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## COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments

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1 COVID-19 mortality in hospitalized cancer patients is not  
2 significantly affected by chemotherapy or other anti-cancer  
3 treatments.  
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17 **\*Joint first Author:** Lennard YW Lee, Institute of Cancer and Genomic Sciences, University of Birmingham, Edgbaston,  
18 Birmingham B15 2TT, UK. L.lee.2@bham.ac.uk, 0121 414 3511 & Jean-Baptiste Cazier, Centre for Computational Biology,  
19 University of Birmingham, Institute of Cancer and Genomic Sciences, University of Birmingham, Edgbaston, Birmingham B15  
20 2TT, UK. J.Cazier@bham.ac.uk, 0121 414 6480

21

22 **\*Joint Senior Author:** Gary Middleton, Institute of Immunology and Immunotherapy, University of Birmingham, Edgbaston,  
23 Birmingham B15 2TT, UK. g.middleton@bham.ac.uk, 0121 414 7144 & Rachel Kerr, Department of Oncology, Old Road  
24 Campus Research Building, University of Oxford, Oxford OX3 7DQ, 01865 617331

25

**Corresponding Author:**

26

Lennard YW Lee, Institute of Cancer and Genomic Sciences, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK.  
27 L.lee.2@bham.ac.uk, 0121 414 3511

28

**Conflicts of Interest:** The authors declare no potential conflicts of interest.

29

**Running Title:** No significant effect on mortality for hospitalized cancer patients with COVID-19 on chemotherapy,  
30 immunotherapy, radiotherapy or hormonal treatment.

31

32 **Keywords:** cancer, coronavirus, COVID-19, SARS-CoV-2, United Kingdom, Public Health, chemotherapy, Systemic anti-  
33 cancer treatments, Live clinical data dissemination system,

34 **Abstract**

35

36 **Background**

37 Individuals with cancer, particularly those who are receiving systemic anti-cancer treatments, have been  
38 postulated to be at increased risk of mortality from SARS-CoV-2 related coronavirus disease (COVID-19).  
39 This conjecture has considerable impact on the treatment of cancer patients and large, multi-centre data  
40 to support this assumption is lacking due to the contingencies of the pandemic.

41

42 **Methods**

43 The cancer community of the United Kingdom (UK) has launched the *UK Coronavirus Cancer Monitoring*  
44 *Project* (UKCCMP). The UKCCMP is the first COVID-19 clinical registry that enables near real-time  
45 reports to frontline doctors about the effect of COVID-19 on cancer patients.

46

47 **Findings**

48 An analysis of the first 800 cancer patients with symptomatic COVID-19 disease entered into the  
49 UKCCMP registry has been performed. Approximately half of these patients have a mild COVID-19  
50 disease course (52%). Mortality was observed in 226 patients (28%) and risk of death was significantly  
51 associated with advancing patient age, sex (M>F) and the presence of other co-morbidities.  
52 Approximately one third had received cytotoxic chemotherapy within 4 weeks prior to testing positive for  
53 COVID-19. After adjusting for age, sex and comorbidities, recent receipt of chemotherapy had no  
54 significant effect on mortality from COVID-19 disease, when compared to cancer patients who had not  
55 received recent chemotherapy. No significant effect on mortality was also observed for patients with recent  
56 immunotherapy, hormonal therapy, targeted therapy or radiotherapy use.

57

58 **Interpretation**

59 Mortality from COVID-19 in cancer patients appears to be principally driven by age, sex and co-  
60 morbidities. We are not able to identify evidence that cancer patients on cytotoxic chemotherapy or other  
61 anti-cancer treatment are at significantly increased risk of mortality from COVID-19 disease compared to  
62 those not on active treatment.

63

64 **Introduction**

65

66 It is clear from data arising from the Office for National Statistics that the risk of morbidity and mortality  
67 from COVID-19 disease as a consequence of SARS-CoV-2 infection is not uniform across the population.  
68 Cancer patients on systemic anti-cancer treatments have been generally assumed by many to be at a  
69 higher risk than their counterparts who are not currently receiving anti-cancer treatment. The evidence to  
70 support this claim is scanty and limited to retrospective series arising from China, the epicentre of the  
71 current pandemic, and involving very small numbers of patients. <sup>1,2,3</sup> However despite these severe  
72 limitations, the promulgation of this hypothesis has led to widespread, global changes to chemotherapy  
73 and anti-cancer treatment prescribing patterns. <sup>4</sup> In a global health emergency, it is critical that oncologists  
74 secure evidence from a larger dataset, which can then inform their risk benefit analyses for individual  
75 patients in terms of the use of anti-cancer treatments. <sup>5,6</sup>

