

COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study



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Summary

Background Individuals with cancer, particularly those who are receiving systemic anticancer treatments, have been postulated to be at increased risk of mortality from COVID-19. This conjecture has considerable effect on the treatment of patients with cancer and data from large, multicentre studies to support this assumption are scarce because of the contingencies of the pandemic. We aimed to describe the clinical and demographic characteristics and COVID-19 outcomes in patients with cancer.

Methods In this prospective observational study, all patients with active cancer and presenting to our network of cancer centres were eligible for enrolment into the UK Coronavirus Cancer Monitoring Project (UKCCMP). The UKCCMP is the first COVID-19 clinical registry that enables near real-time reports to frontline doctors about the effects of COVID-19 on patients with cancer. Eligible patients tested positive for severe acute respiratory syndrome coronavirus 2 on RT-PCR assay from a nose or throat swab. We excluded patients with a radiological or clinical diagnosis of COVID-19, without a positive RT-PCR test. The primary endpoint was all-cause mortality, or discharge from hospital, as assessed by the reporting sites during the patient hospital admission.

Findings From March 18, to April 26, 2020, we analysed 800 patients with a diagnosis of cancer and symptomatic COVID-19. 412 (52%) patients had a mild COVID-19 disease course. 226 (28%) patients died and risk of death was significantly associated with advancing patient age (odds ratio 9.42 [95% CI 6.56–10.02]; $p < 0.0001$), being male (1.67 [1.19–2.34]; $p = 0.003$), and the presence of other comorbidities such as hypertension (1.95 [1.36–2.80]; $p < 0.001$) and cardiovascular disease (2.32 [1.47–3.64]). 281 (35%) patients had received cytotoxic chemotherapy within 4 weeks before testing positive for COVID-19. After adjusting for age, gender, and comorbidities, chemotherapy in the past 4 weeks had no significant effect on mortality from COVID-19 disease, when compared with patients with cancer who had not received recent chemotherapy (1.18 [0.81–1.72]; $p = 0.380$). We found no significant effect on mortality for patients with immunotherapy, hormonal therapy, targeted therapy, radiotherapy use within the past 4 weeks.

Interpretation Mortality from COVID-19 in cancer patients appears to be principally driven by age, gender, and comorbidities. We are not able to identify evidence that cancer patients on cytotoxic chemotherapy or other anticancer treatment are at an increased risk of mortality from COVID-19 disease compared with those not on active treatment.

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Introduction

The risk of morbidity and mortality from COVID-19 as a consequence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is not uniform across the UK population.¹ Patients with cancer receiving systemic anticancer treatments have been generally assumed by many to be at a higher risk from the disease than their counterparts are who are not receiving anticancer treatment. The evidence to support this claim is scarce and limited to retrospective series arising from China, the epicentre of the COVID-19 pandemic, and involving small numbers of patients.^{2–4} However, despite these severe limitations, the promulgation of this hypothesis has led to widespread global changes to

patterns of prescribing chemotherapy and anticancer treatment.⁵ In a global health emergency, oncologists must secure evidence from a large dataset, which can then inform their risk-benefit analyses for individual patients in terms of the use of anticancer treatments.^{6,7}

On March 18, 2020, we launched the UK Coronavirus Cancer Monitoring Project (UKCCMP), with widespread support across our national cancer network.⁸ Within 5 weeks, the UKCCMP had generated the largest prospective database of COVID-19 in patients with cancer that had been generated to date. We aimed to describe the clinical and demographic characteristics and COVID-19 outcomes in this cohort of patients with cancer and symptomatic COVID-19, and attempted to assess how

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For more on the UKCCMP see <https://ukcoronaviruscancermonitoring.com>

Research in context

Evidence before this study

We searched PubMed for all studies related to the effect of severe acute respiratory syndrome coronavirus 2, the cause of COVID-19, on patients with cancer, using the search terms "COVID-19", "SARS-CoV-2", "cancer", "treatment", "chemotherapy", "immunotherapy", "radiotherapy", "targeted therapy", "outcomes," "death", "mortality", and "risk". We included publications in English only. To date, only two studies have described the effect of cancer treatments on COVID-19 outcomes. Both studies consist of small retrospective analyses from China in a few cancer centres. One study reported four patients who had chemotherapy or surgery in the past month, and identified that three had a clinically severe disease course. Another study described a cohort of 105 cancer patients with COVID-19, 17 of whom had received chemotherapy within the past 40 days and six had received immunotherapy. The authors reported that four of the six patients on immunotherapy had critical symptoms. No conclusions were drawn about chemotherapy and the authors stressed the importance of a further study with a large case population. In summary, to date, no high-quality evidence exists to identify risks from use of recent anticancer treatments during the COVID-19 pandemic.

