Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Original Research

Mortality in patients with cancer and coronavirus disease 2019: A systematic review and pooled analysis of 52 studies

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Abstract ***Background:*** Patients with coronavirus disease 2019 (COVID-19) who have underlying malignancy have a higher mortality rate compared with those without cancer, although the magnitude of such excess risk is not clearly defined. We performed a systematic review and pooled analysis to provide precise estimates of the mortality rate among patients with both cancer and COVID-19.

Methods: A systematic literature search involving peer-reviewed publications, preprints and conference proceedings up to July 16, 2020, was performed. The primary end-point was the case fatality rate (CFR), defined as the rate of death among patients with cancer and COVID-19. The CFR was assessed with a random effects model, which was used to derive a pooled CFR and its 95% confidence interval (CI).

Results: Fifty-two studies, involving a total of 18,650 patients with both COVID-19 and cancer, were selected for the pooled analysis. A total of 4243 deaths were recorded in this

Abbreviations: AACR, American Association of Cancer Research; ASCO, American Society of Clinical Oncology; COVID-19, coronavirus disease 2019; CCC-19, COVID-19 and Cancer Consortium; ESMO, European Society for Medical Oncology; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TERAVOLT, Thoracic cancERs international coVid 19 cOLlaboraTion.

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population. The probability of death was 25.6% (95% CI: 22.0%–29.5%; $I^2 = 48.9\%$) in this patient population.
Conclusions: Patients with cancer who develop COVID-19 have high probability of mortality. Appropriate and aggressive preventive measures must be taken to reduce the risk of COVID-19 in patients with cancer and to optimally manage those who do contract the infection.

1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by the beta-coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread globally and resulted in more than 635,000 deaths as of July 24, 2020 [1]. Among patients with COVID-19, those with cancer have worse outcomes compared with those without underlying malignancy, but mortality rates differ significantly among studies, ranging from 3.7% to 61.5% [2,3].

Even larger studies have significantly different mortality rates – for example, a prospective observational cohort study from the UK reported a mortality rate of 35.4% (617 deaths among 1743 patients with COVID-19 and cancer) [4], while the most recent update from the COVID-19 and Cancer Consortium (CCC-19) showed a death rate of 15.8% (433 deaths in a cohort of 2749 patients with both diseases) [5].

Many of the studies reporting outcomes of patients with both cancer and COVID-19 to date have included relatively small numbers of such patients. Data related to this subpopulation are rapidly increasing but are mostly fragmented. The aim of this systematic review and pooled analysis is to provide a more robust estimate of the mortality rate among SARS-CoV-2–infected patients with underlying cancer.

2. Methods

2.1. Literature search

A systematic literature review of PubMed, Google Scholar, MedRxiv and conference proceedings from the American Association of Cancer Research (AACR), American Society of Clinical Oncology, European Society for Medical Oncology 2020 up to July 16, 2020, was performed by two coauthors (KSS and MT), and disagreement was resolved by consensus with all authors. Multiple combinations of search terms were used: (COVID OR coronavirus OR SARS-CoV-2) AND (cancer OR tumour OR tumour OR malignancy OR malignancies OR neoplasia) AND (mortality OR death). The included study references were cross searched for additional studies. The duplicated reports were removed. The CCC-19 data were updated to reflect the keynote address at the AACR Virtual Meeting: COVID-19 and Cancer by Dr Solange Peters on July 21, 2020.

2.2. Study selection

Inclusion criteria were as follows: (i) studies reporting mortality rate in patients with cancer and COVID-19; (ii) any type of study (including retrospective studies, randomised controlled trials, prospective cohort studies and case series); (iii) studies involving adults; (iv) studies published in English, Spanish or French language.

Exclusion criteria were as follows: (i) studies with less than 10 patients with both cancer and COVID-19; (ii) studies reported in languages other than the aforementioned ones.

2.3. Data extraction

Data were independently extracted by two authors (KSS and MT). Extracted data consisted of first author's name, type of publication (i.e. peer reviewed, preprint or conference proceeding), reported number of patients with cancer and COVID-19, the number of deaths among the study population, study time period, institution or country involved and type of cancer.

2.4. Statistical analysis

Primary end-point was the case fatality rate (CFR), defined as the rate of death among patients with cancer and COVID-19. The CFR was assessed with a random effects model, which was used to derive a pooled CFR and its 95% confidence interval (CI). Heterogeneity was assessed with the I^2 test (substantial heterogeneity whenever $I^2 \geq 50\%$). A sensitivity analysis was performed excluding reports including less than 100 patients.

