The risk of contracting SARS-CoV-2 or developing COVID-19 for people with cancer: A systematic review of the early evidence

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ARTICLE INFO

ABSTRACT

Background: The early COVID-19 literature suggested that people with cancer may be more likely to be infected with SARS-CoV-2 or develop COVID-19 than people without cancer, due to increased health services contact and/or immunocompromise. While some studies were criticised due to small patient numbers and methodological limitations, they created or reinforced concerns of clinicians and people with cancer. These risks are also important in COVID-19 vaccine prioritisation decisions. We performed a systematic review to critically assess and summarise the early literature.

Methods and findings: We conducted a systematic search of Medline/Embase/BioRxiv/MedRxiv/SSRN databases including peer-reviewed journal articles, letters/commentaries, and non-peer-reviewed pre-print articles for 1 January–1 July 2020. The primary endpoints were diagnosis of COVID-19 and positive SARS-CoV-2 test. We assessed risk of bias using a tool adapted from the Newcastle-Ottawa Scale.

Twelve studies were included in the quantitative synthesis. All four studies of COVID-19 incidence (including 24,181,727 individuals, 125,649 with pre-existing cancer) reported that people with cancer had higher COVID-19 incidence rates. Eight studies reported SARS-CoV-2 test positivity for > 472,000 individuals, 48,370 with pre-existing cancer. Seven of these studies comparing people with any and without cancer, were pooled using random effects [pooled odds ratio 0.91, 95 %CI: 0.57–1.47; unadjusted for age, sex, or comorbidities]. Two studies suggested people with active or haematological cancer had lower risk of a positive test. All 12 studies had high risk of bias; none included universal or random COVID-19/SARS-CoV-2 testing.

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Conclusions: The early literature on susceptibility to SARS-CoV-2/COVID-19 for people with cancer is characterised by pervasive biases and limited data. To provide high-quality evidence to inform decision-making, studies of risk of SARS-CoV-2/COVID-19 for people with cancer should control for other potential modifiers of infection risk, including age, sex, comorbidities, exposure to the virus, protective measures taken, and vaccination, in addition to stratifying analyses by cancer type, stage at diagnosis, and treatment received.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported to infect humans in Wuhan, China in December 2019. Infection with SARS-CoV-2 can lead to the development of coronavirus disease (COVID-19) which was declared a pandemic on 11 March 2020. COVID-19 has a wide range of presentations, from mild disease to severe pneumonia and respiratory distress requiring hospitalisation and mechanical ventilation, organ failure, and death.

The pandemic has presented unprecedented challenges to health care systems, public health agencies, governments, and populations, raising concerns about the safety of vulnerable groups, including people with cancer. In particular, there have been concerns that people with cancer may be at higher risk of developing COVID-19 due to increased exposure to SARS-CoV-2 (e.g. visiting high-risk settings such as hospitals), and/or increased susceptibility due to compromised immune responses resulting from either cancer itself and/or cancer treatment. People with cancer who developed COVID-19 were also hypothesised to be at higher risk of progressing to severe disease and death. Further, people with lung cancer may be at an elevated risk of developing COVID-19 and progressing to severe disease due to existing lung damage and reduced lung capacity, and those with haematological cancer may be at higher risk due to the direct effects of cancer on the immune system.

Early studies such as Liang et al. [1] (published 14 Feb 2020) and Yu et al. [2] (published 25 Mar 2020) did indeed report a higher risk of developing COVID-19 among people with cancer. However, as noted in later commentaries [3–5], these studies were based on only 12 and 18 people with cancer, respectively, and did not account for differences in age or comorbidities.

Given the critical role of early evidence in decision-making during the pandemic, we conducted a systematic review of studies published in the first months of the pandemic (to 1 July 2020) to address the question, "Are people with a pre-existing cancer diagnosis more likely to contract SARS-CoV-2 or develop COVID-19 than the general population or people without a pre-existing diagnosis of cancer?". We also conducted a separate systematic review, reported in a companion article, to examine the early evidence for whether people with cancer who developed COVID-19 were at higher risk of death.

The aim of this systematic review was to synthesise and critically examine the early evidence. To aid interpretation of this evidence, we also characterise sources of bias and other methodological limitations, and examine how these impacted the results.

2. Methods

The protocol for this systematic review was registered on PROSPERO (CRD42020191913).

2.1. Definitions and eligibility criteria

We were initially interested in the effect of a previous cancer diagnosis on susceptibility to COVID-19, the symptomatic disease resulting from infection with SARS-CoV-2. However, some studies referred to people with asymptomatic SARS-CoV-2 infection as having COVID-19. Due to limitations in the early studies, we also considered studies that assessed SARS-CoV-2 positivity without quantifying the proportion of people who were asymptomatic.

Cohort or cross-sectional studies reporting incidence of COVID-19, or SARS-CoV-2 test positivity for people with cancer (exposed) compared to people without cancer or the general population in published journal articles or preprints were eligible for inclusion.

Incidence was defined as the proportion of people newly diagnosed with COVID-19. The ideal study would be one in which the entire population underwent testing, or a selected representative cohort was tested periodically, with adjustments made for potential contact with the virus, and extensive information recorded on potential modifiers and confounders. Such studies were not identified. Rather the available studies reported the incidence of COVID-19 or SARS-CoV-2 infection for populations in which not everyone was tested and testing was not random. Test positivity was defined as the proportion of SARS-CoV-2 positive cases amongst those who were tested.

Eligible exposures were previous diagnosis of any cancer, active cancer (cancer diagnosed or treated in the last year, or described as active), or specifically lung cancer or haematological cancer (in line with biological hypotheses suggesting higher risks for people with these cancer types). Where the exposure was described as cancer with no further details provided, we classified this as "any cancer".

2.2. Information sources and search strategy

On 3 July 2020, all Medline and Embase databases were searched for English-language articles published 1 January-1 July 2020, by combining text terms for COVID-19 and cancer or comorbidities (Supplementary Table 1). We also searched BioRxiv and MedRxiv (based on all preprints on COVID-19 or SARS-CoV-2 listed on https://connect.biorxiv.org/relate/content/181) and the SSRN website (https://www.ssrn.com/index.cfm/en/coronavirus/) for abstracts mentioning cancer or comorbidities posted during the same period. Reference lists of included articles and systematic reviews identified in the searches were checked for additional potentially relevant studies.

2.3. Selection process

Titles and abstracts of published articles were screened by two reviewers (CC or DC) with 10 % assessed by both to check concordance. Titles and abstracts of pre-prints were screened by a single reviewer (SH). The full texts of potentially relevant articles were independently assessed for inclusion by teams of two reviewers (CC, DC, VF, or SH) using pre-specified selection criteria. Discrepancies between reviewers were resolved by consensus or adjudication by a third reviewer. When there was both a preprint and published version of the same study available before 1 July 2020, only the published version was included.