76

77 On 18<sup>th</sup> March 2020, we launched the *UK Coronavirus Cancer Monitoring Project* (UKCCMP) with  
78 widespread support across our national cancer network. <sup>7,8</sup> Within 5 weeks the UKCCMP had generated  
79 the largest prospective database and interrogation of COVID-19 disease in cancer patients generated to  
80 date. Here we describe the clinical and demographic characteristics and COVID-19 outcomes in this  
81 cohort of patients with cancer and symptomatic COVID-19 and attempt to assess how the presence of  
82 cancer and the receipt of cytotoxic chemotherapy and other anti-cancer treatments impacts upon COVID-  
83 19 disease phenotype.

84

85 **Methods**

86

87 **Study Design and Participants**

88 The UKCCMP database of United Kingdom (UK) cancer patients with a COVID-19 infection was launched  
89 with the support of the UK oncology professional bodies, including the *Association of Cancer Physicians*  
90 (*ACP*), *The Royal College of Radiologists (RCR)*, the *National Oncology Trainees Research Collaborative*  
91 *for Healthcare Research (NOTCH)*, patient support groups including *Macmillan Cancer Support*, charities  
92 including *Action Radiotherapy* and our national research body, *Cancer Research UK (CRUK)*.<sup>9,10</sup> It was  
93 designed as a Public Health Surveillance registry to support rapid clinical decision-making, in accordance  
94 with the UK Policy Framework for Health and Social Care Research, the UK National Research Ethics  
95 Service and the UK Governance Arrangement for Research Ethic Committees. At an institutional level,  
96 this cohort study was approved according to local information governance processes. All patients with  
97 active cancer and presenting to our network of cancer centres from March 18<sup>th</sup> 2020 to April 26<sup>th</sup> 2020  
98 with COVID-19 were eligible for enrolment into the UKCCMP. In keeping with international practice,  
99 patients were deemed to have COVID-19 if there was a positive SARS-CoV-2 Real-Time Reverse  
100 Transcription Polymerase Chain Reaction (RT-PCR) assay test from a throat/nose swab. Patients with a  
101 radiological or clinical diagnosis of COVID-19, without a positive RT-PCR test were not included in this  
102 analysis. As such, these patients are, by definition, symptomatic, requiring secondary care review for  
103 potential hospitalization. They were not part of a proactive surveillance program. 'Patients with active  
104 cancer' was defined as those with metastatic cancer, or on anti-cancer treatment in any setting  
105 (curative/radical/adjuvant/neoadjuvant setting) or treated within the past 12 months with surgery/cytotoxic  
106 chemotherapy/radiotherapy. Stage of tumour was divided into those into those that were *Primary Tumour*  
107 *Localized-* localized to organ and therefore potentially resectable, *Primary Tumour- locally advanced-*  
108 where it had spread locally from the primary organ and not resectable, *Metastatic-* where there is distant  
109 spread (stage 4) and those presently in *Remission*. Patients were assessed as to whether they had  
110 received chemotherapy (which did not include denosumab), immunotherapy, hormonal therapies or  
111 radiotherapy within 4 weeks of contraction of SARS-CoV-2. Non-palliative chemotherapy was defined as  
112 chemotherapy that was used in a neoadjuvant/adjuvant/radical setting. For the purposes of the present  
113 analysis, outcomes were monitored up to April 26<sup>th</sup> 2020.

114

115

116 **Data Collection**

117 Prospective data collection was performed by the newly formed pan-UK cancer centre emergency  
118 response network. Case reporting was led by a COVID-19 Emergency Response Reporting Individual  
119 (ERRI), supported by a Local Emergency Response Reporting Group (LERRG) at each centre. The role  
120 of the LERRG was to ensure near continuous reporting of cases in situations of absence of the ERRI due  
121 to off-days, illness, compassionate leave, self-isolation or re-deployment. The UKCCMP encouraged all  
122 local reporting sites to enter data in a real time basis, as soon as a positive SARS-CoV-2 test had been  
123 identified. The data fields were then re-updated as soon as treatment and outcomes had been identified  
124 and also to reflect the worse COVID-19 severity scores during hospitalization. The ERRI was a trained/in  
125 training oncologist who performed data review, annotation and entry. In a small number of centres, data  
126 entry was performed by data managers but with direct oversight by the ERRI. All registry entries were de-  
127 identified at source to ensure data anonymity to researchers. Data was entered into a Research Electronic  
128 Data Capture (REDCap) browser-based metadata driven electronic data capture (EDC) software system.

