-CoV-2 is highly transmissible and escapes vaccine-induced immunity. We aimed to describe outcomes due to COVID-19 during the omicron outbreak compared with the prevaccination period and alpha (B.1.1.7) and delta (B.1.617.2) waves in patients with cancer in Europe.

Methods In this retrospective analysis of the multicentre OnCovid Registry study, we recruited patients aged 18 years or older with laboratory-confirmed diagnosis of SARS-CoV-2, who had a history of solid or haematological malignancy that was either active or in remission. Patient were recruited from 37 oncology centres from UK, Italy, Spain, France, Belgium, and Germany. Participants were followed up from COVID-19 diagnosis until death or loss to follow-up, while being treated as per standard of care. For this analysis, we excluded data from centres that did not actively enter new data after March 1, 2021 (in France, Germany, and Belgium). We compared measures of COVID-19 morbidity, which were complications from COVID-19, hospitalisation due to COVID-19, and requirement of supplemental oxygen and COVID-19-specific therapies, and COVID-19 mortality across three time periods designated as the prevaccination (Feb 27 to Nov 30, 2020), alpha-delta (Dec 1, 2020, to Dec 14, 2021), and omicron (Dec 15, 2021, to Jan 31, 2022) phases. We assessed all-cause case-fatality rates at 14 days and 28 days after diagnosis of COVID-19 overall and in unvaccinated and fully vaccinated patients and in those who received a booster dose, after adjusting for country of origin, sex, age, comorbidities, tumour type, stage, and status, and receipt of systemic anti-cancer therapy. This study is registered with ClinicalTrials.gov, NCT04393974, and is ongoing.

Findings As of Feb 4, 2022 (database lock), the registry included 3820 patients who had been diagnosed with COVID-19 between Feb 27, 2020, and Jan 31, 2022. 3473 patients were eligible for inclusion (1640 [47·4%] were women and 1822 [52·6%] were men, with a median age of 68 years [IQR 57–77]). 2033 (58·5%) of 3473 were diagnosed during the prevaccination phase, 1075 (31·0%) during the alpha-delta phase, and 365 (10·5%) during the omicron phase. Among patients diagnosed during the omicron phase, 113 (33·3%) of 339 were fully vaccinated and 165 (48·7%) were boosted, whereas among those diagnosed during the alpha-delta phase, 152 (16·6%) of 915 were fully vaccinated and 21 (2·3%) were boosted. Compared with patients diagnosed during the prevaccination period, those who were diagnosed during the omicron phase had lower case-fatality rates at 14 days (adjusted odds ratio [OR] 0·32 [95% CI 0·19–0·61) and 28 days (0·34 [0·16–0·79]), complications due to COVID-19 (0·26 [0·17–0·46]), and hospitalisation due to COVID-19 (0·17 [0·09–0·32]), and had less requirements for COVID-19-specific therapy (0·22 [0·15–0·34]) and oxygen therapy (0·24 [0·14–0·43]) than did those diagnosed during the alpha-delta phase. Unvaccinated patients diagnosed during the omicron phase had similar crude case-fatality rates at 14 days (ten [25%] of 40 patients *vs* 114 [17%] of 656) and at 28 days (11 [27%] of 40 *vs* 184 [28%] of 656) and similar rates of hospitalisation due to COVID-19 (18 [43%] of 42 *vs* 266 [41%] of 652) and complications from COVID-19 (13 [31%] of 42 *vs* 237 [36%] of 659) as those diagnosed during the alpha-delta phase.

Interpretation Despite time-dependent improvements in outcomes reported in the omicron phase compared with the earlier phases of the pandemic, patients with cancer remain highly susceptible to SARS-CoV-2 if they are not vaccinated against SARS-CoV-2. Our findings support universal vaccination of patients with cancer as a protective measure against morbidity and mortality from COVID-19.

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Introduction

The evolving nature of pandemics is the product of the dynamic interplay between pathogen, environment, and host,[1] and the SARS-CoV-2 pandemic is no exception.[2] Since March, 2020, the evolution of viral transmission has resulted in multiple outbreaks across the world intercalated by steady states. Morbidity, mortality, and socioeconomic consequences of the COVID-19 pandemic have been substantially affected by the succession of emerging variants of concern of SARS-CoV-2, each characterised by various degrees of virulence.[3]

On Nov 26, 2021, the omicron (B.1.1.529) variant was identified in South Africa and Botswana as a new and highly transmissible variant of concern and was subsequently the cause of a pandemic surge in Europe and the USA in late 2021 to early 2022.[4]

Although data from the general population suggest that the clinical course of infection with the omicron variant is milder than with the previous variants, as a result of the reduced cellular tropism for cells of the lower respiratory tract overexpressing transmembrane protease serine 2,[5,6] the substantial immune-escape potential of this variant remains a key concern for those who are at highest risk.[7,8]

Patients with cancer are especially susceptible to COVID-19, both acutely and chronically.[9] Although improving trends in mortality had been seen even before the introduction of SARS-CoV-2 vaccines,[10] universal vaccination and boosting of immunity have been set out as clear objectives to protect patients with cancer from the persistent threat of COVID-19.[11] Despite initial evidence of lower case-fatality rates during the omicron wave of the pandemic than during previous waves,[5] whether the improved prognosis of patients with cancer is the result of a multifactorial process, which includes the effective implementation of immunisation and booster campaigns,[12] enhancement of public health measures and improved management of the disease,[10] or just a consequence of inherent biological differences of the emerging variant is unknown.[13] Similarly, there are no large real-world case series describing uptake and effectiveness of SARS-CoV-2 vaccine booster doses in patients with cancer.

In this study from the OnCovid registry, we compared morbidity and mortality in patients with cancer diagnosed with COVID-19 during the omicron outbreak in Europe against previous phases of the pandemic. We also assessed whether receipt of two or three doses of

Research in context

Evidence before this study

The emerging omicron (B.1.1.529) variant of SARS-CoV-2 is characterised by increased transmissibility and immune escape potential and is responsible of the late 2021 into early 2022 COVID-19 pandemic surge across Europe. COVID-19 illness due to omicron variant has been reported to be less severe than with previous variants. Patients with cancer are especially vulnerable to COVID-19; however, outcomes in this patient population during the omicron wave have not been characterised. We searched PubMed for publications in English, from database inception to Feb 28, 2022, on the effect of omicron-related COVID-19 in patients with cancer using the search terms ("COVID-19" OR "SARS-CoV-2") AND ("oncology" OR "cancer" OR "malignancy") AND ("omicron" OR "B.1.1.529"). Although registry studies have provided evidence of decreasing case-fatality rates over time, even in patients with cancer, there is no evidence to clearly infer whether omicron-related COVID-19 is characterised by decreased severity in this specific population. Additionally, published studies derived information on vaccine and booster dose efficacy through the assessment of their immunogenicity potential without a direct measure of their clinical efficacy.

Added value of this study

To our knowledge, this is the largest retrospective registry study of patients with cancer in Europe to report data on omicron to date. In this study, we found that patients with cancer diagnosed with COVID-19 during the omicron outbreak in Europe had significantly lower mortality than did those diagnosed during previous phases of the pandemic. Measures of COVID-19 morbidity, such as hospitalisation and complication rates, were similarly improved. However, we found that the major determinant of the improved outcomes was previous SARS-CoV-2 vaccination. In unvaccinated patients diagnosed during the omicron phase of the pandemic, mortality was as high as that recorded in previous phases of the pandemic. Receipt of full vaccination and boosting was associated with improvement in COVID-19 outcomes in comparison with unvaccinated patients, independently of demographics and oncological features.