Added value of this study

This UK Coronavirus Cancer Monitoring Project study is a national monitoring project. We have analysed the interaction between recent anticancer treatments and COVID-19 morbidity and mortality in the largest cohort of patients with cancer with COVID-19 presented to date, consisting of 800 patients. Recent chemotherapy use in patients with cancer before severe acute respiratory syndrome coronavirus 2 infection was not significantly associated with increased mortality. Although the numbers of patients are smaller, we did not observe any significant risk from recent use of immunotherapy, hormonal therapy, targeted therapy, or radiotherapy.

Implications of all the available evidence

Our data are strongly indicative that COVID-19 mortality in patients with cancer is principally driven by advancing age and the presence of other non-cancer comorbidities. At a population level, our data do not suggest that chemotherapy or anticancer treatments will necessarily increase the risk of mortality from COVID-19, and gives confidence to oncologists and other clinicians that delivery of effective anticancer regimens should continue during this difficult time.

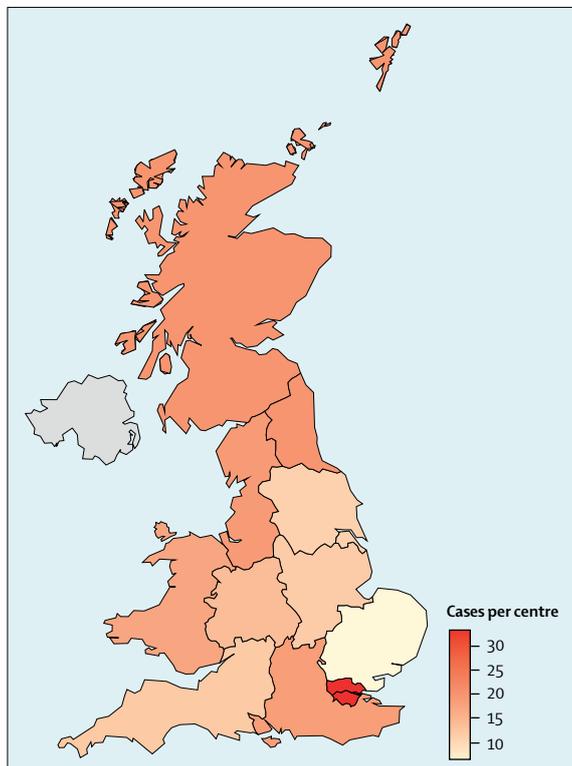


Figure 1: Prevalence of COVID-19 in Scotland, Wales, and regions of England
Data are the average numbers of cases from reports per cancer centre region, up to April 26, 2020. Grey indicates no data available.

the presence of cancer and the receipt of cytotoxic chemotherapy and other anticancer treatments affects the COVID-19 disease phenotype.

Methods

Study design and participants

The UKCCMP database of UK patients COVID-19 who have cancer with was launched with the support of the UK oncology professional bodies, including the Association of Cancer Physicians, the Royal College of Radiologists, the National Oncology Trainees Research Collaborative for Healthcare Research, patient support groups including Macmillan Cancer Support, and charities including Action Radiotherapy.⁹ The database was designed as a public health surveillance registry to support rapid clinical decision making, in accordance with the UK Policy Framework for Health and Social Care Research, the UK National Research Ethics Service, and the UK Governance Arrangement for Research Ethic Committees. At an institutional level, this cohort study was approved according to local information governance processes.

All patients with active cancer and presenting to our network of 55 cancer centres from March 18, 2020, to April 26, 2020, with COVID-19 were eligible for enrolment into the UKCCMP. In keeping with international practice, patients were deemed to have COVID-19 if an RT-PCR assay test from a throat or nose swab was positive for SARS-CoV-2. Patients with a radiological or clinical diagnosis of COVID-19, without a positive RT-PCR test were not included in this analysis. As such, these patients