129 <sup>11</sup> This secure EDC platform is hosted by the Institute of Translational Medicine at the University of

130 Birmingham. Patient demographics, treatment details, COVID-19 disease course and cancer features  
131 were obtained from the direct assessment of the ERRI/LERRG and/or through hospital medical records.  
132 COVID-19 Severity Score was determined according to the WHO guidelines.<sup>12</sup> Cancer type was defined  
133 according to ICD-10 diagnostic codes.

134

135

#### 136 **UKCCMP data processing and analysis**

137 The data through the REDCap platform is transferred securely through to the Compute and Storage for  
138 Life Science (CaStLeS) infrastructure as part of the Birmingham Environment for Academic Research  
139 local Cloud (BEARCloud)<sup>13</sup> at the Centre for Computational Biology, University of Birmingham.

140

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

146

147

#### 148 **Statistical analysis & Data visualisation**

149

150 In this study, we report on the clinical outcomes of cancer patients who developed COVID-19 disease,  
151 assessing whether the patient died or eventually achieved discharge, and observing the effect of anti-  
152 cancer treatment on outcomes. The two-sided Welch's t-test was used to compare continuous data and  
153 two-sided Fisher's exact test was used to compare categorical data from different categories with  
154 multivariate Bonferroni (multi-test) adjustment. A primary endpoint of all-cause mortality was defined *a*  
155 *priori*. This included deaths described as related to COVID-19 during this admission, as well as deaths  
156 reported as a consequence of any other cause during this admission, such as due to cancer progression  
157 or treatment toxicity. This was used for all regression analyses. Multivariate analyses were performed in  
158 SPSS, version 26 and Fisher's Exact tests in R version 3.6.3 utilising the Fisher.test () function.  
159 Multivariable logistic regression was used to estimate odd ratios and 95% confidence intervals of each  
160 factor after adjustment for clinically relevant potential confounders of age, sex, diabetes, hypertension,  
161 COPD or other comorbidities at admission. Goodness of fit was checked using Hosmer-Lemeshow test  
162 and, unless otherwise reported, had  $p > 0.05$ . Where this goodness of fit criteria was not met, further  
163 multivariable logistic regression models using the above potential confounders was performed using a  
164 forward selection of  $p < 0.10$ . Patients with either 'no information/missing relevant data' were not included  
165 in these regression analyses. Sub-group analyses of patients on chemotherapy was performed in order  
166 to better identify risk in this cohort of patients. This included an analysis of non-palliative vs. palliative  
167 chemotherapy, first line vs. later lines of palliative chemotherapy, palliative chemotherapy vs. no anti-  
168 cancer treatment, palliative chemotherapy vs. no recent chemotherapy. The justification for these  
169 analyses is that the cancer chemotherapy group is heterogenous. These subgroup analyses have a well-  
170 established oncology/clinical rationale, for example, non-palliative (curative) chemotherapy aims to  
171 prevent recurrence or eradicate disease, whereas palliative chemotherapy aims to maintain quality of life,  
172 or extend life usually by a matter of months, and both patient and chemotherapy treatment (drugs, dose  
173 and intensity) necessarily evolve as a patient progresses from 1<sup>st</sup> line to later lines of chemotherapy.<sup>14</sup>  
174 Data processing and visualisation utilised R (version 3.6.3) packages.

175 **Project funding**

176 This project was funded by the University of Birmingham (data collection and time of JPC, LL, UKCCMP  
177 and GM) and the University of Oxford (RK time). The University of Birmingham had no formal role in  
178 data collection, analysis, interpretation or decision to submit.

179

180

181

182 **Results**

183

184 Fifty-five Cancer centres had appointed a COVID-19 local emergency response reporting group (LERRG)  
185 and form part of this clinical network of cancer centres. Together this network covered a patient population  
186 of nearly 1.5 million patients who were living with active cancer, with good coverage across all regions of  
187 the United Kingdom (Figure 1).