Implications of all the available evidence

The major determinants of the significantly improved outcomes are most likely immunisation and booster campaigns, as suggested by the high mortality rate reported for unvaccinated patients. SARS-CoV-2 vaccines are confirmed to be the most valuable instrument to protect patients with cancer from COVID-19 and their widespread distribution should continue to be promoted.

SARS-CoV-2 vaccine affected COVID-19 outcomes in these patients versus those who were unvaccinated.

Methods

Study design and participants

OnCovid is an ongoing European registry study collecting data from consecutive patients from 37 oncology centres in the UK, Italy, Spain, France, Belgium, and Germany (appendix p 5). Patients are eligible for inclusion if they are aged 18 years or older, with an RT-PCR confirmed SARS-CoV-2 infection, and history of solid or haematological malignancy either active or in remission at the time of COVID-19 diagnosis (appendix pp 2–4). To ensure consecutive accrual and comparability of outcomes, we excluded data from three centres (in France, Germany, and Belgium) that did not actively enter new data after March 1, 2021, which was the date of database lock from a previous study. We also excluded patients for whom the date of COVID-19 diagnosis was missing.

OnCovid was granted central approval by the UK Health Research Authority (20/HRA/1608) and by the corresponding research ethics committees at each participating institution. Full waiver of consent due to the retrospective nature of the study was granted by the UK Health Research Authority.

Procedures

Core study data were collated from electronic medical records into a case report form designed using the REDCap (version 11.1.29) software. Multisite access and data curation were coordinated by the Medical Statistics Unit in Novara, Italy.

The overarching objective of this study was to describe COVID-19 morbidity and mortality in patients with cancer during the omicron outbreak in Europe in comparison with previous phases of the pandemic and to assess clinical outcomes in patients who had received a full vaccination course against SARS-CoV-2 with or without a third booster dose compared with unvaccinated individuals.

We assessed the distribution of patient characteristics, COVID-19 severity, and mortality across three predefined phases reflective of the evolution of the COVID-19 pandemic in Europe. We divided groups according to date of COVID-19 diagnosis as follows: the prevaccination phase (Feb 27 to Nov 30, 2020), the alpha (B.1.1.7)–delta (B.1.617.2) variants phase (Dec 1, 2020, to Dec 14, 2021),[14] and the omicron (B.1.1.529) variant phase (Dec 15, 2021, to Jan 31, 2022).[15]

The main clinical endpoints were all-cause case-fatality rates at 14 days and 28 days after diagnosis.[10] We then analysed outcomes reflective of COVID-19 severity that we described in previous publications,[10,16–19] including rates of hospitalisation due to COVID-19, complications from COVID-19 (acute respiratory failure and acute respiratory distress syndrome, kidney injury, secondary infections, sepsis, septic shock, acute cardiac injury, acute liver injury, and others or unspecified complications), and requirement for supplemental oxygen therapy and COVID-19-specific therapy (including chloroquine–hydroxychloroquine, antibiotics, steroids, antivirals, interleukin [IL]-6 inhibitors, and others or unspecified therapy).

We also assessed, in univariable analyses only, the experience of at least one COVID-19-related symptom (which included fever, cough, fatigue, dyspnoea, anosmia, dysgeusia, coryzal symptoms, diarrhoea, headache, myalgia, nausea or vomiting, sore throat, and others or unspecified symptoms), and rate of pre-existing hospitalisations across the three phases.

Statistical analysis

Patient observation started from the date of COVID-19 diagnosis until patient death, loss to follow-up, or data cutoff (Feb 4, 2022) for censored patients, whichever occurred first. Patients were censored if they were alive at their last follow-up, and they were considered as lost to follow-up if they did not attend planned appointments for any reason. Although patients who were lost to follow-up were excluded from the outcome analyses, those with incomplete follow-up (marked as censored but with an observation period of <14 days from COVID-19 diagnosis) were included in the 14-day case-fatality rate and 28-day case-fatality rate analyses to maximise the sample size of the omicron phase.

We summarised baseline characteristics as categorical variables and then using descriptive statistics. Missing values were excluded from the denominator when calculating proportions and for any formal subgroup comparisons; however, missing data proportions were calculated using the whole reference population. We tested associations between categorical variables using Fisher's exact test and the Pearson χ^2 test, as appropriate. We present COVID-19 outcomes using crude rates and Poisson 95% CI. We used the binomial Clopper-Pearson method to calculate 95% CIs for groups with limited sample sizes as appropriate.

Risk of each COVID-19 outcome of patients diagnosed during the alpha-delta and the omicron phases were compared with those of patients diagnosed during the prevaccination phase using separated fixed multivariable logistic regression models and presented as adjusted odds ratios (ORs) with 95% CI. We used the following covariates, which were based on established prognostic factors in patients with COVID-19 and cancer:[10,16,17,19] country (UK *vs* Spain *vs* Italy), sex (male *vs* female), age (continuous), number of comorbidities (0–1 *vs* ≥2), primary tumour (clustered as breast, gastrointestinal, genitourinary or gynaecological, thoracic, haematological, and others), tumour stage at time of COVID-19 diagnosis (advanced *vs* non-advanced), tumour status at time of COVID-19 diagnosis (active *vs* non-active), and the receipt of systemic anticancer therapy within 4 weeks before COVID-19 diagnosis (yes *vs* no). Patients with missing information for any of the covariates were

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See Online for appendix

excluded from this analysis. We assessed risk of death at 28 days using the same fixed multivariable modelling through the Cox regression, with results presented as adjusted hazard ratios (HR) with 95% CIs.

To provide additional insight on the role of SARS-CoV-2 vaccines on the evolution of the pandemic and on COVID-19 outcomes in patients diagnosed with COVID-19 during the omicron phase, we assessed demographics and oncological characteristics among unvaccinated patients diagnosed during the alpha-delta and omicron phases, and then we described COVID-19-associated morbidity and mortality among unvaccinated and vaccinated patients (defined as those who received at least one dose of a SARS-CoV-2 vaccine) across the predefined phases. Given the substantially unbalanced sample size of the unvaccinated subgroups, we did two propensity score-matching procedures between unvaccinated patients from the omicron phase and unvaccinated patients from the alpha-delta phase, and between unvaccinated patients from the omicron phase and patients from the prevaccination phase to offer a comparison of the 14-day case-fatality rate of unvaccinated patients across the phases. For the propensity-score matching, we used a 1:3 ratio and a caliper of 0·2 SD, and we estimated its balancing ability using standardised mean differences (SMD) of the matched characteristics.

To assess vaccination trends and their effectiveness, we assessed COVID-19-associated morbidity and mortality at 14 and 28 days after diagnosis among patients diagnosed from the date of the first SARS-CoV-2 breakthrough infection reported in a boosted patient onwards (ie, from Nov 17, 2021, to database lock on Feb 4, 2022). We used this approach to ensure comparability of vaccination subgroups, given the already established strong and significant time-dependent changes in demographics, oncological characteristics, and COVID-19 outcomes in patients with cancer.[10] Patients with unknown vaccination status were excluded from the analysis.