2.4. Data collection

Pre-specified data items were extracted from each included study independently by teams of two reviewers (CC, DC, VF, or SH), using a form developed and tested for this purpose. Differences in extracted data between reviewers were resolved by consensus or adjudication by a third reviewer.

The following characteristics and data were extracted: study design, country, publication status and type, population characteristics, setting, recruitment period, definitions of exposure and comparator, method of SARS-CoV-2 detection or COVID-19 diagnosis, frequencies with and without the exposure and outcome and, where reported, the effect estimate and its 95 % confidence interval (CI) and covariates included in

analyses.

2.5. Study risk of bias assessment

Risk of bias of included studies was assessed using a modified version of the Newcastle-Ottawa Scale adapted to assess the risk of bias of observational aetiological cohort studies (Supplementary Table 2) [6]. Risk of bias for each study included in the quantitative synthesis was evaluated independently by teams of two reviewers (CC, DC, VF, or SH). We assessed cohort selection, nature and measurement of exposure and outcome, completeness of and differences in follow up, exclusions due to missing data, and if applicable, control of confounding; where possible, we used the effect estimate adjusted for the largest number of covariates. Age, sex, access to testing, exposure to high-risk settings and comorbidities were considered important confounders. Differences in ratings between reviewers were resolved by consensus or adjudication by a third reviewer. An overall rating was assigned to each study: 'high' if high risk of bias in any domain, 'moderate' if moderate risk of bias in one or more domains and not high risk in any domains, or 'low' if low risk of bias in all domains.

2.6. Effect measures

Effect estimates for the association between a pre-existing cancer diagnosis and the incidence of COVID-19 or SARS-CoV-2 test positivity were adjusted and/or unadjusted odds ratios (ORs) and 95 % CIs (no study reported hazard ratios or relative risks). When ORs were not reported for a study, we calculated unadjusted ORs and 95 % CIs from exposure-outcome cross tabulations with 0.5 added to each cell when there were zero cells [7]. Unadjusted rate ratios were calculated for studies with a general population comparator.

2.7. Data synthesis

All analyses were conducted separately for combinations of effect measure, exposure, and comparator for both outcomes. If different studies reported overlapping study samples, only the study with the largest number of people with cancer was included. Articles with insufficient or inconsistent data were excluded from the quantitative synthesis. As our aim was to assess the reported data and highlight methodological and reporting limitations in the early evidence, we did not contact study authors to confirm or obtain additional data.

Where possible, pooled effect estimates and 95 % CIs, were obtained from Stata version 14.0 (Stata Corp, College Station, TX) using generic inverse variance random-effects analysis. Rate ratios were not pooled with ORs in the same meta-analysis. Pooled ORs and rate ratios greater than 1.00 indicate higher COVID-19 incidence or SARS-CoV-2 positivity for people with cancer and values less than 1.00 indicate higher COVID-19 incidence or SARS-CoV-2 positivity for those without cancer.

2.8. Assessment of heterogeneity

Heterogeneity between study-specific effect estimates was assessed using the χ^2 and the I^2 statistics [8]. We interpreted the I^2 statistic according to guidance provided in the Cochrane Handbook Version 6.2 [9].

2.9. Subgroup analyses

Pre-specified subgroup analyses were by country, source of population, type of COVID-19 diagnostic test, and publication status (original journal article, preprint); however, these were not conducted due to small numbers of studies in all analyses.

2.10. Reporting bias assessment

No meta-analysis included 10 or more studies, so we did not assess risk of bias due to missing results, publication bias and/or small-study effects.

3. Results

Searches of published and preprint literature identified 10,153 unique records with an additional 156 records identified from citations (Fig. 1). Most articles were ineligible as they were an excluded publication type or study design, were a letter or comment without relevant primary data, or did not include a population of interest (Supplementary Table 3). Sixteen cohort studies met the inclusion criteria of which four were excluded from the quantitative synthesis due to insufficient or inconsistent data (Supplementary Table 4) [10–13]. Of the remaining 12 studies (Table 1), four measured COVID-19 incidence [2,14–16] and eight measured Sars-CoV-2 test positivity [17–24].

All four studies of COVID-19 incidence included > 1000 people with cancer (Table 1) and were conducted in different settings: general population, a large healthcare organisation, and cancer patients from a single hospital compared to the general population. Overall, our data synthesis of COVID-19 incidence studies included 24,181,727 individuals, of whom 125,649 (0.5 %) had a known previous diagnosis of cancer (Table 2). Five analyses comparing people with any cancer or active cancer to those without cancer or the general population were possible; each comprised a single study (Table 2). No studies of COVID-19 incidence considered haematological or lung cancers separately. All cohorts included both tested and untested individuals; no studies had universal or random SARS-CoV-2 testing. Only one study (Analysis 2) adjusted for confounders (age, sex, country, date at entry, body mass index, history of diabetes, heart disease, lung disease, kidney disease, and current smoker status) [15], with unadjusted effect estimates reported or calculated by us for the remaining studies (Table 2).

Across all analyses, COVID-19 incidence was significantly higher for people with cancer with ORs or rate ratios between 1.33 and 6.61 (Table 2).

All COVID-19 incidence studies were rated as high risk of bias (Table 3). A major source of bias was confounding, particularly as no study adjusted for level of potential viral contact such as number of recent health care visits. Differences and completeness in follow-up were also major potential sources of bias. Furthermore, no study reported the criteria used for SARS-CoV-2 testing or testing uptake. The criteria for COVID-19 diagnosis were also unclear or not reported in three of the studies (Table 1).

Across the eight studies of SARS-CoV-2 test positivity, the number of people with cancer varied widely (4 to nearly 27,000), with only three studies including > 1000 people with cancer (Table 1). Two studies were population-based, two were based in large healthcare organisations, three were hospital-based, and one included cancer patients from a single hospital compared with the general population. Two studies provided data for people with haematological cancer [17,18] and one for people with lung cancer [17]. Only one study adjusted for confounders (sex, age, residence, Charlson Comorbidity Index and healthcare use in the year prior to testing) [18], with unadjusted measures of association either reported in the remaining studies, or calculated by us.

Our data synthesis SARS-CoV-2 test positivity studies included 472,683 individuals, of whom 48,370 (11.4 %) had a known previous cancer diagnosis (Table 4). Seven studies compared people with and without cancer and the unadjusted ORs were pooled using a random effects model (Analysis 6; pooled OR 0.91, 95 %CI: 0.57–1.47; high heterogeneity $I^2 = 97.8$ %, p < 0.0001; Supplementary Fig. 1).