188

189 This early patient cohort consists of the first 800 patients with active cancer who had a documented SARS-  
190 CoV-2 infection presenting as symptomatic COVID-19 disease. As presented in Table 1, 56% of patients  
191 were male with a median age of 69.0 years (IQR 59-76). Comorbidities were common, including  
192 hypertension (n=247, 31%), diabetes (n=131, 16%), cardiovascular disease (n=109, 14%), COPD (n=61,  
193 8%). One hundred and sixty-nine cancer patients were listed as having no comorbidities apart from their  
194 cancer diagnosis (21%). Approximately half of the patients had current ongoing metastatic cancer (n=347,  
195 43%), of which malignant neoplasia of the digestive organs (n=150, 19%), haematological malignancies  
196 (n=109, 14%), breast (n=102, 13%) and respiratory and thoracic organs (n=90, 11%) were the commonest  
197 primary tumour sites. The median time from identification of documented COVID-19 disease until study  
198 end points were met (death or discharge from hospital) was 5 days (range 0-38).

199

200 In terms of the pattern of COVID-19 presentation, most presented with fever (n=484, 61%), cough (n=377,  
201 47%), and/or shortness of breath (n=312, 39%). However, diarrhoea (n=51, 6%), nausea and vomiting  
202 (n=39, 5%), ageusia (n=13, 2%) and anosmia (n=9, 1%) were also identified as less common presenting  
203 symptoms.

204

205 A number of correlates of severity of COVID-19 were measured, according to WHO criteria.<sup>12</sup> A mild  
206 COVID-19 severity score was recorded in 412 patients (52%), with 96 patients (12%) not requiring  
207 hospitalization. 315 patients required oxygen (39%), and 53 patients received ITU-level care (7%). Of  
208 these 53 patients, at the time of analysis, 6 were discharged (11%), 23 died (43%) and 24 were either still  
209 in ITU and/or did not have a final recorded outcome (45%). The ITU admission rate was notably low and  
210 reflective of findings from the UK intensive care national audit and research centre (ICNARC)<sup>15</sup>.

211

212 Death in this cohort was the final outcome in 226 patients (28%) with reporting stating that the death was  
213 principally attributable to COVID-19 in the majority of these cases (n=211, 93%). This mortality rate is  
214 higher than reported literature in the 'general' population, and likely to reflect the relative severity of  
215 symptoms of cancer patients who seek help from secondary care. Compared to the rest of the cancer  
216 cohort, patients who died were significantly older (median 73.0 years vs. 66.0 years, p<0.001) (Figure 2),  
217 more were male (mortality 33%, 146/449) than female (mortality 23%, 80/349) and those who died also  
218 displayed higher rates of comorbidities including cardiovascular disease (21% vs 11%, p<0.001) and  
219 hypertension (41% vs 27%) (p<0.001). They were also more likely to present with symptoms of shortness  
220 of breath (57% vs 32%) (p<0.001).

221

222 Across the cohort, 22% of patients were reported by sites as having their anti-cancer treatments  
223 interrupted due to the COVID-19 pandemic, though, the exact nature of this interruption was not captured  
224 in this study.

225



226 Compared to patients who had not received chemotherapy within 4 weeks of testing positive for COVID-  
227 19, those who had received recent chemotherapy did not suffer increased mortality when analysed by  
228 univariate analysis (27% death rate with chemotherapy vs 29% death rate without recent chemotherapy).  
229

230 In order to explore this relationship in greater detail, an in-depth analysis of the 281 patients who had  
231 received recent chemotherapy use was therefore performed (Figure 3). There were no significant  
232 differences in underlying cancer primary site in the recent chemo versus no chemo group. However,  
233 compared to cancer patients who had not received recent chemotherapy, the chemotherapy positive  
234 cohort was younger (median age 64.0 years vs. 71.0 p<0.001). Therefore, a multivariate analysis with  
235 adjustment for age, sex and comorbidities was performed and we found that deaths in COVID-19 cancer  
236 patients who had received recent chemotherapy were still no more likely than those that had not (OR  
237 1.18, 95% CI [0.81 to 1.72]; p=0.380) (Table 2). This analysis had a borderline fit (Hosmer-Lemeshow test  
238 p value=0.048). To be more confident of our findings, we also performed a forward regression model  
239 (Hosmer-Lemeshow goodness of fit p=0.476) with similar findings (OR 1.15, 95% CI [0.79 to 1.66],  
240 p=0.467).