Patients who received two doses of the BNT162b2 (Pfizer–BioNTech), mRNA-1273 (Moderna), and ChAdOx1-S (Oxford–AstraZeneca) vaccines before diagnosis with COVID-19, or patients who were diagnosed at least 28 days after a single dose of the Ad26.COV2.S (Johnson & Johnson) vaccine, were defined as fully vaccinated. Patients who had received at least one dose of the BNT162b2, mRNA-1273, or ChAdOx1-S vaccine, without meeting these criteria, were considered to be partially vaccinated, and patients who had received a third dose of either the BNT162b2 or mRNA-1273 vaccine (or a second dose after the Ad26.COV2.S vaccine) were considered to be boosted.

After having assessed with univariable analysis all COVID-19 outcomes between unvaccinated, fully and partially vaccinated, and boosted patients, we adopted a two-tiered approach. First, we reported COVID-19 outcomes between unvaccinated and vaccinated patients, including all patients who received at least one dose of vaccine. We then explored vaccination subgroups by comparing the 14-day case-fatality rate and 28-day case-fatality rate separately between boosted, fully and partially vaccinated, and unvaccinated patients, and then between fully and partially vaccinated patients and boosted patients. Considering the comparatively smaller sample size of the unvaccinated subgroup, we used inverse probability of treatment weighting (IPTW) accounting for selected demographic and oncological characteristics across subgroups of interest, to optimise numerosity and ensure comparability of COVID-19 outcomes in the fitted multivariable analyses. Variables with missing data were included in the IPTW by grouping them as reference terms in case of less than 5% missingness and as an unknown category in case of 5% missingness or higher. The following covariates were included in the first-tier vaccination analysis: country (UK *vs* Spain *vs* Italy), sex (male *vs* female), age (≥65 years *vs* <65 years), number of comorbidities (≥2 *vs* 0–1), tumour status at time of COVID-19 diagnosis (active *vs* non-active), tumour stage at time of COVID-19 diagnosis (advanced *vs* non-advanced *vs* unknown), and receipt of systemic anti-cancer therapy at time of COVID-19 diagnosis (yes *vs* no *vs* unknown). Because of the reduced sample size, only sex, age, comorbidities, and tumour status were included in the IPTW for the second-tier vaccination analysis. We assessed the balancing ability of each IPTW through the distribution of unweighted and weighted variables with relevant p values and SMD.

We then fitted propensity score-weighted logistic regression models for each COVID-19 outcome of interest, using the weighted covariates. We estimated the variance for the IPTW using a cluster-robust standard error evaluation for each variable.

Considering that the data source consisted of 37 institutions, we corrected all multivariable models for the main pandemic phases and SARS-CoV-2 vaccination analyses using a clustered-robust standard error adjustment for participating centre, with results presented using corrected 95% CIs, and unadjusted standard errors and p values.

Finally, we report COVID-19 outcomes among patients with solid tumours and haematological malignancies[20] included in the vaccination analysis to determine the potential different effectiveness of SARS-CoV-2 vaccines between the two categories.

We considered p value of less than 0·05 to be significant. This study is registered with ClinicalTrials.gov, NCT04393974.

Role of the funding source

Neither study sponsor nor the study funders had any role in study design, data collection, data analysis, data interpretation, or writing of the report.

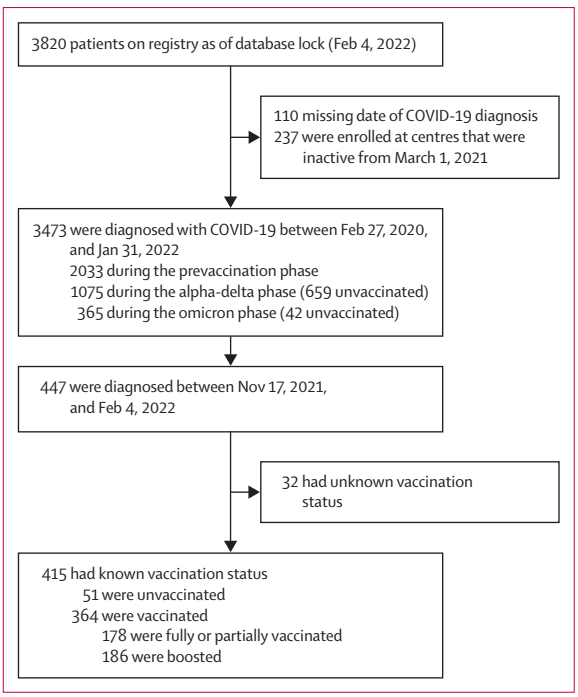

Figure 1: **Study flow diagram**

Results

By the database lock on Feb 4, 2022, the registry included 3820 patients diagnosed with COVID-19 between Feb 27, 2020, and Jan 31, 2022. 347 patients were excluded, such that 3473 (90·9%) eligible patients from 34 centres across three countries (UK, Spain, and Italy) were included in this analysis (figure 1). 2033 (58·5%) of 3473 patients were diagnosed during the prevaccination phase, 1075 (31·0%) during the alpha-delta phase, and 365 (10·5%) during the omicron phase, with 226 cases diagnosed per month in the prevaccination phase, 85 during the alpha-delta phase, and 243 during the omicron phase.

Demographic and clinical characteristics of eligible patients are shown in table 1. Overall, 1640 (47·4%) of 3462 patients with data were women and 1822 (52·6%) were men, with a median age of 68 years (IQR 57–77). Data on ethnicity and race were not collected. Patients diagnosed during the omicron phase were more likely to be younger than 65 years (p=0·0041), and with fewer than two comorbidities (p=0·0013) than those diagnosed in the prevaccination or alpha-delta phases. However, a greater proportion of patients diagnosed during the omicron phase had advanced stage tumours (p<0·0001) and were receiving systemic anticancer therapy at the time of COVID-19 diagnosis (p<0·0001). The proportions of fully vaccinated and boosted patients were higher during the omicron phase than the alpha-delta phase (p<0·0001 for both). None of the patients diagnosed during the prevaccination phase received experimental vaccine therapy. Country of origin (p<0·0001) and