Fong et al. [17] compared those with active cancer and the general population (Analysis 9; unadjusted rate ratio 0.28, 95 %CI 0.10–0.75) and Ji et al. [18] compared people with haematological cancers versus no cancer (Analysis 10; Analysis 11; adjusted OR 0.39, 95 %CI
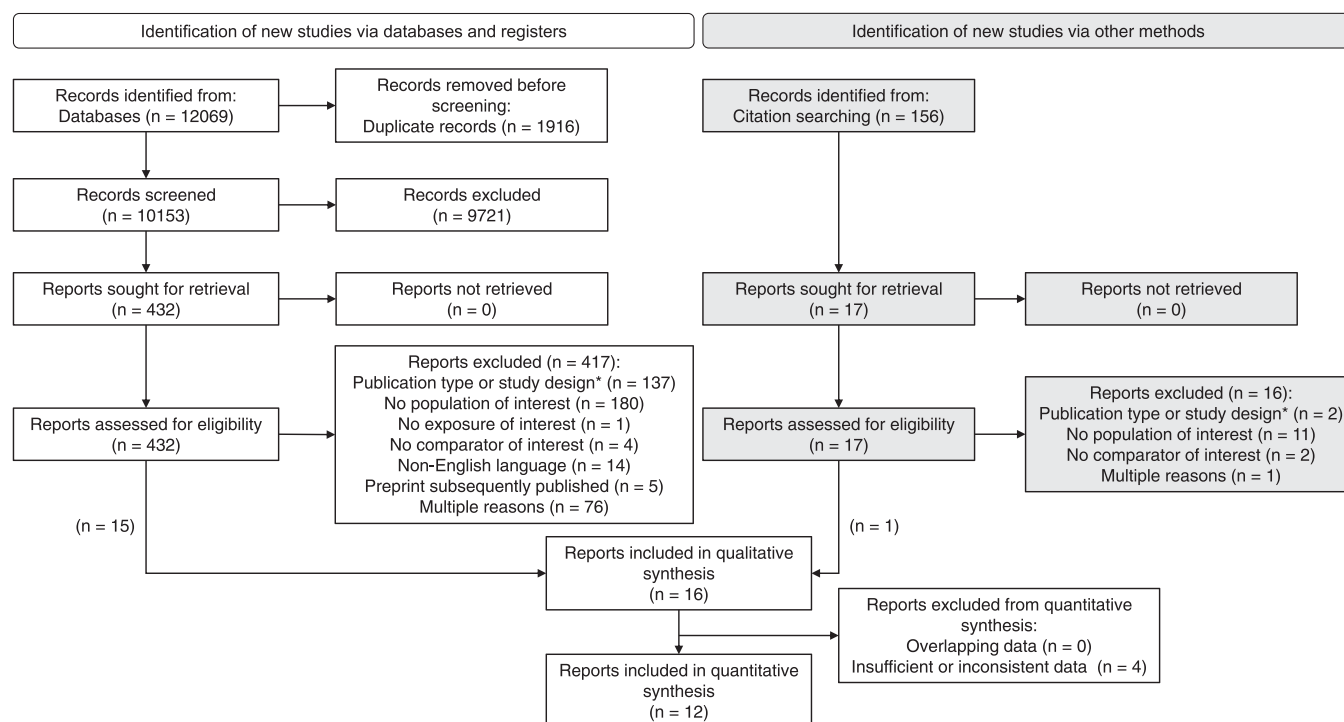
Fig. 1. Flow diagram based on the PRISMA 2020 flow chart summarising the article screening process. * excluded publication type or study design, or letter or comment without relevant primary data.

0.19–0.79). There was no significant association between cancer status (active, haematological or lung) and test positivity in the remaining analyses (Analyses 7, 8, 12, 13; Table 4).

All eight studies reporting SARS-CoV-2 test positivity had high risk of bias (Table 5). Confounding was a key source of potential bias, with only one study adjusting for age and other potential important confounders. Differences and completeness in follow up were also major sources of potential bias, as testing in the studies was either not random or testing criteria were not described.

4. Discussion

Our systematic review identified, appraised and synthesised early evidence from 12 studies including > 24 million people (> 170,000 people with pre-existing cancer). Studies of COVID-19 incidence reported higher risk for people with cancer, but did not adjust for characteristics such as age, sex and level of potential viral contact, and did not incorporate systematic or random COVID-19 testing of the population. Studies that examined SARS-CoV-2 test positivity had heterogeneous results. This is likely to be due to differences in testing criteria/policies and the availability of SARS-COV2 testing infrastructure in different settings (e.g. variation between countries, general population testing versus testing of hospital patients) and at different stages of local outbreaks and public health measures. Two studies reported lower SARS-CoV-2 test positivity for people with cancer with no significant differences detected in other studies and a meta-analysis.

This review provides the first systematic assessment of evidence on the risk of contracting SARS-CoV-2 or developing COVID-19 for people with a pre-existing cancer diagnosis that includes an in-depth evaluation of risk of bias. We found that the early studies provided only limited information due to important sources of bias. None of these studies were based on random testing which was not unexpected as widespread testing was rarely if at all available in the early stages of the pandemic. Thus, it is unclear whether apparent increased incidence of COVID-19 among people with cancer reflected greater susceptibility, increased exposure to the virus, more intensive testing, or a combination of these

factors. Studies reporting SARS-CoV-2 test positivity had similar limitations. These findings were consistent with prior comments on the quality of evidence available early in the pandemic [1,2].

Our review process had some limitations. Titles and abstracts were not screened independently by two reviewers (although we found good agreement for the 10 % of studies screened by both reviewers), and we did not contact authors of original studies seeking additional information or data. Nonetheless, this review also has several strengths including a comprehensive assessment of the early literature, and tailored considerations of risk of bias for studies of COVID-19 incidence and SARS-CoV-2 test positivity.

Recently, concerns about risk of SARS-CoV-2 exposure and severity of COVID-19 for people with cancer have influenced discussions on vaccine prioritisation. Multiple organisations in different countries have called for people with cancer to be prioritised for vaccination [25], including the American Association for Cancer Research [26], the National Comprehensive Cancer Network [27], and the European Society for Medical Oncology [28]. Even if biological susceptibility to COVID-19 is not higher for people with cancer, frequent hospital visits for treatment and potential higher risk of severe disease may be reasons to prioritise appropriate subgroups for vaccination (see also our parallel systematic review on risk of death after developing COVID-19).