241  
242 Patients receiving chemotherapy are a heterogeneous group and so further exploratory subgroup  
243 analyses were performed. On further multivariate analysis of the group of patients who had received  
244 recent chemotherapy, decreased odds of death was found in patients receiving non-palliative  
245 chemotherapy (neoadjuvant/adjuvant/radical) compared to those receiving palliative chemotherapy (16%  
246 vs 35%) (OR 0.40 CI [0.17 to 0.96]; p=0.040) following adjustments for age, sex and comorbidities.  
247 However, the odds of death in these palliative chemotherapy patients was still not significantly different to  
248 cancer patients with no anti-cancer treatment at all (OR 1.05, 95% CI [0.63 to 1.76]; p=0.854), but there  
249 was a non-significant trend compared to those with no recent chemotherapy (OR 1.48, 95% CI [0.93 to  
250 2.36]; p=0.102). There was no significant differences in mortality in those patients receiving first line  
251 palliative chemotherapy compared to those receiving later lines of palliative treatment (OR 0.84, 95% CI  
252 [0.36 to 1.98]; p=0.690) following adjustments for age, sex and comorbidities.

253  
254 Finally, we analysed the use of other forms of anti-cancer therapies within 4 weeks of testing positive for  
255 SARS-CoV-2 infection and presenting with COVID-19 disease. Compared to the rest of the cohort who  
256 were not on these therapies, patients on immunotherapy (n=44, OR 0.59, 95% CI [0.27 to 1.27]; p=0.177),  
257 hormonal therapy (n= 64, OR 0.90, 95% CI [0.49 to 1.68]; p=0.744), radiotherapy (n=76, OR 0.65, 95%  
258 CI [0.36 to 1.18]; p=0.159) and targeted therapies (n= 72, OR 0.83, 9% CI [0.45 to 1.54]; p=0.559) were  
259 also not at any additional risk of death following adjustment for age, sex and comorbidities (Figure 4).

260

261

262

263 **Discussion**

264

265 Global healthcare systems are currently dealing with the COVID-19 pandemic, a disease caused by  
266 SARS-CoV-2 infection; a situation which is set to be a generational challenge to all clinicians. At the time  
267 of writing, the clinical phenotype and interactions of SARS-CoV-2 infection/ COVID-19 disease with pre-  
268 existing disease and systemic anti-cancer treatments agents is poorly described and based on very small  
269 retrospective studies.

270

271 The disruption from the pandemic to normal oncological care has been huge for a number of reasons.  
272 Firstly, cancer clinicians and the rest of the cancer team are under unprecedented pressures, with  
273 increasing concern from patients about their perceived 'vulnerability', cancelled cancer operations, a  
274 significant drive to do telemedicine rather than face to face consultations, and a high degree of absence  
275 from work across the cancer team, due to personal illness and self / household isolation. Secondly, many  
276 oncologists are being redeployed to general or acute medicine roles to support the large number of  
277 COVID-19 admissions requiring intensive medical support and input. Thirdly, a couple of small studies  
278 reporting COVID-19 outcomes in cancer patients has resulted in the community being fearful of giving  
279 effective anticancer treatments. These studies concluded that cancer patients are not only more  
280 susceptible to contracting the virus, but also at risk of developing more severe sequelae.<sup>3,2</sup> In the largest  
281 cohort of 105 cancer patients consisting of only 17 on chemotherapy, 6 patients on immunotherapy and  
282 4 on targeted therapies, strong recommendations were made about the COVID-19 risk from anti-cancer  
283 treatments.<sup>1</sup> All of these studies are small cohorts and limited to a very restricted number of cancer centres.  
284 We felt that the studies raised important hypotheses but were in no way unequivocal and indeed there  
285 are contradictory studies from a single centre study from the United States of America.<sup>16</sup> To clarify the  
286 relationship between cancer, anti-cancer treatments and COVID-19 infection, it is clear that larger-scale  
287 datasets are necessary.

288

289 Because of the limited prevalence of the coexistence of cancer and COVID-19 disease, individual health  
290 care centres and physicians will only encounter small numbers of patients with both diseases. In addition,  
291 because of the fire-fighting nature of pandemic healthcare, much of the usual infrastructure of medical  
292 professional data dissemination has been completely dismantled: local, national, and international clinical  
293 meetings have been delayed or cancelled as part of public health measures to prevent COVID-19 spread.  
294 It is therefore of even greater importance that national and international strategies to share data quickly  
295 and effectively are created during this time of unprecedented need for rapid learning and evidence  
296 regarding best practice.