	Overall population (N=3473)	Prevaccination phase (n=2033)	Alpha-delta phase (n=1075)	Omicron phase (n=365)	p value
Country	..	..	..	..	<0·0001
UK	1348 (38·8%)	688 (33·8%)	535 (49·8%)	125 (34·2%)	..
Spain	1041 (30·0%)	631 (31·0%)	274 (25·5%)	136 (37·3%)	..
Italy	1084 (31·2%)	714 (35·1%)	266 (24·7%)	104 (28·5%)	..
Sex	..	..	..	..	0·37
Female	1640/3462 (47·4%)	941/2028 (46·4%)	526/1073 (49·0%)	173/361 (47·9%)	..
Male	1822/3462 (52·6%)	1087/2028 (53·6%)	547/1073 (51·0%)	188/361 (52·1%)	..
Missing*	11 (0·3%)	5 (0·2%)	2 (0·2%)	4 (1·1%)	..
Age	..	..	..	..	0·0041
<65 years	1430/3453 (41·4%)	801/2024 (39·6%)	454/1069 (42·5%)	175/360 (48·6%)	..
≥65 years	2023/3453 (58·6%)	1223/2024 (60·4%)	615/1069 (57·5%)	185/360 (51·4%)	..
Missing*	20 (0·6%)	9 (0·4%)	6 (0·6%)	5 (1·4%)	..
Comorbidities	..	..	..	..	0·0013
0–1	1883 (54·2%)	1059 (52·1%)	598 (55·6%)	226 (61·9%)	..
≥2	1590 (45·8%)	974 (47·9%)	477 (44·4%)	139 (38·1%)	..
Smoking history	..	..	..	..	0·10
Never smokers	1410/2858 (49·3%)	857/1682 (51·0%)	414/874 (47·4%)	139/302 (46·0%)	..
Former or current smokers	1448/2858 (50·7%)	825/1682 (49·0%)	460/874 (52·6%)	163/302 (54·0%)	..
Missing*	615 (17·7%)	351 (17·3%)	201 (18·7%)	63 (17·3%)	..
Primary tumour	..	..	..	..	<0·0001
Breast	616/3448 (17·9%)	395/2024 (19·5%)	164/1062 (15·4%)	57/362 (15·7%)	..
Gastrointestinal	881/3448 (25·6%)	501/2024 (24·8%)	275/1062 (25·9%)	105/362 (29·0%)	..
Gynaecological or genitourinary	653/3448 (18·9%)	391/2024 (19·3%)	217/1062 (20·4%)	45/362 (12·4%)	..
Thoracic	563/3448 (16·3%)	293/2024 (14·5%)	197/1062 (18·5%)	73/362 (20·2%)	..
Others	238/3448 (6·9%)	134/2024 (6·6%)	85/1062 (8·0%)	19/362 (5·2%)	..
Haematological	497/3448 (14·4%)	310/2024 (15·3%)	124/1062 (11·7%)	63/362 (17·4%)	..
Missing*	25 (0·7%)	9 (0·4%)	13 (1·2%)	3 (0·8%)	..
Tumour stage	..	..	..	..	<0·0001
Non-advanced	1560/3228 (48·3%)	967/1895 (51·0%)	465/995 (46·7%)	128/338 (37·9%)	..
Advanced	1668/3228 (51·7%)	928/1895 (49·0%)	530/995 (53·3%)	210/338 (62·1%)	..
Missing*	245 (7·1%)	138 (6·8%)	80 (7·4%)	27 (7·4%)	..

(Table 1 continues on next page)

	Overall population (N=3473)	Prevaccination phase (n=2033)	Alpha-delta phase (n=1075)	Omicron phase (n=365)	p value
(Continued from previous page)					
Status at COVID-19 diagnosis	..	..	..	..	0·11
Remission or non-measurable	1403/3434 (40·9%)	826/2002 (41·3%)	447/1069 (41·8%)	130/363 (35·8%)	..
Active malignancy	2031/3434 (59·1%)	1176/2002 (58·7%)	622/1069 (58·2%)	233/363 (64·2%)	..
Missing*	39 (1·1%)	31 (1·5%)	6 (0·6%)	2 (0·5%)	..
Systemic anticancer therapy at COVID-19 diagnosis†	..	..	..	..	<0·0001
No	1892/3289 (57·5%)	1179/1952 (60·4%)	561/1000 (56·1%)	152/337 (45·1%)	..
Yes	1397/3289 (42·5%)	773/1952 (39·6%)	439/1000 (43·9%)	185/337 (54·9%)	..
Chemotherapy (monotherapy and combination therapy)	716/3289 (21·8%)	383/1952 (19·6%)	237/1000 (23·7%)	96/337 (28·5%)	0·0003
Immune checkpoint inhibitor-only regimens	130/3289 (4·0%)	58/1952 (3·0%)	46/1000 (4·6%)	26/337 (7·7%)	0·0001
Endocrine therapy	201/3289 (6·1%)	133/1952 (6·8%)	53/1000 (5·3%)	15/337 (4·5%)	0·10
Tyrosine kinase inhibitors, monoclonal antibodies, and other systemic anticancer therapy	346/3289 (10·5%)	195/1952 (10·0%)	103/1000 (10·3%)	48/337 (14·2%)	0·061
Missing*	184 (5·3%)	81 (4·0%)	75 (6·9%)	28 (7·7%)	..
SARS-CoV-2 vaccination status	..	..	..	..	<0·0001
Unvaccinated	2734/3287 (83·2%)	2033 (100%)	659/915 (72·0%)	42/339 (12·4%)	..
Partially vaccinated	102/3287 (3·1%)	NA	83/915 (9·1%)	19/339 (5·6%)	..
Fully vaccinated	265/3287 (8·1%)	NA	152/915 (16·6%)	113/339 (33·3%)	..
Boosted	186/3287 (5·6%)	NA	21/915 (2·3%)	165/339 (48·7%)	..
Missing*	186 (5·3%)	NA	160 (14·9%)	26 (7·1%)	..
Incomplete follow-up (ie, <14 days)	215 (6·2%)	75 (3·7%)	67 (6·2%)	73 (20·0%)	..

Data are n (%) or n/N (%). NA=not applicable. *Missing values were excluded from denominator when calculating proportions and for any formal subgroup comparisons; however, missing data proportions were calculated using the whole reference population. †Defined as within 4 weeks before COVID-19 diagnosis.

Table 1: **Baseline characteristics of the overall population across the predefined phases of the pandemic**

distribution of primary tumour types (p<0·0001) were significantly different across phases, with a higher proportion of patients diagnosed during the omicron phase than during the other phases having haematological, thoracic, and gastrointestinal malignancies (table 1).

Among 265 fully vaccinated patients, 111 (41·9%) received BNT162b2, 48 (18·1%) received mRNA-1273, 64 (24·2%) received ChAdOx1-S, and three (1·1%) received the Ad.26.COV2.S vaccine, with 39 (14·7%) patients having an unspecified vaccine administered. Among 102 partially vaccinated patients, 30 (29·4%) received the BNT162b2 vaccine, 31 (30·4%) received mRNA-1273, and 16 (15·7%) received the ChAdOx1-S vaccine, with 25 (24·5%) having an unspecified vaccine administered. Among 186 boosted patients, 88 (47·3%) received BNT162b2, 49 (26·3%) received mRNA-1273, 32 (17·2%) received ChAdOx1-S, and three (1·6%) received the Ad.26.COV2.S vaccine, with 14 (7·5%) having an unspecified vaccine administered (appendix p 6).

The median observation period was 89 days (IQR 13–382) for the prevaccination phase, 53 days (18–216) for the alpha-delta phase, and 20 days (13–28) for the omicron phase. COVID-19 outcomes across the predefined phases are shown in figure 2A and table 2. Patients diagnosed during the omicron phase had improved 14-day case-fatality rate (p<0·0001) and 28-day case-fatality rate (p<0·0001), reduced hospitalisations due to COVID-19 (p<0·0001), reduced COVID-19 complications (p<0·0001), and reduced need for COVID-19-specific therapy (p<0·0001) and oxygen therapy (p<0·0001) compared with the alpha-delta and prevaccination phases.