Prospective representative cohorts with systematic and periodic testing for SARS-CoV-2 and/or COVID-19, can provide valuable information both on future disease dynamics and on potential differences in vaccine efficacy between population subgroups, especially people with cancer [25]. Ideally, cancer and vaccination status would be established through linkage of these cohorts to population-wide registries or comprehensive and complete medical records, including vaccine type and timing of doses. As COVID-19 risk has been hypothesised to differ by cancer type, time since diagnosis, and cancer treatment received (especially immunosuppressive treatments), further examination of these factors in the context of existing and emerging variants is required. Important confounders to consider include, at a minimum, age, sex and comorbidities. To test for differences in biological susceptibility, adjustment for level of SARS-CoV-2 exposure is required (including

Table 1
Characteristics of studies included in the quantitative synthesis.

Study	Country	Publication type	Population				Exposure (Cancer)			Comparator		Outcome
			Setting	N	Age (by COVID-19 status if NR overall) (years)	Male (%)	Definition	Cancer type	n	Definition	n	Method of COVID-19 diagnosis
INCIDENCE – Tested and untested population												
Lee et al.[a] [15]	UK, USA, Sweden	Preprint	General population	1,789,197	NR	42.7	Active cancer	NR	4904	No cancer	1,784,293	NR
			General population	1,807,559	NR	42.9	NR	NR	23,266	No cancer	1,784,293	NR
Dagan et al. [14]	Israel	Preprint	Healthcare organisation[b]	4,631,168	NR	NR	Active or non-active cancer	NR	99,790	No cancer	4,531,378	PCR
Yu et al. [2]	China	Original journal article	Single hospital vs general population	11,081,000	NR	NR	Active cancer	Mixed	1524	General population	11,081,000	Unclear
Rogado et al. [16]	Spain	Original journal article	Single hospital vs general population	6,662,000	NR	NR	Active or non-active cancer	Mixed	1069	General population	6,662,000	Unclear
TEST POSITIVITY – Tested population only												
Reilev et al. [20]	Denmark	Preprint	General population	228,677	49[c] (positive) 47[c] (negative)	37.3	Active or non-active cancer	NR	18,969	No cancer	209,708	PCR
Ji et al. [18]	Korea	Original journal article	General population	219,961	47.1[d] (positive) 49.5[d] (negative)	47.4	NR	**Mixed**	26,921	No cancer	193,040	PCR
				194,779	NR	NR	NR	**Haematological**	1739	No cancer	193,040	PCR
Rentsch et al. [21]	USA	Preprint	Healthcare organisation	3789	66	90.2	NR	NR	571	No cancer	3218	PCR
Marcello et al. [19]	USA	Preprint	Healthcare organisation	16,420	NR	NR	NR	NR	1554	No cancer	14,866	PCR
Zhu et al. [24]	China	Original journal article	Multiple hospitals	116	40	NR	NR	NR	4	No cancer	112	PCR
Solodky et al. [23]	France	Letter to the Editor	Single hospital	329	NR	NR	NR	NR	85	No cancer	244	Antibody test
Shah et al. [22]	USA	Preprint	Single hospital	316	63[c] (positive) 62[c] (negative)	51.9	Active or non-active cancer	NR	71	No cancer	245	PCR
				316	63[c] (positive) 62[c] (negative)	51.9	Active cancer	NR	47	No active cancer	269	PCR
				292	NR	NR	Active cancer	NR	47	No cancer	245	PCR
Fong et al. [17]	Italy	Original journal article	Single hospital vs general population	3075	NR	NR	Active cancer	**Mixed**	219	General population	3075	PCR
				3075	NR	NR	Active cancer	**Haematological**	63	General population	3075	PCR
				3075	NR	NR	Active cancer	**Lung**	23	General population	3075	PCR

NR = not reported; PCR = (real-time reverse transcriptase) polymerase chain reaction assay.

[a] Lee et al. [15] is a prospective cohort study. All other studies are retrospective cohort studies.

[b] Based on an integrated payer-provider healthcare organisation covering > 50 % of the population.

[c] Median.

[d] Mean.

Table 2

Numbers of studies, COVID-19 cases and non-cases and results for each analysis for COVID incidence.

Analysis	Measure of effect	Exposure group	Comparison group	Number of studies	Cancer COVID-19 negative or not tested~	Cancer COVID-19 positive~	Comparator COVID-19 negative or not tested~	Comparator COVID-19 positive~	Total participants	Effect estimate (95 % CI)
1	Unadjusted OR	Any cancer	No cancer	1	99,646	144	4,526,477	4901	4,631,168	1.33 (1.12, 1.58)
2	Adjusted OR	Any cancer	No cancer	1	23,111	155	1,774,044	10,249	1,807,559	1.60 (1.36, 1.88)
3	Unadjusted rate ratio	Any cancer	General population	1	1024	45	6,619,550	42,450	6,662,000[a]	6.61 (4.97, 8.79)
4	Unadjusted OR	Active cancer	No cancer	1	4854	50	1,774,044	10,249	1,789,197	1.78 (1.34, 2.36)
5	Unadjusted rate ratio	Active cancer	General population	1	1512	12	11,039,848	41,152	11,081,000[a]	2.12 (1.20, 3.73)
	Total across all analyses 1–5[b]:			5	130,147	406	25,733,963	109,001	25,970,924	
	Total in one or more analyses 1–5[c]:			4	125,293	356	23,959,919	98,752	24,181,727	

[a] For studies where the comparator is "General population", people with cancer in the exposure group are a subset of the comparator group; however, they are only counted once in the total column.

[b] Totals include multiple counts of the same studies and people included in different analyses.

[c] Totals counting studies and people only once.

Table 3

Risk of bias of studies assessing incidence of COVID-19 infection which were included in the quantitative synthesis.

Study	1	2	3	4	5	6	7	8a	8b	8c	Overall rating
Lee et al. [15]	Low	High	Low	High	High	High	Low	Moderate	High	High	High
Dagan et al. [14]	Low	Low	Low	Low	High	High	Low	High	NA	NA	High
Yu et al. [2]	High	Moderate	Low	High	High	High	Low	High	NA	NA	High
Rogado et al. [16]	High	Moderate	Low	High	High	High	Low	High	NA	NA	High

1 = Exposed and comparison (unexposed) populations and selection of cohort(s); 2 = Nature and measurement of exposure; 3 = Timing of outcome of interest and exposure measurement (reverse causation); 4 = Nature and measurement of outcome; 5 = Completeness of follow up; 6 = Differences in follow up; 7 = Exclusions due to missing data on any variables; 8a = Control of confounding: Comparability of exposed and unexposed cohorts with respect to potentially important confounding variables; 8b = Control of confounding: Reliability of the assessment of the presence or absence of prognostic factors; 8c = Control of confounding: Covariates are appropriately included in the analysis; NA = not applicable.

information on health service use, social contacts and preventive measures such as mask wearing). An example of such a prospective cohort set up to examine COVID-19 incidence is the UK Biobank subcohort with additional recruitment of participants' children and grandchildren (total n ~ 20,000), although no results by cancer status have been published to date [29].