297

298 The UKCCMP was designed to serve as a Public Health Surveillance registry to answer important  
299 questions about the interaction of cancer, its treatments and COVID-19, and to support rapid clinical  
300 decision-making. Close alignment of healthcare systems, physicians, and patients has meant that the  
301 project was launched and produced clinically meaningful output over the course of four weeks.

302

303 In this paper, the UKCCMP describes the demographics of cancer patients with COVID-19 and explores  
304 the effect of cytotoxic chemotherapy and other anti-cancer treatments on the trajectory of that disease.  
305 We have identified that the phenotype of diagnosed COVID-19 disease in over half of cancer patients is  
306 mild, but death from COVID-19 in this cohort was observed in a significant percentage of patients. This  
307 mortality is higher than that observed in the general non-cancer UK population,<sup>17</sup> and may be reflective

308 of the severity of symptoms of the cancer patients who choose to seek treatment in secondary healthcare  
309 setting. It is interesting to note that the rate of admission to ITU was low at about 6% compared to a death  
310 rate of approximately 28%. Our dataset is currently unable to answer the question as to whether this might  
311 arise as a result of advance patient healthcare directives, hospital/ITU admission policy, a reluctance of  
312 treating physicians to utilise ITU resources for cancer patients or historically lower numbers of ITU beds  
313 available in the United Kingdom <sup>18</sup>. This does raise questions as to whether having a diagnosis of cancer  
314 decreases the potential access of these patients to the most intensive support.

315

316 From this early dataset, using multivariate analysis, we conclude that cytotoxic chemotherapy given within  
317 4 weeks prior to confirmed COVID-19 disease is not a significant contributor to a more severe disease or  
318 a predictor of death from COVID-19, compared to cancer patients who have not received chemotherapy  
319 in that period. Whilst numbers are smaller, similar observations were observed for immunotherapy,  
320 hormonal therapy, targeted therapy and radiotherapy. Again, further interrogation with higher numbers  
321 will allow us to confirm or refute this finding.

322

323 Overall, in interpreting these data, and putting them into context, we suggest that it is important to continue  
324 to shield cancer patients from exposure to SARS-CoV-2, though self-isolation, minimising hospital visits  
325 where they can be avoided (which may mean a substitution or more oral agents in place of intravenous  
326 drugs), avoiding the mixing of COVID negative and COVID positive workstreams within the hospital  
327 environment; and by mitigating the risk of neutropenia to avoid the risk of simultaneous COVID-19 and  
328 bacterial septicaemia. It is also important to ensure that cancer patients have equivalent access to ITU  
329 care. However, in answer to the frequent question from patients as to whether chemotherapy or anti-  
330 cancer treatments will increase their risk of dying from COVID-19, in addition to the increased risk due to  
331 their cancer, our answer should be, not necessarily so. In patients presenting to NHS trusts or cancer  
332 centres, our data is strongly indicative that cancer COVID-19 mortality is principally driven by advancing  
333 age and the presence of other non-cancer co-morbidities. We conclude that withholding effective cancer  
334 treatments from significant numbers of cancer patients during the current pandemic runs the very real risk  
335 of increasing cancer morbidity and mortality, perhaps much more so than COVID-19 itself.

336

337 It is important to note the current limitations of the UKCCMP. Our analysis is partly dependent on the UK  
338 national COVID-19 testing policy, which is currently is less permissive than other nations <sup>19,20</sup> and also  
339 relies on RT-PCR which has a well described false negative result. <sup>21</sup> The project may therefore  
340 underreport total COVID-19 cases in cancer patients, particularly those with no/mild symptoms and who  
341 do not require or present to healthcare centres. On the other hand, because we are in such close and  
342 frequent contact with our patients, and have a high index of suspicion on their behalf, we may also repeat  
343 testing and potentially over report SARS-CoV-2 infection compared to the general population. One might  
344 argue that there could be a selection bias, in that those patients that were *not* on chemotherapy may have  
345 been taken off because of a poorer performance status, thus increasing their risk of death from COVID-  
346 19 disease, and reducing our ability to assess the real risk of anticancer treatments in a better performance  
347 status 'healthier' population. However, we have attempted to address this through multivariate analyses  
348 with age and co-morbidity correction. Finally, we do not comment on overall incidence of COVID-19  
349 positivity amongst cancer patients because we do not yet have secure numerators and denominators for  
350 that calculation. However, total number of cases remain thankfully low, likely reflecting effective cancer  
351 social isolation policies.