	All patients (n=800)	Patients who died (n=226)	Patients who survived (n=574)
Sex			
Male	449 (56%)	146 (65%)	303 (53%)
Female	349 (44%)	80 (35%)	269 (47%)
Other*	2 (0%)	0 (0%)	2 (0%)
Age, years			
	69 (59–76)	73 (66–80)	66 (57–74)
Comorbidities			
Cardiovascular disease	109 (14%)	48 (21%)	61 (11%)
Chronic obstructive pulmonary disease	61 (8%)	24 (11%)	37 (6%)
Diabetes	131 (16%)	46 (20%)	85 (15%)
Hypertension	247 (31%)	92 (41%)	155 (27%)
None	169 (21%)	27 (12%)	142 (25%)
Other†	336 (42%)	108 (48%)	228 (40%)
No information	123 (15%)	28 (12%)	95 (17%)
Cancer type			
Lip, oral cavity, and pharynx	27 (3%)	4 (2%)	23 (4%)
Digestive organs	150 (19%)	42 (19%)	108 (19%)
Respiratory and intrathoracic organs	90 (11%)	32 (14%)	58 (10%)
Melanoma (skin)	27 (3%)	4 (2%)	23 (4%)
Breast	102 (13%)	18 (8%)	84 (15%)
Female genital organs	45 (6%)	5 (2%)	40 (7%)
Male genital organs	78 (10%)	30 (13%)	48 (8%)
Urinary tract	50 (6%)	16 (7%)	34 (6%)
Central nervous system	15 (2%)	3 (1%)	12 (2%)
Lymphoma	60 (8%)	20 (9%)	40 (7%)
Other haematological	109 (14%)	40 (18%)	69 (12%)
Other or unspecified‡	47 (6%)	12 (5%)	35 (6%)
Cancer stage			
Primary tumour localised	149 (19%)	40 (18%)	109 (19%)
Primary tumour locally advanced	78 (10%)	14 (6%)	64 (11%)
Metastatic	347 (43%)	103 (46%)	244 (43%)
Remission	21 (3%)	3 (1%)	18 (3%)
No information	205 (25%)	66 (29%)	139 (24%)

(Table 1 continues in next column)

are, by definition, symptomatic, requiring secondary care review for potential hospitalisation. These patients were not part of a proactive surveillance programme. Patients with active cancer were defined as those with metastatic cancer, or on anticancer treatment in any setting (curative, radical, adjuvant, or neoadjuvant setting) or treated within the past 12 months with surgery cytotoxic chemotherapy, or radiotherapy.

Stages of tumour were divided into those into primary tumour localised, which were localised to organ and therefore potentially resectable; primary tumour locally advanced, which had spread locally from the primary organ and was not resectable; metastatic, when there has been distant spread (stage IV); and patients in remission.

	All patients (n=800)	Patients who died (n=226)	Patients who survived (n=574)
(Continued from previous column)			
Cancer treatment within 4 weeks of COVID-19 diagnosis			
Chemotherapy	281 (35%)	75 (33%)	206 (36%)
Hormone therapy	64 (8%)	21 (9%)	43 (7%)
Immunotherapy	44 (6%)	10 (4%)	34 (6%)
Radiotherapy	76 (10%)	18 (8%)	58 (10%)
Surgery	29 (4%)	7 (3%)	22 (4%)
Targeted treatment	72 (9%)	16 (7%)	56 (10%)
Other§	60 (8%)	13 (6%)	47 (8%)
None	272 (34%)	92 (41%)	180 (31%)
No information	10 (1%)	1 (0%)	9 (2%)
COVID-19 severity category			
Mild	412 (52%)	22 (10%)	390 (68%)
Severe	187 (23%)	59 (26%)	128 (22%)
Critical	173 (22%)	140 (62%)	33 (6%)
No information	28 (3%)	5 (2%)	23 (4%)
COVID-19 treatment			
Intensive therapy unit	53 (7%)	23 (10%)	30 (5%)

Data are n (%), or median (IQR). UKCCMP=UK Coronavirus Cancer Monitoring Project. ICD10=International Classification of Diseases. *Includes patients who do not identify as either male or female. †Includes comorbidities that were not listed in the table. ‡Includes ICD10 cancer types including malignant neoplasia of the bone and articular tissue, endocrine glands, mesothelioma and soft tissue, and any other tumour type that was not included in the table. §Includes cancer treatments that did not fall into the cancer treatment types defined in the table.

Table 1: Clinical features of patients in the UKCCMP registry

Patients were assessed by the local teams and review of their medical history as to whether they had received chemotherapy (which did not include treatment with denosumab), immunotherapy, hormonal therapies, or radiotherapy within 4 weeks of contraction of COVID-19. Non-palliative chemotherapy was defined as chemotherapy that was used in a neoadjuvant, adjuvant, or radical setting. Outcomes were monitored until April 26, 2020.