We also note that test choice may influence the results from such studies: polymerase chain reaction (PCR) tests for SARS-CoV-2 can provide information on current infection status, but would require frequent testing to avoid confounding by varying durations of infection persistence. While antibody tests can also identify people who have been infected in the past, the results may be confounded by different degrees of antibody production among people who did or did not receive treatments affecting their immune system or have a haematological cancer [30]. With increasing vaccination in many countries and resulting development of antibodies in those who have been vaccinated, future studies would also need to use antibody tests that can distinguish response to vaccination from past SARS-CoV-2 infection. For both PCR and antibody tests, the distinction between asymptomatic and more severe COVID-19 will also be vital due to differential impacts on individual patients and health systems.

In a separate systematic review, we have examined the early evidence on risk of COVID-19-related death and identified a wide range of methodological concerns. However, several high-quality studies of the risk of severe COVID-19 have been reported after the period covered in this review, including the OpenSAFELY [31] and QCOVID [32] studies in the UK, which have extensive linked data for 8–23 million people. Nevertheless, in these studies, SARS-CoV-2 testing was not performed systematically or at random and the testing criteria and availability were influenced by complex factors that likely also differed between jurisdictions in the UK.

In the early stages of the pandemic, concerns regarding the risk of SARS-CoV-2 exposure, susceptibility to infection, and severity of COVID-19 for people with cancer led to cancer treatment changes in different countries and settings [33–39]. The precautionary principle is important in early and urgent decision-making; however, treatment changes can also have negative effects, so it is crucial to generate high-quality timely evidence on the magnitude of risks to inform more nuanced decisions. Where health care services are safe due to effective risk-reduction measures, cancer diagnosis and treatment disruptions should be minimised to reduce the unintended long-term negative impacts of the pandemic [40]. Having an accurate understanding of COVID-19 risk is also important to reduce the anxiety experienced by people with cancer, and those supporting them [41,42]. Acknowledging the challenges experienced in many contexts, especially in the first months of the pandemic, it is important to create and support research infrastructure that allows prompt provision of high-quality evidence to inform policy and health system responses to the emergence of new SARS-CoV-2 variants of concern and future crises. National and international collaborations and data sharing are also crucial for producing large, well-powered studies.

Given recent concerns about risks posed by emerging SARS-CoV-2 variants of concern for people with pre-existing health conditions, our systematic review processes provide a platform for the ongoing review and analysis of the expanding data on COVID-19 risk, facilitating future efforts with timely identification and synthesis of the high-quality evidence. This is a key focus of the COVID-19 and Cancer Global Modelling Consortium (CCGMC.org) comprising modelling platforms and teams that can provide informed advice to support decision-making in cancer control both during and after the pandemic. In this context, robust estimates of COVID-19 risk for people with cancer are essential model inputs to identify the best strategies for minimising cancer control

Table 4
Numbers of studies, COVID-19 cases and non-cases in each analysis for SARS-CoV-2 test positivity.

Analysis	Measure of effect	Exposure group	Comparison group	Number of studies	Cancer SARS-CoV-2 negative	Cancer SARS-CoV-2 positive	Comparator SARS-CoV-2 negative	Comparator SARS-CoV-2 positive	Total participants[a]	Effect estimate (95 % CI)	Heterogeneity I² (p value)
6	Unadjusted OR	Any cancer	No cancer	7	46,004	2171	395,907	25,526	469,608	0.91 (0.57, 1.47)	97.8 % (p < 0.0001)
7	Unadjusted OR	Active cancer	No cancer	1	42	5	222	23	292	1.15 (0.43, 3.10)	NA
8	Unadjusted OR	Active cancer	No active cancer	1	42	5	241	28	316	1.02 (0.38, 2.72)	NA
9	Unadjusted rate ratio	Active cancer	General population	1	215	4	2875	200	3075[a]	0.28 (0.10, 0.75)	NA
10	Unadjusted OR	Haematological cancers	No cancer	1	1731	8	186,038	7002	194,779	0.12 (0.06, 0.24)	NA
11	Adjusted OR	Haematological cancers	No cancer	1	1731	8	186,038	7002	194,779	0.39 (0.19, 0.79)	NA
12	Unadjusted rate ratio	Active Haematological cancers	General population	1	61	2	2875	200	3075[a]	0.49 (0.13, 1.92)	NA
13	Unadjusted rate ratio	Active Lung cancer	General population	1	23	0	2875	200	3075[a]	0.33 (0.02, 5.45)	NA
		Total across all analyses 6–13[b]:		**14**	**49,849**	**2203**	**777,071**	**40,181**	**868,999**		
		Total in one or more analyses 6–13[c]:		**8**	**46,200**	**2170**	**398,801**	**25,731**	**472,683**		
		Total across all analyses 1–13[b]:		**19**	**179,996**	**2609**	**26,511,034**	**149,182**	**26,839,923**		
		Total in one or more analyses 1–13[c]:		**12**	**171,493**	**2526**	**24,358,720**	**124,483**	**24,654,410**		

NA = not applicable.
[a] For studies where the comparator is "General population", people with cancer in the cancer group are a subset of the comparator group; however, they are only counted once in the totals column.
[b] Totals include multiple counts of the same studies and people included in different analyses.
[c] Totals counting studies and people only once.

Table 5

Risk of bias of studies assessing SARS-CoV-2 test positivity which were included in the quantitative synthesis.

Study	1	2	3	4	5	6	7	8a	8b	8c	Overall rating
Reilev et al. [20]	Low	Low	Low	Low	High	High	Low	High	NA	NA	High
Ji et al. [18]	Low	Low	Low	Low	High	High	Low	Low	Low	Low	High
Rentsch et al. [21]	Low	Low	Low	Low	High	High	Low	High	NA	NA	High
Marcello et al. [19]	Low	High	Low	Low	High	High	Moderate	High	NA	NA	High
Zhu et al. [24]	Low	High	Low	Low	High	High	Low	High	NA	NA	High
Solodky et al. [23]	High	Moderate	Low	Low	High	High	Low	High	NA	NA	High
Shah et al. [22]	Low	Low	Low	Low	High	High	Low	High	NA	NA	High
Fong et al. [17]	High	Moderate	Low	High	High	High	Low	High	NA	NA	High

1 = Exposed and comparison (unexposed) populations and selection of cohort(s); 2 = Nature and measurement of exposure; 3 = Timing of outcome of interest and exposure measurement (reverse causation); 4 = Nature and measurement of outcome; 5 = Completeness of follow up; 6 = Differences in follow up; 7 = Exclusions due to missing data on any variables; 8a = Control of confounding: Comparability of exposed and unexposed cohorts with respect to potentially important confounding variables; 8b = Control of confounding: Reliability of the assessment of the presence or absence of prognostic factors; 8c = Control of confounding: Covariates are appropriately included in the analysis; NA = not applicable

disruptions and resulting harms.