After adjusting for country of origin, sex, age, comorbidities, tumour stage, tumour status, and receipt of systemic anticancer therapy at time of COVID-19 diagnosis, and after the cluster adjustment for participating centre, compared with patients diagnosed during the prevaccination phase, patients diagnosed during the omicron phase had a lower case-fatality rate at 14 days (adjusted OR 0·32 [95% CI 0·19–0·61]) and at 28 days (0·34 [0·16–0·79]), and risk of complications from COVID-19 (0·26 [0·17–0·46]), hospitalisation due to COVID-19 (0·17 [0·09–0·32]), and requirement for COVID-19-specific therapy (0·22 [0·15–0·34]) and oxygen therapy (0·24 [0·14–0·43]; appendix pp 6–10). Similarly, compared with patients diagnosed during the prevaccination phase, those diagnosed during the omicron phase had a lower risk of death at 28 days (adjusted HR 0·48 [95% CI 0·34–0·67]) than did those diagnosed during the alpha-delta phase (0·73 [0·62–0·85]; appendix p 10).

Improving trends for COVID-19 outcomes were reported for both patients with solid and haematological malignancies, despite worse COVID-19 severity reported among patients with haematological malignancies than in those with solid malignancies across the three phases (appendix p 11).

Overall, 659 (72·0%) of 955 patients diagnosed during the alpha-delta phase and 42 (12·4%) of 339 diagnosed during the omicron phase were unvaccinated. Distribution

of demographic and clinical characteristics for unvaccinated patients is shown in the appendix (p 12). Unvaccinated patients diagnosed during the omicron phase had similar COVID-19 morbidity and mortality to those diagnosed during the alpha-delta phase (14-day case-fatality rate: ten [25%] of 40 patients diagnosed during omicron phase *vs* 114 [17%] of 656 diagnosed during alpha-delta phase) and the 28-day case-fatality rate (11 [27%] of 40 *vs* 184 [28%] of 656). Hospitalisation due to COVID-19 (18 [43%] of 42 *vs* 266 [41%] of 652), rates of COVID-19 symptoms (38 [90%] of 42 *vs* 541 [82%] of 659), and complications from COVID-19 (13 [31%] of 42 *vs* 237 [36%] of 659) were comparable, alongside requirements for COVID-19 specific therapy (18 [49%] of 37 *vs* 331 [54%] of 618) and supplemental oxygen therapy (14 [39%] of 36 *vs* 283 [46%] of 617; figure 2B; appendix p 13). After propensity-score matching, 42 unvaccinated patients from the omicron phase were matched with 122 patients from the prevaccination phase and with 121 patients from the alpha-delta phase (appendix p 13). Analysis of this propensity score-matched populations showed no evidence of difference in 14-day case-fatality rate between unvaccinated patients across the predefined pandemic phases (omicron *vs* prevaccination: OR 0·53 [95% CI 0·23–1·19]; omicron *vs* alpha-delta: 0·84 [0·37–1·91]).

447 (12·9%) of patients were diagnosed between the date of the first breakthrough SARS-CoV-2 infection in a boosted patient (Nov 17, 2021) and Jan 31, 2022. 32 patients had unknown vaccination status, leaving 415 eligible patients for the analysis of whether a booster dose was associated with improved COVID-19 outcomes. 51 (12·3%) of 415 patients were unvaccinated, 178 (42·9%) were vaccinated, of whom 152 were fully vaccinated and 26 partially vaccinated, and 186 (44·8%) had received a booster dose. Distribution of demographic and clinical characteristics across the vaccination subgroups is shown in the appendix (p 14). The most frequent tumour type among boosted patients was haematological malignancy (p=0·016). Country of origin was significantly associated with vaccination (p=0·0003); however, we found no other associations between vaccination status and baseline features, including sex, age, comorbidities, smoking history, tumour stage, tumour status, and the receipt of systemic anticancer therapy at the time of COVID-19 diagnosis, with the exception of increasing proportions of patients receiving tyrosine kinase inhibitors and monoclonal antibodies among vaccinated and boosted patients (p=0·023; appendix p 14).

The median observation period of the population included in the vaccine analysis was 22 days (IQR 14–30). Compared with unvaccinated controls, boosted and vaccinated patients had significant improvements in 14-day case-fatality rate (p=0·0011) and 28-day case-fatality rate (p=0·015), hospitalisation due to COVID-19 (p=0·0011), and complications from COVID-19 (p=0·015); no improvements were seen in the other COVID-19 outcomes (table 3).

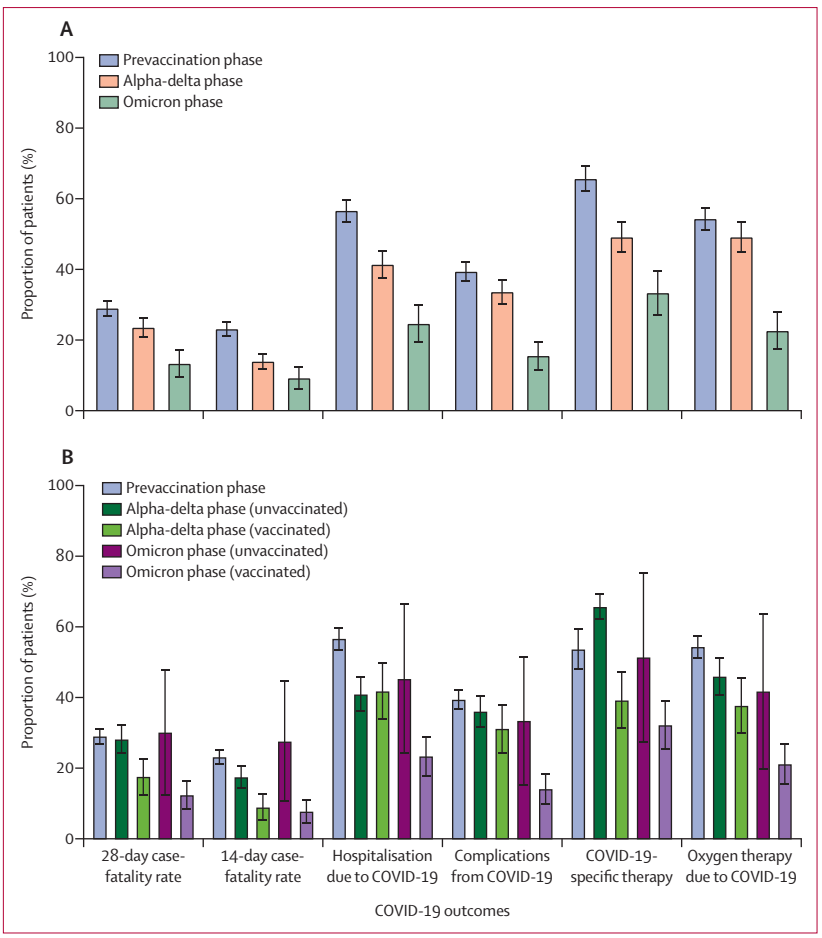

Figure 2: **COVID-19-related outcomes across the predefined phases for the overall population (A) and according to the vaccination status for patients from the alpha-delta and omicron phases (diagnosed between Nov 17, 2021, and Feb 4, 2022; B)**

Error bars denote 95% CIs. Vaccination status included all patients who received at least one dose of a SARS-CoV-2 vaccine.