352

353 Despite these noted limitations, the UKCCMP is unique in covering the majority of the UK cancer  
354 population, with universal access to cancer care and has been achieved through the rapid set up of a  
355 dedicated and coordinated emergency cancer network. The UKCCMP will continue to update our data  
356 weekly and share our outcomes with the oncological community.

357

358 With greater numbers analysed we will be able to answer more nuanced questions and guide further  
359 research. It will be important to investigate if the grading of COVID-19 could be further refined, to add  
360 granularity to our understanding the heterogeneity between different tumour subtypes, to clarify the risks  
361 of specific anti-cancer treatments, to determine if there are risks relating to more specific timing of anti-  
362 cancer treatments, and to gain a better understanding of the interaction between the host immune  
363 response and risk from COVID-19. There are some very interesting questions surrounding the differential  
364 impact of various anticancer treatments on different components of the immune system (neutrophils,  
365 cytotoxic T-cells, regulatory T cells and macrophages) and how these will interplay with the risk of  
366 contracting SARS-CoV-2 infection, or with the possibility of severe COVID-19 disease sequelae such as  
367 the cytokine storm.

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**Table 1: Clinical features of patients in the UKCCMP registry, 16<sup>th</sup> April 2020, with breakdown by all- cause mortality. Data are displayed as number of cases, except for age which is median age.**

Patient features	All patients (n=800)	Patients Died (n=226)	Patients Survived (n=574)
<b>Sex and age</b>			
- Male	449 (56%)	146 (65%)	303 (53%)
- Female	349 (44%)	80 (35%)	269 (47%)
- Other <sup>a</sup>	2 (0%)	0 (0%)	2 (0%)
- Median age/years	69	73	66
<b>Co-morbidities</b>			
- Cardiovascular disease	109 (14%)	48 (21%)	61 (11%)
- COPD	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 <sup>b</sup>	336 (42%)	108 (48%)	228 (40%)
- No information	123 (15%)	28 (12%)	95 (17%)
<b>Cancer type</b>			
- 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 <sup>c</sup> /unspecified	47 (6%)	12 (5%)	35 (6%)
<b>Cancer Stage</b>			
- 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%)
<b>Cancer treatment within 4 weeks</b>			
- 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 <sup>d</sup>	60 (8%)	13 (6%)	47 (8%)
- None	272 (34%)	92 (41%)	180 (31%)
- No information	10 (1%)	1 (0%)	9 (2%)
<b>COVID-19 Severity Score</b>			
- 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%)
<b>COVID-19 treatment</b>			
- ITU	53 (7%)	23 (10%)	30 (5%)

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<sup>a</sup> Patient features- other, identifies patient where the patient does not identify as either male/female

<sup>b</sup> Co-morbidities- other, identifies co-morbidities which are not any of the co-morbidities included in the tables

<sup>c</sup> Cancer type- other, identifies ICD10 cancer types including malignant neoplasia of the bone and articular tissue, endocrine glands, mesothelioma and soft tissue and any other tumour type which was not included in the table.

<sup>d</sup> Cancer type- other, identifies cancer treatments which do not fall into the cancer treatment types defined in the table

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**Table 2: Regression analysis and odds of death based on features of patients in the UKCCMP. Univariate analysis was conducted with presence compared to 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 performed. Multivariate analysis was conducted correcting for age, sex and patient co-morbidities.**