In conclusion, the early literature on COVID-19 susceptibility for people with cancer was characterised by pervasive biases and limitations in the available data, resulting in highly uncertain evidence. To support rapid evidence-based decision making in changing circumstances, including the emergence of new virus variants, it is important to establish an infrastructure that enables enhanced data collection and prioritises conduct of high-quality studies to reflect near real-time disease dynamics in both the overall population and in specific vulnerable subgroups. This infrastructure is also needed to enable ongoing research efforts to support continued public health responses to the COVID-19 pandemic.

CRediT authorship contribution statement

KC and D'OC conceived the study. KC, D'OC, JS, SE, SH, VF, CC, DC designed the study. CC, SH, VF, DC, SE analysed the data. CC, SH, VF, DC accessed and verified the data. CC, SH, VF, DC, SE, DO'C and JS wrote the manuscript. All authors contributed to data interpretation, reviewed, revised, and approved the manuscript, and accept responsibility to submit for publication.

Competing interests

Prof Karen Canfell reports is co-PI of an investigator-initiated trial of cervical screening, "Compass", run by the Australian Centre for Prevention of Cervical Cancer (ACPCC), which is a government-funded not-for-profit charity. Compass receives infrastructure support from the Australian government and the ACPCC has received equipment and a funding contribution from Roche Molecular Diagnostics, USA. KC is also co-PI on a major implementation program *Elimination of Cervical Cancer in the Western Pacific* which has received support from the Minderoo Foundation and the Frazer Family Foundation and equipment donations from Cepheid Inc. Dr. Michael Caruana is also an investigator on Compass.

Neither KC or MC nor their institution (the Daffodil Centre, a joint venture between Cancer Council NSW and The University of Sydney) receive direct funding from commercial organisations.

Other authors declare no conflict of interest.

Data availability

All of the original data of this study are available upon reasonable request to the corresponding authors (KC or JS).

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jcpo.2022.100338.

References

[1] W. Liang, W. Guan, R. Chen, W. Wang, J. Li, K. Xu, C. Li, Q. Ai, W. Lu, H. Liang, S. Li, J. He, Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China, Lancet Oncol. 21 (3) (2020) 335–337, https://doi.org/10.1016/S1470-2045 (20)30096-6.

[2] J. Yu, W. Ouyang, M.L.K. Chua, C. Xie, SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China, JAMA Oncol. 6 (7) (2020) 1108–1110, https://doi.org/10.1001/jamaoncol.2020.0980.

[3] S.A. Cannistra, B.G. Haffty, K. Ballman, Challenges faced by medical journals during the COVID-19 pandemic, J. Clin. Oncol. 38 (19) (2020) 2206–2207, https://doi.org/10.1200/JCO.20.00858.

[4] H. Wang, L. Zhang, Risk of COVID-19 for patients with cancer, Lancet Oncol. 21 (4) (2020), e181, https://doi.org/10.1016/S1470-2045(20)30149-2.

[5] Y. Xia, R. Jin, J. Zhao, W. Li, H. Shen, Risk of COVID-19 for patients with cancer, Lancet Oncol. 21 (4) (2020), e180, https://doi.org/10.1016/S1470-2045(20) 30150-9.

[6] M. Kirk, K. Smurthwaite, J. Braunig, S. Trevenar, C. D'Este, R. Lucas, A. Lal, R. Korda, A. Clements, J. Mueller, B. Armstrong. The PFAS Health Study: Systematic Literature Review. Canberra. 2018.

[7] R. Lawson, Small sample confidence intervals for the odds ratio, Commun. Stat. Simul. Comput. 33 (4) (2004) 1095–1113, https://doi.org/10.1081/SAC-200040691.

[8] J.P. Higgins, S.G. Thompson, Quantifying heterogeneity in a meta-analysis, Stat. Med. 21 (11) (2002) 1539–1558, https://doi.org/10.1002/sim.1186.

[9] J. Higgins, J. Thomas, J. Chandler, M. Cumpston, T. Li, M. Page, V. Welch, (ed.), Cochrane Handbook for Systematic Reviews of Interventions Version 6.2, 2021, ⟨www.training.cochrane.org/handbook⟩, (Accessed 01 July 2021).

[10] B. Fattizzo, J.A. Giannotta, M. Sciumè, D. Cattaneo, C. Bucelli, N.S. Fracchiolla, F. Onida, L. Baldini, W. Barcellini, A. Iurlo, Reply to "COVID-19 in persons with haematological cancers": a focus on myeloid neoplasms and risk factors for mortality, Leukemia 34 (7) (2020) 1957–1960, https://doi.org/10.1038/s41375-020-0877-y.

[11] W. Li, D. Wang, J. Guo, G. Yuan, Z. Yang, R.P. Gale, Y. You, Z. Chen, S. Chen, C. Wan, X. Zhu, W. Chang, L. Sheng, H. Cheng, Y. Zhang, Q. Li, J. Qin, L. Meng, Q. Jiang, COVID-19 in persons with chronic myeloid leukaemia, Leukemia 34 (7) (2020) 1799–1804, https://doi.org/10.1038/s41375-020-0853-6.

[12] M. Luong-Nguyen, H. Hermand, S. Abdalla, N. Cabrit, C. Hobeika, A. Brouquet, D. Goere, A. Sauvanet, Nosocomial infection with SARS-Cov-2 within departments of digestive surgery, J. Visc. Surg. 157 (3S1) (2020) S13–S18, https://doi.org/10.1016/j.jviscsurg.2020.04.016.

[13] A.H. Norooznezhad, F. Najafi, P. Riahi, M. Moradinazar, E. Shakiba, S. Mostafaei, Primary symptoms, comorbidities, and outcomes of 431 hospitalized patients with confirmative RT-PCR results for COVID-19, Am. J. Trop. Med. Hyg. 24 (2020) 24, https://doi.org/10.4269/ajtmh.20-0512.

[14] N. Dagan, N. Barda, D. Riesel, I. Grotto, S. Sadetzki, R. Balicer, A score-based risk model for predicting severe COVID-19 infection as a key component of lockdown exit strategy, medRxiv (2020), https://doi.org/10.1101/2020.05.20.20108571.

[15] K.A. Lee, W. Ma, D.R. Sikavi, J. Wolf, C.J. Steves, T.D. Spector, A.T. Chan, Cancer and risk of COVID-19 through a general community survey, medRxiv (2020), https://doi.org/10.1101/2020.05.20.20103762.