Baseline characteristics before and after weighting distribution for the first-tier analysis comparing all vaccinated patients with unvaccinated patients are reported in the appendix (p 15) alongside IPTW-fitted multivariable logistic regression models for each COVID-19 outcome. After adjusting for sex, age, number of comorbidities, country of origin, tumour status, tumour stage, and receipt of systemic anticancer therapy at time of COVID-19 diagnosis, and accounting for cluster adjustment by participating centre, we found that vaccinated patients had reduced 14-day case-fatality rate and 28-day case-fatality rate, and reduced need for COVID-19-specific therapy and oxygen therapy, reduced rate of complications from COVID-19, and reduced hospitalisations due to COVID-19 compared with unvaccinated patients (figure 3; appendix pp 15–16).

Patient characteristics before and after weighting for the second-tier analysis and the fitted multivariable logistic regression models for the 14-day case-fatality rate and 28-day case-fatality rate are summarised in the appendix

	Overall population (N=3473)	Prevaccination phase (n=2033)	Alpha-delta phase (n=1075)	Omicron phase (n=365)	p value
Symptoms from COVID-19	3002 (86·4% [83·3–89·6])*	1832 (90·1% [86·0–94·3])*	868 (80·7% [75·5–86·4])*	302 (82·7% [73·6–92·6])*	<0·0001
Oxygen therapy	1530 (47·6% [45·2–50·1])	1029 (54·3% [51·1–57·7])	430 (43·0% [38·9–47·2])	71 (22·4% [17·4–28·2])	<0·0001
Missing†	261 (7·5%)	139 (6·8%)	74 (6·9%)	48 (13·1%)	..
COVID-19-specific therapy	1830 (57·1% [54·5–59·8])	1225 (65·7% [62·0–69·4])	495 (49·1% [44·8–53·6])	110 (33·1% [27·2–39·9])	<0·0001
Missing†	268 (7·7%)	168 (8·2%)	67 (6·2%)	33 (9·0%)	..
Complications from COVID-19	1218 (35·1% [33·1–37·1])	801 (39·4% [36·7–42·2])	361 (33·6% [30·2–37·2])	56 (15·3% [11·5–19·9])	<0·0001
Hospitalisation	..	..	..	..	<0·0001
Due to COVID-19	1665 (48·6% [46·3–51·0])	1142 (56·6% [53·4–60·0])	437 (41·4% [37·5–45·4])	86 (24·4% [19·4–30·1])	..
Pre-existing hospitalisation	836 (24·4 [22·8–26·1])	417 (20·7% [18·7–22·7])	323 (30·6% [27·3–34·1])	96 (27·2% [22·0–33·2])	..
Missing†	48 (1·4%)	17 (0·8%)	19 (1·8%)	12 (3·3%)	..
14-day case-fatality rate	645 (18·9% [17·4–20·3])	466 (23·1% [21·1–25·3])	148 (13·9% [11·7–16·3])	31 (9·0% [6·1–12·7])	<0·0001
Missing†	54 (1·5%)	20 (0·9%)	13 (1·2%)	21 (5·8%)	..
28-day case-fatality rate	879 (25·7% [24·0–27·4])	584 (29·0% [26·7–31·4])	250 (23·5% [20·7–26·6])	45 (13·1% [9·5–17·5])	<0·0001
Missing†	54 (1·5%)	20 (0·9%)	13 (1·2%)	21 (5·8%)	..

Data are n (frequency [95% CI]) or n (%). *Clopper-Pearson (exact) binomial CIs. †Missing values were excluded from the denominator when calculating frequency of COVID-19 outcomes and for any formal subgroup comparisons; however, missing data percentages were computed using the whole reference population.

Table 2: **Univariable analysis of COVID-19 outcomes across the predefined phases of the pandemic**

	Overall population (n=415)	Unvaccinated (n=51)	Fully and partially vaccinated (n=178)	Boosted (n=186)	p value
Symptoms from COVID-19	338 (81·4% [77·4–85·1])*	45 (88·2% [76·1–95·5])*	136 (76·4% [69·4–82·4])*	157 (84·4% [78·3–89·3])*	0·059
Oxygen therapy	87 (23·8% [19·1–29·4])	18 (40·0% [23·7–63·2])	35 (23·2% [16·1–32·2])	34 (20·1% [13·9–28·1])	0·020
Missing†	50 (12·0%)	6 (11·8%)	27 (15·2%)	17 (9·1%)	..
COVID-19 specific therapy	129 (34·0% [28·4–40·4])	22 (48·9% [30·6–74·0])	47 (29·7% [21·8–39·5])	60 (34·1% [26·0–43·9])	0·057
Missing†	36 (8·7%)	6 (11·8%)	20 (11·2%)	10 (5·4%)	..
Complications from COVID-19	71 (17·1% [13·3–21·6])	16 (31·3% [17·9–50·9])	28 (15·7% [10·4–22·7])	27 (14·5% [9·6–21·1])	0·015
Hospitalisation	..	..	..	..	0·0011
Due to COVID-19	103 (25·7% [20·9–31·2])	21 (41·2% [25·5–62·9])	35 (20·6% [14·3–28·6])	47 (26·1% [19·2–34·7])	..
Pre-existing hospitalisation	110 (27·4% [22·5–33·1])	13 (25·5% [13·5–43·6])	62 (36·5% [27·9–46·7])	35 (19·4% [3·5–27·0])	..
Missing†	14 (3·4%)	0	8 (4·5%)	6 (3·2%)	..
14-day case-fatality rate	35 (8·8% [6·1–12·2])	11 (22·4% [11·2–40·2])	12 (6·9% [3·6–12·1])	12 (6·8% [3·5–11·8])	0·0011
Missing†	17 (4·1%)	2 (3·9%)	6 (3·4%)	9 (4·8%)	..
28-day case-fatality rate	54 (13·5% [10·2–17·7])	13 (26·5% [14·1–45·3])	22 (12·7% [8·0–19·3])	19 (10·7% [6·4–16·7])	0·015
Missing†	17 (4·1%)	2 (3·9%)	6 (3·4%)	9 (4·8%)	..

Data are n (frequency [95% CI]) or n (%). 32 patients with unknown vaccination status were excluded from these analyses. *Clopper-Pearson (exact) binomial CIs. †Missing values were excluded from the denominator when calculating COVID-19 outcomes and for any formal subgroup comparisons; however, missing data proportions were calculated using the whole reference population.

Table 3: **Univariable analysis of COVID-19 outcomes among patients diagnosed with COVID-19 from Nov 17, 2021, to Jan 1, 2022, by vaccination status**

(pp 17–18). After adjusting for sex, age, number of comorbidities, country of origin, tumour status, tumour stage, and receipt of systemic anticancer therapy at the time of COVID-19 diagnosis, 28-day case-fatality rate was improved in boosted patients (adjusted OR 0·20 [95% CI 0·11–0·38]) and fully vaccinated and partially vaccinated patients (0·29 [0·15–0·53]), whereas no significant differences in 14-day case-fatality rate (0·97 [0·52–1·81]) and 28-day case-fatality rate (0·90 [0·53–1·52]) were reported between boosted patients and full and partially vaccinated patients.