3. Results

After the systematic literature search, 682 references (including 216 preprints) were retrieved, of which 598 were excluded on the basis of their titles and 32 on the basis of their abstract or full text due to various reasons

Table 1
Mortality data from 52 studies on patients with cancer and COVID-19.

S No.	First author	Type of study	Total patients with cancer and COVID-19	Deaths in patients with cancer and COVID-19	Time period	Institution or country	Type of cancer
1	Burn *et al.* [11]	Preprint	6656	1317	1 Mar to 6 May 2020	Catalonia, Spain	Any
2	Peters [5]	Conference proceedings	2749	433	17 Mar to 26 June 2020	COVID-19 and Cancer Consortium (CCC-19), USA, Canada, Spain	Any
3	Docherty *et al.* [4]	Peer reviewed	1743	617	6 Feb to 19 Apr 2020	UK	Any
4	Fratino *et al.* [12]	Peer reviewed	909	150	Upto 30 Mar 2020	Italy	Any
5	Lee *et al.* [13]	Peer reviewed	800	226	18 Mar to 26 Apr 2020	UK Coronavirus Cancer Monitoring Project (UKCCMP)	Any
6	Montopoli *et al.* [14]	Peer reviewed	430	75	Upto 1 Apr 2020	68 hospitals, Veneto, Italy	Any (but population restricted to men only)
7	Robilotti *et al.* [15]	Peer reviewed	423	51	10 Mar to 7 Apr 2020	New York, USA	Any
8	Horn *et al.* [16]	Conference proceedings	400	141	26 Mar to 12 Apr 2020	TERAVOLT Registry (8 countries)	Thoracic cancers only
9	Miyashita *et al.* [17]	Peer reviewed	334	37	1 Mar to 6 Apr 2020	Mt Sinai Health System, New York, USA	Any
10	Graselli *et al.* [18]	Peer reviewed	331	202	Upto 22 Apr 2020	Lombardy, Italy	Any
11	Wang *et al.* [19]	Preprint	283	50	17 Dec 2019 to 18 Mar 2020	Hubei, China	Any
12	COVIDSurg Collaborative [20]	Peer reviewed	239	66	1 Jan to 31 Mar 2020	24 countries	Any (COVID-19 was diagnosed based on lab, clinical or radiological features)
13	Tian *et al.* [21]	Peer reviewed	232	46	13 Jan to 18 Mar 2020	9 hospitals in Wuhan, China	Any
14	Mehta *et al.* [22]	Peer reviewed	218	61	18 Mar to 8 Apr 2020	New York, USA	Any
15	Yang *et al.* [23]	Peer reviewed	205	30	13 Jan to 18 Mar 2020	9 hospitals from Hubei, China	Any
16	Pinato *et al.* [24]	Peer reviewed	204	59	Upto 6 Mar 2020	8 hospitals in the UK, Italy and Spain	Any
17	Scarfò *et al.* [25]	Peer reviewed	190	55	28 Mar to 22 May 2020	Europe	Chronic lymphocytic leukaemia only
18	de Melo *et al.* [26]	Preprint	181	60	30 Apr to 26 May 2020	Brazilian National Cancer Institute	Any
19	Martinez-Lopez *et al.* [27]	Preprint	167	56	1 Mar to 30 Apr 2020	73 hospitals in Spain	Multiple myeloma only
20	Russel *et al.* [28]	Preprint	156	34	29 Feb to 12 May 2020	Guys Hospital, London, UK	Any
21	Basse *et al.* [29]	Preprint	141	26	13 Mar to 25 Apr 2020	Institute Curie Hospital, Paris, France	Any
22	Barlesi *et al.* [30]	Conference proceedings	137	20	14 Mar to 15 Apr 2020	Gustave Roussy Cancer Campus, Villejuif, France	Any
23	Angelis *et al.* [31]	Peer reviewed	113	29	1 Mar to 30 Apr 2020	Royal Marsden, London, UK	Any
24	Gupta *et al.* [32]	Peer reviewed	112	60	4 Mar to 4 Apr 2020	65 hospitals, USA	Any
25	Zhang *et al.* [33]	Peer reviewed	107	23	5 Jan to 18 Mar 2020	5 hospitals from Wuhan, China	Any
26	Deng *et al.* [34]	Peer reviewed	107	6	Upto 11 Feb 2020	China	Any
27	Dai *et al.* [35]	Peer reviewed	105	12	1 Jan to 24 Feb 2020	14 hospitals from Hubei, China	Any
28	Luo *et al.* [36]	Peer reviewed	102	25	12 Mar to 6 May 2020	New York, USA	Lung cancer only
29	Hultcrantz *et al.* [37]	Preprint	100	18	10 Mar to 30 Apr 2020	New York, USA	Multiple myeloma only
30	Cook *et al.* [38]	Peer reviewed	75	41	Upto 18 May 2020	UK	Multiple myeloma only