[16] J. Rogado, B. Obispo, C. Pangua, G. Serrano-Montero, A. Martin Marino, M. Perez-Perez, A. Lopez-Alfonso, P. Gullon, M.A. Lara, Covid-19 transmission, outcome and associated risk factors in cancer patients at the first month of the pandemic in a

Spanish hospital in Madrid, Clin. Transl. Oncol. 25 (12) (2020) 25, https://doi.org/10.1007/s12094-020-02381-z.

[17] D. Fong, S. Rauch, C. Petter, E. Haspinger, M. Alber, M. Mitterer, Infection rate and clinical management of cancer patients during the COVID-19 pandemic: experience from a tertiary care hospital in northern Italy, ESMO Open 5 (3) (2020), e000810, https://doi.org/10.1136/esmoopen-2020-000810.

[18] W. Ji, K. Huh, M. Kang, J. Hong, G.H. Bae, R. Lee, Y. Na, H. Choi, S.Y. Gong, Y. H. Choi, K.P. Ko, J.S. Im, J. Jung, Effect of underlying comorbidities on the infection and severity of COVID-19 in Korea: a nationwide case-control study, J. Korean Med. Sci. 35 (25) (2020), e237, https://doi.org/10.3346/jkms.2020.35.e237.

[19] R.K. Marcello, J. Dolle, S. Grami, R. Adule, Z. Li, K. Tatem, C. Anyaogu, S. Apfelroth, R. Ayinla, N. Boma, T. Brady, B.F. Cosme-Thormann, R. Costarella, K. Ford, K. Gaither, J. Jacobson, M. Kanter, S. Kessler, R.B. Kristal, J.J. Lieber, V. Mukherjee, V. Rizzo, M. Rowell, D. Stevens, E. Sydney, A. Wallach, D. A. Chokshi, N. Davis, Characteristics and outcomes of COVID-19 patients in New York City's public hospital system, medRxiv (2020), https://doi.org/10.1101/2020.05.29.20086645.

[20] M. Reilev, K.B. Kristensen, A. Pottegård, L.C. Lund, J. Hallas, M.T. Ernst, C. F. Christiansen, H.T. Sørensen, N.B. Johansen, N.C. Brun, M. Voldstedlund, H. Støvring, M.K. Thomsen, S. Christensen, S. Gubbels, T.G. Krause, K. Mølbak, R. W. Thomsen, Characteristics and predictors of hospitalization and death in the first 9519 cases with a positive RT-PCR test for SARS-CoV-2 in Denmark: a nationwide cohort, medRxiv (2020), https://doi.org/10.1101/2020.05.24.20111823.

[21] C.T. Rentsch, F. Kidwai-Khan, J.P. Tate, L.S. Park, J.T. King, M. Skanderson, R. G. Hauser, A. Schultze, C.I. Jarvis, M. Holodniy, V.L. Re, K.M. Akgün, K. Crothers, T.H. Taddei, M.S. Freiberg, A.C. Justice, Covid-19 testing, hospital admission, and intensive care among 2,026,227 United States veterans aged 54–75 years, medRxiv (2020), https://doi.org/10.1101/2020.04.09.20059964.

[22] S.J. Shah, P.N. Barish, P.A. Prasad, A.L. Kistler, N. Neff, J. Kamm, L.M. Li, C. Y. Chiu, J.M. Babick, M.C. Fang, Y. Abe-Jones, F.N. Alvarez, O. B. Botvinnik, J.M. Davis, G.D. Castenada, C. Consortium, R.M. Dadasovich, X. Deng, J.L. DeRisi, A.M. Detweiler, S. Federman, J.R. Haliburton, S.L. Hao, A. D. Kerkhoff, R. Kumar, K. Malcolm, S.A. Mann, S.P. Martinez, R. Marya, E. Mick, L. L. Mwakibete, N. Najafi, M.J. Peluso, M.S. Phelps, A.O. Pisco, K. Ratnasiri, L. A. Rubio, A.B. Sellas, K.D. Sherwood, J. Sheu, N. Spottiswoode, M. Tan, G. Yu, K. N. Kangelaris, C. Langelier, Clinical features, diagnostics, and outcomes of patients presenting with acute respiratory illness: a comparison of patients with and without COVID-19, medRxiv (2020), https://doi.org/10.1101/2020.05.02.20082461.

[23] M.L. Solodky, C. Galvez, B. Russias, P. Detourbet, V. N'Guyen-Bonin, A.L. Herr, P. Zrounba, J.Y. Blay, Lower detection rates of SARS-COV2 antibodies in cancer patients versus health care workers after symptomatic COVID-19, Ann. Oncol.: Off. J. Eur. Soc. Med. Oncol. 31 (8) (2020) 1087–1088, https://doi.org/10.1016/j.annonc.2020.04.475.

[24] W. Zhu, K. Xie, H. Lu, L. Xu, S. Zhou, S. Fang, Initial clinical features of suspected coronavirus disease 2019 in two emergency departments outside of Hubei, China, J. Med. Virol. 92 (9) (2020) 1525–1532, https://doi.org/10.1002/jmv.25763.

[25] A. Desai, J.F. Gainor, A. Hegde, A.M. Schram, G. Curigliano, S. Pal, S.V. Liu, B. Halmos, R. Groisberg, E. Grande, T. Dragovich, M. Matrana, N. Agarwal, S. Chawla, S. Kato, G. Morgan, P.M. Kasi, B. Solomon, H.H. Loong, H. Park, T. K. Choueiri, I.M. Subbiah, N. Pemmaraju, V. Subbiah, & the COVID 19 and Cancer Clinical Trials Working Group, COVID-19 vaccine guidance for patients with cancer participating in oncology clinical trials, Nat. Rev. Clin. Oncol. 18 (2021) 313–319, https://doi.org/10.1038/s41571-021-00487-z.

[26] A. Ribas, R. Sengupta, T. Locke, S.K. Zaidi, K.M. Campbell, J.M. Carethers, E. M. Jaffee, E.J. Wherry, J.-C. Soria, G. Souza, Priority COVID-19 vaccination for patients with cancer while vaccine supply is limited, Cancer Discov. 11 (2) (2021) 233, https://doi.org/10.1158/2159-8290.CD-20-1817.

[27] National Comprehensive Cancer Network, Preliminary recommendations of the NCCN COVID-19 Vaccination Advisory Committee* Version 1.0 1/22/2021, 2021. ⟨https://www.nccn.org/covid-19/pdf/COVID-19_Vaccination_Guidance_V1.0.pdf⟩, (Accessed 13 March 2021).

[28] M.C. Garassino, M. Vyas, E.G.E. de Vries, R. Kanesvaran, R. Giuliani, S. Peters, The ESMO call to action on COVID-19 vaccinations and patients with cancer: vaccinate. Monitor. Educate, Ann. Oncol. 32 (5) (2021) 579–581, https://doi.org/10.1016/j.annonc.2021.01.068.