Patient features	Univariate analysis			
	Odds Ratio (95% CI)	<i>p value</i>	<i>p adjusted</i>	
<b>Sex and age</b>				
- Sex	1.67 (1.19-2.34)	0.003	0.006	**
- Age	9.42 (6.56-10.02)	<0.0001	<0.0001	****
<b>Co-morbidities</b>				
- Cardiovascular disease	2.32 (1.47-3.64)	0.0003	0.0019	**
- COPD	1.80 (1.00-3.27)	0.063	ns	
- Diabetes	1.61 (1.03-2.48)	0.032	ns	
- Hypertension	1.95 (1.36-2.80)	0.0003	0.0015	**
<b>Cancer type</b>				
- Lip, oral cavity and pharynx	0.42 (0.13-1.21)	0.116	ns	
- Digestive organs	0.91 (0.60-1.38)	0.680	ns	
- Respiratory and intrathoracic organs	1.50 (0.91-2.45)	0.121	ns	
- Melanoma (Skin)	0.37 (0.12-1.14)	0.079	ns	
- Breast	0.48 (0.28-0.84)	0.009	ns	
- Female genital organs	0.31 (0.11-0.81)	0.010	ns	
- Male genital organs	1.99 (1.14-3.48)	0.015	ns	
- Urinary tract	1.10 (0.58-2.12)	0.745	ns	
- Central nervous system	0.64 (0.15-2.32)	0.760	ns	
- Lymphoma	1.30 (0.71-2.30)	0.373	ns	
- Other Haematological	1.57 (1.01-2.42)	0.040	ns	
<b>Cancer Stage</b>				
- Primary Tumour - Localised	1.04 (0.67-1.64)	0.912	ns	
- Primary Tumour - Locally Advanced	0.58 (0.29-1.09)	0.111	ns	
- Metastatic	1.34 (0.90-2.01)	0.145	ns	
- Remission	0.42 (0.10-1.43)	0.204	ns	
<b>Cancer treatment within 4 weeks</b>				
- Chemotherapy	0.78 (0.55-1.11)	0.173	ns	
- Hormone Therapy	1.16 (0.64-2.06)	0.659	ns	
- Immunotherapy	0.60 (0.27-1.24)	0.179	ns	
- Radiotherapy	0.66 (0.37-1.17)	0.178	ns	
- Surgery	0.83 (0.32-2.15)	0.825	ns	
- Targeted Treatment	0.56 (0.30-1.01)	0.058	ns	
<b>COVID-19 Severity Score</b>				
- 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	****
<b>COVID-19 treatment</b>				
- ITU	1.95 (1.09-3.52)	0.027	0.027	*
<b>Treatment features</b>	Multivariate analysis			
	Odds Ratio (95% CI)	<i>p value</i>		
<b>Recent ant-cancer treatments</b>				
- 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		
<b>Cytotoxic Chemotherapy</b>				
- Non-palliative chemo vs palliative chemo	0.40 (0.17-0.96)	0.040		
- Palliative 1st line chemo vs other line	0.84 (0.36-1.98)	0.690		
- Palliative chemo vs no chemo	1.48 (0.93-2.36)	0.102		
- Palliative chemo vs no treatment	1.05 (0.63-1.76)	0.854		

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422 \* denotes statistical significance of *p* adjusted, where \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ , \*\*\*\*  $p < 0.0001$

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439

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441 The following authors were involved in the study design (LL, RK, GM), data collection (LL, JBC, GM, RK,  
442 UKCCMP), analysis (LL, JBC, TS, CT, RK, GM), interpretation (LL, JBC, TS, CT, RK, GM), writing of  
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452 **Declaration of interest**

453

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515 FIGURE LEGENDS

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517

518 *Figure 1: Geographical plot, 26<sup>th</sup> April 2020, demonstrating the prevalence of COVID-19 in the Scotland,*  
519 *Wales and regions of England. Data displayed is average number of cases from reports per cancer centre*  
520 *region.*

521

522 *Figure 2: Horizontal bar plot demonstrating the age distribution of cancer patients in the cohort and relation*  
523 *to patient mortality.*

524

525 *Figure 3: Sankey plot demonstrating relationship of chemotherapy use within 4 weeks of contracting*  
526 *COVID-19 infection and mortality and severity of disease course. The vertical coloured bars denote the*  
527 *patient cohort, split into different groups (purple- severity of COVID19, blue- presence or absence of*  
528 *recent chemotherapy, red/green-patient mortality). The grey horizontal bars denote that associations*  
529 *between the different groups with wider bars denoting more overlap.*

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531 *Figure 4: Forest plots showing effect of anti-cancer treatments and mortality from COVID-19 infection*

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545 **Supplementary Methods**

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547 **Data visualisation and figure generation**

548 Data processing and visualisation utilised R (version 3.6.3) packages including broom, dplyr, gpclib,  
549 ggmap, ggplot2, mapdata, maps, maptools, networkD3, rgdal, rgeos, robustbase and viridis. Data  
550 subsetting was performed using the subset() function of 'robustbase' and data reshaping for visualisation  
551 involved the use of the group\_by() and melt() functions of 'dplyr'. Functions from the ggplot2 R package  
552 were used to generate multiple plots including barplots (geom\_bar) and UK region map (geom\_polygon).  
553 The sankeyNetwork() function of the 'networkD3' R package was also used to generate the Sankey plot.  
554 The shape (.shp) file for the UK region map was publicly available from the UK Office for National  
555 Statistics. <sup>22</sup>

556