Similar improvement in COVID-19 outcomes were seen for vaccinated patients with solid and haematological malignancies compared with unvaccinated patients, with features of COVID-19 morbidity and mortality being concordantly worse among patients with haematological tumours than those with solid tumours across the vaccination categories (appendix p 19).

Discussion

In this analysis from the OnCovid registry study, we found that patients with cancer diagnosed with COVID-19 during the omicron phase had significantly lower mortality rates than did patients diagnosed during earlier phases of the pandemic, with a reduction in acute mortality from more than 30%[9] to less than 10%. In

parallel, patients diagnosed with COVID-19 during the omicron phase typically had lower rates of hospitalisation and complications due to COVID-19 and a lower requirements for oxygen therapy than did those diagnosed in earlier phrases, a finding supports the view of a shift in respiratory tropism of the novel variant.[21]

Such improvements were maintained even adjusting by malignancy type and despite a significantly higher prevalence of adverse prognostic features seen in patients who presented with COVID-19 during the omicron phase, including advanced tumour stage,[9] recent exposure to systemic anticancer therapy,[9] and an increasing proportion of patients with increased susceptibility to COVID-19, such as with underlying haematological and thoracic malignancies.[20,22] Although our findings support the independence of COVID-19 mortality from baseline oncological and demographic features, the time-dependent improvements in COVID-19-related outcomes seen here are unhelpful in ascribing the decreasing COVID-19 morbidity and mortality rates to either changes in virulence of omicron, as opposed to systematic improvement in disease management and health-care system capacity, an aspect shown to affect outcomes ahead of SARS-CoV-2 vaccination campaigns.[10]

Furthermore, when analysing COVID-19 outcomes in unvaccinated patients over time, we found a peak in mortality that coincided with the omicron outbreak, with comparable estimates to those seen during the earlier stages of the pandemic. The 14-day case-fatality rate estimate during the omicron phase among unvaccinated individuals is in fact a highly provocative finding, because it identifies exposure to a vaccine rather than the diminished pathogenicity of new variants of concerns as the key driver behind the improved outcomes from COVID-19 in the evolving stages of the pandemic.

Despite proof of an escaping potential to natural immunity and vaccines of the omicron variant,[7,8] evidence also supports the protective effect of mRNA-based vaccine boosters against the omicron variant for the general population,[23] a finding of particular importance in patients with cancer[24] who might develop an impaired vaccine-induced immunity.[25]

Several studies have confirmed the immunogenicity of SARS-CoV-2 vaccines across different types of cancers and therapeutic methods.[26] However, clinical trials developing SARS-CoV-2 vaccines excluded patients with active malignancy and did not assess the long-term efficacy of booster doses in this patient population.[27]

Here, we present important confirmatory evidence that vaccination and booster doses are associated with a significant improvement in COVID-19-related outcomes in patients with cancer, supporting global efforts aimed at broadening SARS-CoV-2 vaccine cover to patients with haematological and solid malignancies.

The retrospective nature of our study does not allow us to definitively infer a direct causative role between exposure to vaccines and improved mortality in our patient population. However, our analyses show that the effect of vaccine-induced immunity is independent of geographical differences in immunisation uptake and the uneven distribution of tumour groups across vaccinated and boosted patients, a finding that is likely to reflect prioritisation of high-risk patient populations to the delivery of booster doses. Interestingly, detailed analysis of patients who had received three doses of SARS-CoV-2 vaccines showed patients who received a booster had similar COVID-19 mortality rates as those who had received one or two doses, despite a more than 19-times higher cross-neutralisation potential for the omicron variant reported in individuals who received a mRNA-based vaccine booster dose than in the general population who received the standard vaccination course.[23]

Nevertheless, even when assessing the additional benefit of booster doses, the enrichment of the boosted subgroup with more vulnerable patients (eg, those with haematological and thoracic malignancies,[20,22] with impaired immune-response to SARS-CoV-2 vaccines including booster doses[28,29]) needs to be taken into account.

Our analysis has several limitations, primarily the higher proportion of patients with incomplete follow-up during the omicron phase. Retrospective registry studies cannot fully exclude the effect of unmeasured bias and, despite best efforts aimed at controlling for unbalanced prognostic factors, results are inevitably exposed to the risk of selection bias. For instance, case ascertainment cannot be controlled for and because of varying availability of testing across the phases of the pandemic, case-fatality rates might not fully replicate infection-fatality rates overall. Similarly, the effect of COVID-19 on cancer diagnosis and treatment, especially in the earlier phases of the pandemic, might have independently affected outcomes irrespective of SARS-CoV-2 virulence or vaccinal immunity. Another key issue is the paucity of available viral genomic sequences across the evolving waves of the pandemic, leading to the need to define pandemic phases on the basis of

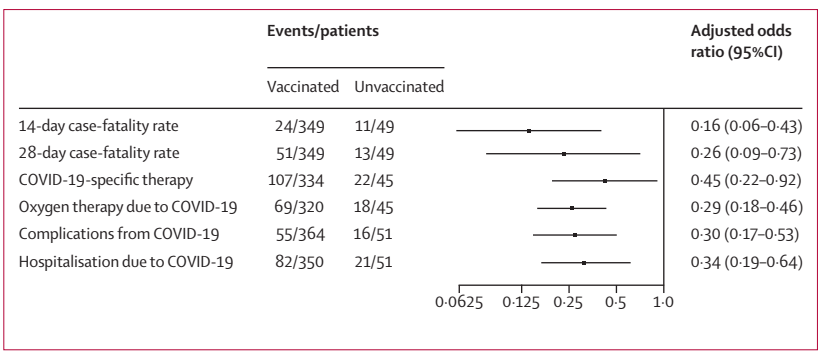

Figure 3: **Adjusted odds ratios of COVID-19 outcomes in vaccinated and unvaccinated individuals**
Vaccination status included all patients who received at least one dose of a SARS-CoV-2 vaccine. The reported adjusted odds ratio and 95% CIs are corrected according to the clustered-robust standard error adjustment for participating centres. The following covariates were included in each model: country (UK *vs* Spain *vs* Italy), sex (male *vs* female), age (≥65 *vs* < 65 years), number of comorbidities (≥2 vs 0–1), tumour status at COVID-19 (non-active *vs* active disease), tumour stage at COVID-19 (advanced *vs* non-advanced *vs* unknown), and receipt of systemic anticancer therapy at COVID-19 (yes *vs* no *vs* unknown).

epidemiological trends. Although this is a legitimate methodological concern, especially when considering patients who were diagnosed during the omicron phase, the extremely rapid course of viral transmission in the late-2021 outbreak was such that dominance of the omicron variant was reported in Europe within a few weeks from initial strain isolation,[15] leaving little opportunity for strains other than omicron to be causative during the latest infection peak recorded in our registry. However, the impact of omicron outside of Europe might be different.

Our analysis of vaccine efficacy depended on timing of vaccination and methods of data collection that were not preplanned but that instead followed standard of care. Although routine SARS-CoV-2 PCR is highly frequent in patients with cancer who re-attend hospital, determination bias with potential underestimation of breakthrough infections is a risk that should be taken into account when interpreting our findings and all similar registry studies.[30] The effect of missing data was considered when formulating our statistical analysis plan, with core study data being characterised by a high level of completeness of data entry. For approximately 13% of vaccinated patients, the specific type of vaccine could not be determined; however, we decided to include these individuals in the analyses because of evidence of largely similar efficacy of commonly available SARS-CoV-2 vaccines.[27] Finally, outcomes other than acute morbidity and mortality during the omicron phase, including sequelae in vaccinated versus unvaccinated patients, remain poorly characterised in our study and should be assessed with longer-term follow-up.