[29] UK Biobank, COVID-19 hub, 2021. ⟨https://www.ukbiobank.ac.uk/learn-more-about-uk-biobank/covid-19-hub⟩, (Accessed 18 March 2021).

[30] A. Thakkar, K. Pradhan, S. Jindal, Z. Cui, B. Rockwell, A.P. Shah, S. Packer, R. A. Sica, J. Sparano, D.Y. Goldstein, C. Verma, S. Goel, B. Halmos, Patterns of seroconversion for SARS-CoV2-IgG in patients with malignant disease and association with anticancer therapy, Nat. Cancer 2 (4) (2021) 392–399, https://doi.org/10.1038/s43018-021-00191-y.

[31] E.J. Williamson, A.J. Walker, K. Bhaskaran, S. Bacon, C. Bates, C.E. Morton, H. J. Curtis, A. Mehrkar, D. Evans, P. Inglesby, J. Cockburn, H.I. McDonald, B. MacKenna, L. Tomlinson, I.J. Douglas, C.T. Rentsch, R. Mathur, A.Y.S. Wong, R. Grieve, D. Harrison, H. Forbes, A. Schultze, R. Croker, J. Parry, F. Hester, S. Harper, R. Perera, S.J.W. Evans, L. Smeeth, B. Goldacre, Factors associated with COVID-19-related death using OpenSAFELY, Nature 584 (7821) (2020) 430–436, https://doi.org/10.1038/s41586-020-2521-4.

[32] A.K. Clift, C.A.C. Coupland, R.H. Keogh, K. Diaz-Ordaz, E. Williamson, E. M. Harrison, A. Hayward, H. Hemingway, P. Horby, N. Mehta, J. Benger, K. Khunti, D. Spiegelhalter, A. Sheikh, J. Valabhji, R.A. Lyons, J. Robson, M.G. Semple, F. Kee, P. Johnson, S. Jebb, T. Williams, J. Hippisley-Cox, Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study, BMJ 371 (2020) m3731, https://doi.org/10.1136/bmj.m3731.

[33] J.J. Clark, D. Dwyer, N. Pinwill, P. Clark, P. Johnson, A. Hackshaw, The effect of clinical decision making for initiation of systemic anticancer treatments in response to the COVID-19 pandemic in England: a retrospective analysis, Lancet Oncol. 22 (1) (2021) 66–73, https://doi.org/10.1016/S1470-2045(20)30619-7.

[34] T.P. Hanna, G.A. Evans, C.M. Booth, Cancer, COVID-19 and the precautionary principle: prioritizing treatment during a global pandemic, Nat. Rev. Clin. Oncol. 17 (5) (2020) 268–270, https://doi.org/10.1038/s41571-020-0362-6.

[35] A. Kuryba, J.M. Boyle, H.A. Blake, A. Aggarwal, J. van der Meulen, M. Braun, K. Walker, N.S. Fearnhead, Surgical treatment and outcomes of colorectal cancer patients during the COVID-19 pandemic: a national population-based study in England, Ann. Surg. Open 2 (2) (2021), e071, https://doi.org/10.1097/AS9.0000000000000071.

[36] A. Kutikov, D.S. Weinberg, M.J. Edelman, E.M. Horwitz, R.G. Uzzo, R.I. Fisher, A war on two fronts: cancer care in the time of COVID-19, Ann. Intern. Med. 172 (11) (2020) 756–758, https://doi.org/10.7326/M20-1133.

[37] K. Spencer, C.M. Jones, R. Girdler, C. Roe, M. Sharpe, S. Lawton, L. Miller, P. Lewis, M. Evans, D. Sebag-Montefiore, T. Roques, R. Smittenaar, E. Morris, The impact of the COVID-19 pandemic on radiotherapy services in England, UK: a population-based study, Lancet Oncol. 22 (3) (2021) 309–320, https://doi.org/10.1016/S1470-2045(20)30743-9.

[38] A. Sud, B. Torr, M.E. Jones, J. Broggio, S. Scott, C. Loveday, A. Garrett, F. Gronthoud, D.L. Nicol, S. Jhanji, S.A. Boyce, M. Williams, E. Riboli, D.C. Muller, E. Kipps, J. Larkin, N. Navani, C. Swanton, G. Lyratzopoulos, E. McFerran, M. Lawler, R. Houlston, C. Turnbull, Effect of delays in the 2-week-wait cancer referral pathway during the COVID-19 pandemic on cancer survival in the UK: a modelling study, Lancet Oncol. 21 (8) (2020) 1035–1044, https://doi.org/10.1016/s1470-2045(20)30392-2.

[39] J. van de Haar, L.R. Hoes, C.E. Coles, K. Seamon, S. Fröhling, D. Jäger, F. Valenza, F. de Braud, L. De Petris, J. Bergh, I. Ernberg, B. Besse, F. Barlesi, E. Garralda, A. Piris-Giménez, M. Baumann, G. Apolone, J.C. Soria, J. Tabernero, C. Caldas, E. E. Voest, Caring for patients with cancer in the COVID-19 era, Nat. Med. 26 (5) (2020) 665–671, https://doi.org/10.1038/s41591-020-0874-8.

[40] C. Maringe, J. Spicer, M. Morris, A. Purushotham, E. Nolte, R. Sullivan, B. Rachet, A. Aggarwal, The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study, Lancet Oncol. 21 (8) (2020) 1023–1034, https://doi.org/10.1016/S1470-2045(20)30388-0.

[41] K.Y.Y. Ng, S. Zhou, S.H. Tan, N.D.B. Ishak, Z.Z.S. Goh, Z.Y. Chua, J.M.X. Chia, E. L. Chew, T. Shwe, J.K.Y. Mok, S.S. Leong, J.S.Y. Lo, Z.L.T. Ang, J.L. Leow, C.W. J. Lam, J.W. Kwek, R. Dent, J. Tuan, S.T. Lim, W.Y.K. Hwang, K. Griva, J. Ngeow, Understanding the psychological impact of COVID-19 on patients with cancer, their caregivers, and health care workers in Singapore, JCO Glob. Oncol. 6 (2020) 1494–1509, https://doi.org/10.1200/go.20.00374.

[42] D. Sigorski, P. Sobczuk, M. Osmola, K. Kuć, A. Walerzak, M. Wilk, T. Ciszewski, S. Kopeć, K. Hryń, P. Rutkowski, R. Stec, C. Szczylik, L. Bodnar, Impact of COVID-19 on anxiety levels among patients with cancer actively treated with systemic therapy, ESMO Open 5 (5) (2020), e000970, https://doi.org/10.1136/esmoopen-2020-000970.