Data collection

Prospective data collection was done by the pan-UK cancer centre emergency response network. Case reporting was led by a COVID-19 emergency response reporting individual (ERRI), supported by a local emergency response reporting group (LERRG) at each centre. The role of the LERRG was to ensure near continuous reporting of cases in situations of absence of the ERRI. The UKCCMP encouraged all local reporting sites to enter data in a real-time basis, as soon as a positive SARS-CoV-2 test had been identified. The data fields were then updated as soon as treatment and outcomes had been identified and also to reflect the worse COVID-19 severity categories during hospitalisation. The ERRI was an oncologist who was trained or in training, who did data review, annotation, and entry. In a few centres, data entry was done by data managers but with direct oversight by the ERRI. All registry entries were

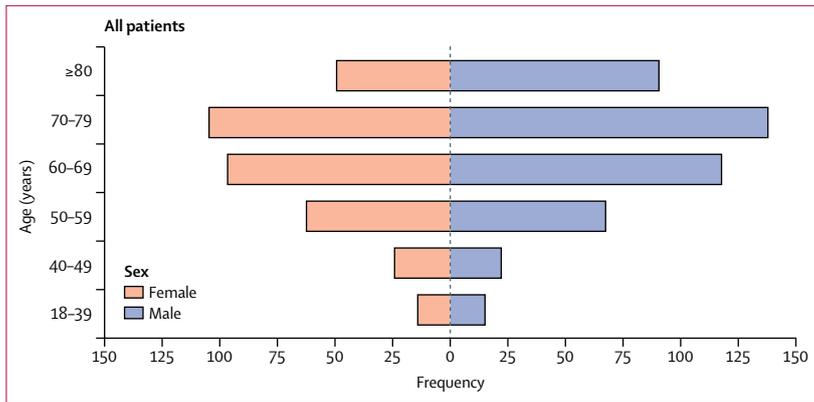


Figure 2: Age distribution of patients with cancer in the cohort and relation to patient mortality

de-identified at source to ensure data anonymity to researchers. Data was entered with the research electronic data capture (REDCap) application, an electronic data capture software system that is browser based and metadata driven.¹⁰ This secure electronic data capture platform is hosted by the Institute of Translational Medicine at the University of Birmingham, Birmingham, UK. Patient demographics, treatment details, COVID-19 disease course, and cancer features were obtained by the direct assessment of the ERRI and LERRG, or through hospital medical records. The COVID-19 severity category was determined according to WHO guidelines.¹¹ Cancer type was defined according to the International Classification of Disease (10th revision) diagnostic codes.

UKCCMP data processing and analysis

The data entered through REDCap was transferred securely through to the Compute and Storage for Life Science (CaStLeS) infrastructure as part of the Birmingham environment for academic research local cloud¹² at the Centre for Computational Biology, University of Birmingham.

Within CaStLeS, the data are curated to avoid duplications and errors, then annotated with further information such as geolocation before they can be analysed and disseminated. The deployment of an automatic workflow system, with human interaction (human-in-the-loop), enables the delivery of near real-time robust data analytics to medical health professionals in oncology through a weekly report in addition to a secured interactive web portal. Importantly, CaStLeS enables delivery of national and local analytics with a dynamic level of granularity.

Statistical analysis and data visualisation

We assessed whether the patient died or eventually achieved discharge, and observed the effect of anticancer treatment on outcomes. The two-sided Welch's *t* test was used to compare continuous data and two-sided Fisher's exact test was used to compare categorical data from different categories with multivariate Bonferroni

(multi-test) adjustment. A primary endpoint of all-cause mortality was defined a priori. This definition included deaths described as related to COVID-19 during admission, as well as deaths reported as a consequence of any other cause during admission, such as due to cancer progression or treatment toxicity. This definition was used for all regression analyses. Multivariate analyses were done in SPSS (version 26.0.0.0) and Fisher's exact tests in R (version 3.6.3), using the `fisher.test()` function. Multivariable logistic regression was used to estimate odd ratios and 95% CIs of each factor after adjustment for clinically relevant potential confounders of age, gender, diabetes, hypertension, chronic obstructive pulmonary disease, or other comorbidities at admission. Goodness of fit was checked using the Hosmer-Lemeshow test and, unless otherwise reported, had $p > 0.05$. Where this goodness of fit criterion was not met, further multivariable logistic regression models using the aforementioned potential confounders was done using a forward selection of $p < 0.10$. Patients with either no information or missing relevant data were not included in these regression analyses. Subgroup analyses of patients on chemotherapy were done to better identify risk in this cohort of patients. These analyses included non-palliative versus palliative chemotherapy, first-line versus later lines of palliative chemotherapy, palliative chemotherapy versus no anti-cancer treatment, and palliative chemotherapy versus no recent chemotherapy (ie, within 4 weeks of admission). The justification for these analyses is that the cancer chemotherapy group is heterogeneous. These subgroup analyses have a well-established oncological and clinical rationale, eg, non-palliative (curative) chemotherapy aims to prevent recurrence or eradicate disease, whereas palliative chemotherapy aims to maintain quality of life, or extend life usually by a matter of months to years, and both the patient's condition and chemotherapy treatment (drugs, dose, and intensity) necessarily evolve as a patient progresses from first-line to later lines of chemotherapy.¹³ We used R (version 3.6.3) for data processing and visualisation.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. GM, RK, JBC, and LYWL had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

55 cancer centres had appointed a COVID-19 LERRG and formed part of this clinical network of cancer centres. This network covered a patient population of nearly 1.5 million patients with active cancer, with good coverage across all regions of the UK (figure 1).