Despite the mentioned limitations, our study provides original and reliable evidence to suggest improving trends in COVID-19 morbidity and mortality during the omicron phase of the pandemic in patients with cancer, mirroring similar results from the general population.[5] However, unvaccinated patients diagnosed in the omicron phase remain exposed to a risk of morbidity and mortality that is similar the findings in previous phases of the pandemic, highlighting the importance of addressing vaccine hesitancy that might persist in some patients with cancer.[31]

Previous SARS-CoV-2 immunisation remains the strongest protective correlate of outcomes in our study, suggesting ongoing efforts aimed at securing broad vaccine cover to be a key strategic objective in protecting patients with cancer against COVID-19. Considering the inherent clinical vulnerability of patients with thoracic and haematological malignancies, who enriched the boosted subgroup in our study, receipt of a booster dose was associated with similar COVID-19-related morbidity and mortality rates, supporting widespread promotion of the delivery of booster doses to more vulnerable patients with cancer.

Contributors

All authors contributed to the publication according to the ICMJE guidelines for the authorship. All authors had access to all the data reported in the study and had final responsibility to submit for publication. All authors read and approved the submitted version of the manuscript (and any substantially modified version that involved the author's contribution to the study). Each author has agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature. AC and DJP accessed and verified the underlying study data. AC and DJP conceived and designed the study. DJP, JA-C, DF, GH, MB RS, OM, ASu, APl, MC, RM, ST, AJ, ADP, TN-D, JH, AS-L, EA, BV, AB, JB, MLa, CMa, PP, FB, ASi, SB, SK, SR, LRo, CMu, KB, MCC-G, RS, DG-I, GR, MP, NS-G, KD, LF, ER, GG, IR-C, RB, APat, CM-V, LC, AZ, RG, FM, EC, ASa, FG, APar, PQ, AA, LRi, APr, MT, MLi, SG, UM, ND, VF, DG, SP, AG, JT, and AC contributed to data acquisition. AC, DF, and DJP analysed and interpreted the data. AC and DJP drafted the manuscript. AC and DF did the statistical analysis. DJP, JA-C, DF, GH, MB, RS, OM, ASu, APl, MC, RM, ST, AJ, ADP, TN-D, JH, AS-L, EA, BV, AB, JB, MLa, CMu, PP, FB, ASi, SB, SK, SR, LRo, CMa, KB, MCC-G, RS, DG-I, GR, MP, NS-G, KD, LF, ER, GG, IR-C, RB, APat, CM-V, LC, AZ, RG, FM, EC, ASa, FG, APar, PQ, AA, LRi, APr, MT, MLi, SG, UM, ND, VF, DG, SP, AG, JT, and AC reviewed and approved the manuscript. DJP obtained funding. AC and DJP supervised the study.

Declaration of interests

DJP has received lecture fees from ViiV Healthcare, Bayer Healthcare, BMS, Roche, Eisai, and Falk Foundation; travel expenses from BMS and Bayer Healthcare; consulting fees for Mina Therapeutics, Eisai, Roche, DaVolterra, and Astra Zeneca; and research funding (to their institution) from MSD and BMS. MLa has acted as consultant for Roche, Novartis, Lilly, AstraZeneca, Exact Sciences, MSD, Pfizer, Seagen, and Gilead; and has received speaker honoraria from Roche, Novartis, Lilly, Pfizer, Takeda, Ipsen, Libbs, Knight, and Sandoz. FM has received consulting fees from Eli Lilly, MSD, Takeda, and Roche; and travel support from Sanofi. SP reported that their spouse is employed by AstraZeneca. ASa has received consulting fees from Arqule, Sanofi, and Incyte; speaker's fees from Takeda, BMS, Roche, AbbVie, Amgen, Celgene, Servier, Gilead, AstraZeneca, Pfizer, Arqule, Eli Lilly, Sandoz, Eisai, Novartis, Bayer, and MSD; and participation on data monitoring committees for BMS, Servier, Gilead, Pfizer, Eisai, Bayer, and MSD. FG has received consulting fees from Novocure, BMS, PharmaMar, and Novartis; speaker's fees from Novocure; travel support from MSD, Novocure, BMS, Boehringer Ingelheim, PharmaMar, Novartis, and Pierre Fabre; and participation on a data safety monitoring board for MSD, BMS, PharmaMar and Novartis. JH has a leadership role with Blood Cancer UK. NS-G has received speakers' fees from Amgen. GG has received consulting fees or had an advisory role for Janssen, AbbVie, AstraZeneca, Roche, Incyte, and BeiGene, and reported speaker fees from Janssen and AbbVie. LRi has received consulting fees from Taiho Oncology, Servier, Amgen, ArQule, AstraZeneca, Basilea, Bayer, BMS, Celgene, Eisai, Exelixis, Genenta, Hengrui, Incyte, Ipsen, IQVIA, Lilly, MSD, Nerviano Medical Sciences, Roche, Sanofi, and Zymeworks; lecture fees from AbbVie, Amgen, Bayer, Eisai, Gilead, Incyte, Ipsen, Lilly, Merck Serono, Roche, and Sanofi; travel expenses from Ipsen; and institutional research funding from Agios, ARMO BioSciences, AstraZeneca, BeiGene, Eisai, Exelixis, Fibrogen, Incyte, Ipsen, Lilly, MSD, Nerviano Medical Sciences, Roche, and Zymeworks. JT reports consulting fees from Array Biopharma, AstraZeneca, Avvinity, Bayer, Boehringer Ingelheim, Chugai, Daiichi Sankyo, F Hoffmann-La Roche, Genentech, HalioDX SAS, Hutchison MediPharma International, Ikena Oncology, Inspirna, IQVIA, Lilly, Menarini, Merck Serono, Merus, MSD, Mirati, Neophore, Novartis, Ona Therapeutics, Orion Biotechnology, Peptomyc, Pfizer, Pierre Fabre, Samsung Bioepis, Sanofi, Seattle Genetics, Scandion Oncology, Servier, Sotio Biotech, Taiho, Tessa Therapeutics, and TheraMyc; speaker's fees from Imedex, Medscape Education, MJH Life Sciences, PeerView Institute for Medical Education, and Physicians Education Resource; and institutional research support from Amgen, Array Biopharma, AstraZeneca Pharmaceuticals, BeiGene, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Debiopharm International, F Hoffmann-La Roche, Genentech, HalioDX, Hutchison MediPharma International, Janssen-Cilag, MedImmune, Menarini, Merck Health, Merck Sharp & Dohme, Merus NV, Mirati, Novartis Farmacéutica, Pfizer, Pharma Mar,

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Data sharing

Individual-level, deidentified participant data and data dictionary can be made available at the request of investigators whose proposed use of the data has been approved by the OnCovid consortium steering committee after review of a methodologically sound research proposal. Data will be made available beginning 6 months after Article publication with no end date. Requests for deidentified data should be made to the study Chief Investigator (DJP).

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