Our patient cohort consisted of the first 800 patients with active cancer who had documented SARS-CoV-2 infection presenting as symptomatic COVID-19 disease.

	Odds ratio (95% CI)	p value	Adjusted p value
Sex	1.67 (1.19–2.34)	0.003	0.006
Age	9.42 (6.56–10.02)	<0.0001	<0.0001
Comorbidities			
Cardiovascular disease	2.32 (1.47–3.64)	0.0003	0.0019
Chronic obstructive pulmonary disease	1.80 (1.00–3.27)	0.063	0.375
Diabetes	1.61 (1.03–2.48)	0.032	0.190
Hypertension	1.95 (1.36–2.80)	0.0003	0.0015
Cancer type			
Lip, oral cavity, and pharynx	0.42 (0.13–1.21)	0.116	1.000
Digestive organs	0.91 (0.60–1.38)	0.680	1.000
Respiratory and intrathoracic organs	1.50 (0.91–2.45)	0.121	1.000
Melanoma (skin)	0.37 (0.12–1.14)	0.079	1.000
Breast	0.48 (0.28–0.84)	0.009	0.141
Female genital organs	0.31 (0.11–0.81)	0.010	0.148
Male genital organs	1.99 (1.14–3.48)	0.015	0.230
Urinary tract	1.10 (0.58–2.12)	0.745	1.000
Central nervous system	0.64 (0.15–2.32)	0.760	1.000
Lymphoma	1.30 (0.71–2.30)	0.373	1.000
Other haematological	1.57 (1.01–2.42)	0.040	1.000
Cancer stage			
Primary tumour localised	1.04 (0.67–1.64)	0.912	1.000
Primary tumour locally advanced	0.58 (0.29–1.09)	0.111	0.442
Metastatic	1.34 (0.90–2.01)	0.145	0.579
Remission	0.42 (0.10–1.43)	0.204	0.815
Cancer treatment within 4 weeks of COVID-19 diagnosis			
Chemotherapy	0.78 (0.55–1.11)	0.173	1.000
Hormone therapy	1.16 (0.64–2.06)	0.659	1.000
Immunotherapy	0.60 (0.27–1.24)	0.179	1.000
Radiotherapy	0.66 (0.37–1.17)	0.178	1.000
Surgery	0.83 (0.32–2.15)	0.825	1.000
Targeted treatment	0.56 (0.30–1.01)	0.058	0.525
COVID-19 severity score			
Mild	0.03 (0.02–0.05)	<0.0001	<0.0001
Severe	1.63 (1.10–2.40)	0.015	0.045
Critical	89.65 (41.64–209.83)	<0.0001	<0.0001
COVID-19 treatment			
Intensive therapy unit	1.95 (1.09–3.52)	0.027	0.027

Univariate analysis was done with presence compared with absence (reference) for each category except for sex and age. Male sex was compared with reference to female sex. A Bonferroni p value adjustment was done.

Table 2: Univariate regression analysis and odds of death based on features of patients in the UK Coronavirus Cancer Monitoring Project

Patient demographics are shown in table 1. Comorbidities were common, including hypertension, diabetes, cardiovascular disease, and chronic obstructive pulmonary disease (table 1). 169 (21%) patients were listed as having no comorbidities apart from their cancer

	Odds ratio (95% CI)	p value
Anticancer treatment within 4 weeks of COVID-19 diagnosis		
Chemotherapy vs no chemotherapy	1.18 (0.81–1.72)	0.380
Hormone therapy vs no hormone therapy	0.90 (0.49–1.68)	0.744
Immunotherapy vs no immunotherapy	0.59 (0.27–1.27)	0.177
Radiotherapy vs no radiotherapy	0.65 (0.36–1.18)	0.159
Targeted treatment vs no targeted treatment	0.83 (0.45–1.54)	0.559
Cytotoxic chemotherapy		
Non-palliative chemo vs palliative chemo	0.40 (0.17–0.96)	0.040
Palliative first-line chemotherapy vs other line	0.84 (0.36–1.98)	0.690
Palliative chemotherapy vs no chemotherapy	1.48 (0.93–2.36)	0.102
Palliative chemotherapy vs no treatment	1.05 (0.63–1.76)	0.854

Multivariate analysis was done correcting for age, sex, and patient comorbidities.

Table 3: Multivariate regression analysis and odds of death based recent anticancer treatment in patients in the UK Coronavirus Cancer Monitoring Project

diagnosis. Approximately half of the patients had metastatic cancer, of which malignant neoplasia of the digestive organs, haematological malignancies, breast and respiratory and thoracic organs were the commonest primary tumour sites (table 1). The median time from identification of documented COVID-19 disease until study endpoints were met (death or discharge from hospital) was 5 days (range 0–38).

In terms of the pattern of COVID-19 presentation, most patients (484 [61%]) presented with fever, cough (377 [47%]), or shortness of breath (312 [39%]). However, diarrhoea (51 [6%]), nausea and vomiting (39 [5%]), ageusia (13 [2%]), and anosmia (nine [1%]) were also identified as presenting symptoms.

A mild COVID-19 severity category was recorded in 412 (52%) patients, with 96 (12%) patients not requiring hospital admission. 315 (39%) patients required oxygen, and 53 (7%) patients received intensive therapy unit (ITU) level care (table 1). Of these 53 patients, six (11%) were discharged, 23 (43%) died and 24 (45%) were either still in ITU or did not have a final recorded outcome.

226 (28%) patients died, with reports stating that the death was principally attributable to COVID-19 in most patients (211 [93%]). Compared with the rest of the cancer cohort, patients who died were significantly older (median 73.0 years vs 66.0 years; $p<0.001$; figure 2), more were male (146 [33%] of 449) than female (80 [20%] of 349), and those who died also displayed higher rates of comorbidities compared with those who did not, including cardiovascular disease (21% vs 11%; $p<0.001$) and hypertension (41% vs 27%; $p<0.001$; table 2). Patients who died were also more likely to present with symptoms of shortness of breath (57% vs 32%; $p<0.001$).

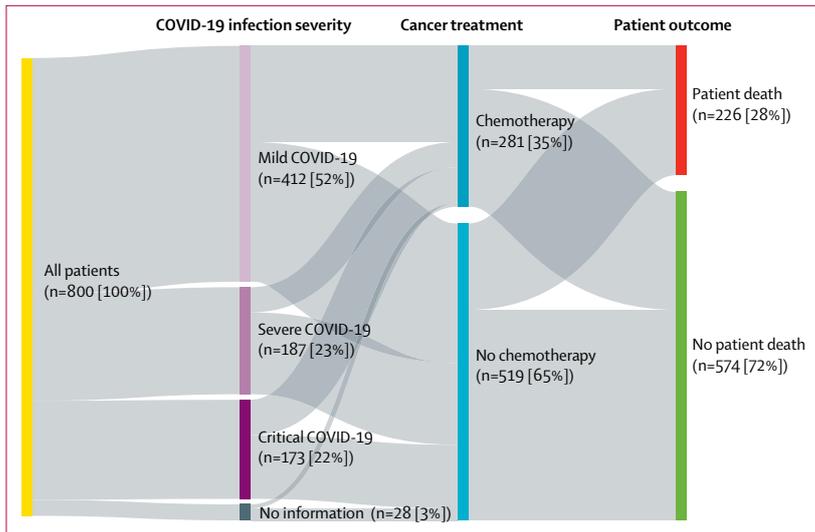


Figure 3: Relationship of chemotherapy use within 4 weeks of confirmed COVID-19 and mortality and severity of disease course
 The vertical coloured bars denote the patient cohort, split into different groups. The grey horizontal bars denote associations between the different groups, with wider bars denoting more overlap.

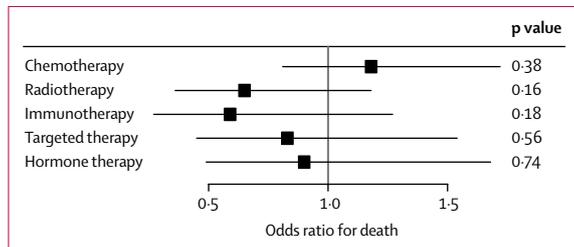


Figure 4: Forest plots showing effect of anticancer treatments and mortality from COVID-19
 Odds ratios were adjusted for age, gender, and comorbidities. Whiskers indicated 95% CI.

Across the cohort, 172 (22%) patients were reported by sites as having their anticancer treatments interrupted because of the COVID-19 pandemic, although, the exact nature of this interruption was not captured in this study.

Compared with patients who had not received chemotherapy within 4 weeks of testing positive for COVID-19, those who had received recent chemotherapy did not suffer increased mortality when analysed by univariate analysis (27% death rate with chemotherapy vs 29% death rate without recent chemotherapy).

To explore this relationship in greater detail, we did an in-depth analysis of the 281 patients who had received recent chemotherapy (ie, within 4 weeks of testing positive for COVID-19; figure 3). We found no significant differences in underlying cancer primary site in the recent chemotherapy versus no chemotherapy group. However, compared with patients who had not received recent chemotherapy, the chemotherapy cohort was younger (median age 64.0 years vs 71.0; $p < 0.001$). Therefore, we did a multivariate analysis with adjustment for age, gender, and comorbidities and found that deaths

in patients with COVID-19 who have cancer who had received recent chemotherapy were still no more likely than in those who had not (table 3). This analysis had a borderline fit (Hosmer-Lemeshow $p = 0.048$). We also did a forward regression model analysis (Hosmer-Lemeshow $p = 0.476$) with similar findings (odds ratio 1.15 [95% CI 0.79–1.66]; $p = 0.467$).

On further multivariate analysis of the group of patients who had received recent chemotherapy, decreased odds of death was found in patients receiving non-palliative chemotherapy (neoadjuvant, adjuvant, or radical) compared with those receiving palliative chemotherapy (16% vs 35%; table 3), after adjustments for age, gender, and comorbidities. However, the odds of death in patients receiving palliative chemotherapy were still not significantly different to those of patients receiving no anticancer treatment at all (table 3), or compared with those with no recent chemotherapy (table 3). We found no significant differences in mortality in patients receiving first-line palliative chemotherapy compared with those receiving later lines of palliative treatment after adjustments for age, gender, and comorbidities (table 3).

Finally, we analysed the use of other forms of anticancer therapies within 4 weeks of testing positive for SARS-CoV-2 infection and presenting with COVID-19. Compared with patients who were not on these therapies, patients on immunotherapy ($n = 44$; OR 0.59 [95% CI 0.27–1.27]; $p = 0.177$), hormonal therapy ($n = 64$; 0.90, [0.49–1.68]; $p = 0.744$), radiotherapy ($n = 76$; 0.65 [0.36–1.18]; $p = 0.159$), and targeted therapies ($n = 72$; 0.83 [0.45–1.54]; $p = 0.559$) were also not at any additional risk of death after adjustment for age, gender, and comorbidities (figure 4).

Discussion

Global health-care systems are dealing with the COVID-19 pandemic, a disease caused by SARS-CoV-2 infection; a situation that is set to be a generational challenge to all clinicians. The clinical phenotype and interactions of COVID-19 with pre-existing disease and systemic anticancer treatments drugs is poorly described and based on small retrospective studies.

The disruption from the pandemic to normal oncological care has been huge for several reasons. First, cancer clinicians and the rest of the cancer team are under unprecedented pressures. These pressures include increasing concern from patients about their perceived vulnerability, cancelled cancer operations, a substantial drive to do telemedicine rather than face-to-face consultations, and a high degree of absence from work across the cancer team due to personal illness and self-isolation. Second, many oncologists are being redeployed to general or acute medicine roles to support the many COVID-19 admissions requiring intensive medical support and input. Third, two small studies^{2,3} reporting COVID-19 outcomes in patients with cancer have resulted in the community being fearful of giving

effective anticancer treatments. These studies concluded that cancer patients are not only more susceptible to contracting the virus compared with the general population, but also at risk of developing more severe sequelae.^{3,4} In the largest cohort of 105 cancer patients, consisting of only 17 on chemotherapy, six patients on immunotherapy, and four on targeted therapies, strong recommendations were made about the COVID-19 risk from anticancer treatments.² All of these studies are small cohorts and limited to a few cancer centres. We felt that the studies raised important hypotheses but were in no way unequivocal and indeed a single-centre study¹⁴ from the USA yielded contradictory results. To clarify the relationship between cancer, anticancer treatments, and COVID-19, larger-scale datasets are necessary.

Because of the low prevalence of the coexistence of cancer and COVID-19, individual health-care centres and physicians will only see a few patients with both diseases. Additionally, because of the nature of the pandemic, much of the usual infrastructure of medical professional data dissemination has been completely dismantled: local, national, and international clinical meetings have been delayed or cancelled as part of public health measures to prevent COVID-19 spread. Therefore, the creation of national and international strategies to share data quickly and effectively is important during this time of unprecedented need for rapid learning and evidence regarding best practice.

The UKCCMP was designed to serve as a public health surveillance registry to answer important questions about the interaction of cancer, cancer treatments, and COVID-19, and to support rapid clinical decision making. Close alignment of health-care systems, physicians, and patients has meant that the project was launched and produced clinically meaningful output over the course of 4 weeks.

We described the demographics of patients with COVID-19 who have cancer and explored the effect of cytotoxic chemotherapy and other anticancer treatments on the trajectory of COVID-19. We identified that the phenotype of diagnosed COVID-19 disease in over half of cancer patients is mild, but death from COVID-19 in this cohort was observed in a substantial proportion of patients. This mortality is higher than that observed in the general non-cancer UK population,¹⁵ and might be reflective of the severity of symptoms of the cancer patients who choose to seek treatment in secondary health-care settings. The rate of admission to ITU was low, at about 6%, compared with a death rate of approximately 28%. Using our dataset, we are unable to answer the question as to whether this finding might arise as a result of advance patient health-care directives, hospital and ITU admission policies, a reluctance of treating physicians to use ITU resources for patients with cancer, or historically fewer ITU beds available in the UK.¹⁶ The ITU admission rate was notably low and reflective of findings from the UK intensive care national

audit and research centre.¹⁷ This finding does raise questions as to whether having a diagnosis of cancer decreases the potential access of these patients to the most intensive support.

From this dataset, using multivariate analysis, we concluded that cytotoxic chemotherapy given within 4 weeks before confirmed COVID-19 is not a significant contributor to a more severe disease or a predictor of death from COVID-19, compared with patients with cancer who have not received chemotherapy in that period. Although numbers of patients were smaller, similar observations were observed for immunotherapy, hormonal therapy, targeted therapy, and radiotherapy. Again, further interrogation with higher numbers of patients will allow us to confirm or refute this finding.

Overall, in interpreting these data and putting them into context, we suggest that continuing to shield patients with cancer from exposure to SARS-CoV-2 is important, through self-isolation, safely minimising the number of hospital visits (which might mean a substitution or oral drugs in place of intravenous drugs), avoiding the mixing of COVID-19-negative and COVID-19-positive workstreams within the hospital environment, and by mitigating the risk of neutropenia to avoid the risk of simultaneous COVID-19 and bacterial septicemia. Patients with cancer must have equivalent access to ITU care. However, in answer to the frequent question from patients as to whether chemotherapy or anticancer treatments will increase their risk of dying from COVID-19, in addition to the increased risk due to their cancer, our answer should be not necessarily so. In patients presenting to UK National Health Service trusts or cancer centres, our data are strongly indicative that cancer plus COVID-19 mortality is principally driven by advancing age and the presence of other non-cancer comorbidities. We concluded that withholding effective cancer treatments from many cancer patients during the pandemic runs the very real risk of increasing cancer morbidity and mortality, perhaps much more so than COVID-19 itself.

The UKCCMP has some limitations. Our analysis is partly dependent on the UK national COVID-19 testing policy, which is less permissive than that of other nations,^{18,19} and also relies on RT-PCR, which has a well described false-negative result.²⁰ The project might therefore under-report total COVID-19 cases in patients with cancer, particularly those with no or mild symptoms and who do not require treatment at or present to health-care centres. However, because we are in such close and frequent contact with our patients, and have a high index of suspicion on their behalf, we might also repeat testing and potentially overreport SARS-CoV-2 infection in these patients compared with in the general population. A selection bias might exist, in that those patients who were not on chemotherapy might have stopped chemotherapy because of a poor performance status, thus increasing the risk of death from COVID-19 disease, and reducing our

ability to assess the real risk of anticancer treatments in a population with a better performance status. However, we have attempted to address this limitation through multivariate analyses with age and comorbidity correction. Finally, we have not commented on overall incidence of COVID-19 positivity among cancer patients because we do not yet have secure numerators and denominators for that calculation. However, the total number of cases remains thankfully low, probably reflecting effective physical distancing measures for cancer patients in hospitals.

Despite these limitations, the UKCCMP covers most of the UK cancer population, with universal access to cancer care and has been achieved through the rapid set up of a dedicated and coordinated emergency cancer network. We will continue to update the UKCCMP register data weekly and share our outcomes with the oncological community.

With greater numbers of patients analysed we will be able to answer more nuanced questions and guide further research. Future studies should investigate whether the grading of COVID-19 could be further refined to add granularity to our understanding of the heterogeneity between different tumour subtypes, to clarify the risks of specific anticancer treatments, to discoverer whether risks relating to more specific timing of anticancer treatments exist, and to gain a better understanding of the interaction between the host immune response and risk from COVID-19. Some interesting questions exist surrounding the differential effects of various anticancer treatments on different components of the immune system (neutrophils, cytotoxic T cells, regulatory T cells, and macrophages) and how these factors will interplay with the risk of contracting SARS-CoV-2 infection, or with the possibility of severe COVID-19 disease sequelae such as the cytokine storm.

Contributors

LYWL, RK, and GM were involved in the study design; LYWL, JBC, GM, RK, and UKCCMP in the data collection; and LYWL, JBC, TS, CDT, RK, and GM in the analysis, interpretation, writing of manuscript, and decision to submit.

Declaration of interests

We declare no competing interests.

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See Online for appendix