(*continued on next page*)

Table 1 (*continued*)

S No.	First author	Type of study	Total patients with cancer and COVID-19	Deaths in patients with cancer and COVID-19	Time period	Institution or country	Type of cancer
31	Booth *et al.* [39]	Peer reviewed	66	34	1 Mar to 6 May 2020	England, UK	Haematological malignancies only
32	Yarza *et al.* [40]	Peer reviewed	63	16	9 Mar to 19 Apr 2020	Hospital Universitario 12 de Octubre, Madrid, Spain	Any
33	Assaad *et al.* [41]	Peer reviewed	55	8	1 Mar to 25 Apr 2020	Centre Léon Bérard, Paris, France	Any
34	Wang *et al.* [42]	Peer reviewed	58	14	1 Mar to 30 Apr 2020	New York, USA	Multiple myeloma only
35	Gonzalez-Cao *et al.* [43]	Preprint	50	13	1 Apr to 17 May 2020	Spain	Melanoma only
36	Suleyman *et al.* [44]	Peer reviewed	49	19	9 Mar to 27 Mar 2020	Henry Ford Health System, Detroit, Michigan, USA	Any
37	Rogado *et al.* [45]	Peer reviewed	45	19	1 Feb to 7 Apr 2020	Hospital Universitario Infanta Leonor of Madrid, Spain	Any
38	Aries *et al.* [46]	Peer reviewed	35	14	11 Mar to 11 May 2020	Barts Cancer Centre, UK	Haematological malignancies only
39	Martín-Moro *et al.* [47]	Peer reviewed	34	11	9 Mar to 17 Apr 2020	Ramón y Cajal University Hospital, Madrid Spain	Haematological malignancies only
40	Zhang *et al.* [48]	Peer reviewed	28	8	13 Jan to 26 Feb 2020	3 hospitals in Wuhan, China	Any
41	Kalinsky *et al.* [2]	Peer reviewed	27	1	10 Mar to 29 Apr 2020	Columbia University Irving Medical Center, USA	Breast cancer only
42	Joharatnam-Hogan *et al.* [49]	Preprint	26	6	12 Mar to 7 Apr 2020	London, UK	Any
43	Stroppa *et al.* [50]	Peer reviewed	25	9	21 Feb to 18 Mar 2020	Piacenza's general hospital, Italy	Any
44	Ciceri *et al.* [51]	Peer reviewed	22	11	25 Feb to 24 Mar 2020	San Raffaele Hospital, Lombardy, Italy	Any
45	Bogani *et al.* [52]	Peer reviewed	19	3	Feb and Mar 2020	Lombardy, Italy	Any
46	Guan *et al.* [53]	Peer reviewed	18	3	11 Dec 2019 to 31 Jan 2020	Wuhan, China	Any
47	Tagliamento *et al.* [54]	Peer reviewed	17	4	10 Mar to 6 Apr 2020	Italy	Solid cancers
48	Wang L *et al.* [55]	Peer reviewed	15	3	1 Jan to 6 Feb 2020	Wuhan, China	Any
49	He *et al.* [3]	Peer reviewed	13	8	23 Jan to 14 Feb 2020	Union Hospital and Wuhan Central Hospital, China	Haematological malignancies only
50	Lattenist *et al.* [56]	Peer reviewed	13	6	13 Mar to 15 May 2020	Universite´ catholique de Louvain, Brussels, Belgium	Haematological malignancies only
51	Yu *et al.* [57]	Peer reviewed	12	3	30 Dec 2019 to 17 Feb 2020	Wuhan, China	Any
52	Wu *et al.* [58]	Peer reviewed	11	4	9 Jan to 20 Mar 2020	Hubei, China	Any, with prior exposure to immune checkpoint inhibitors

COVID-19, coronavirus disease 2019; TERAVOLT, Thoracic cancERs international coVid 19 cOLlaboraTion.

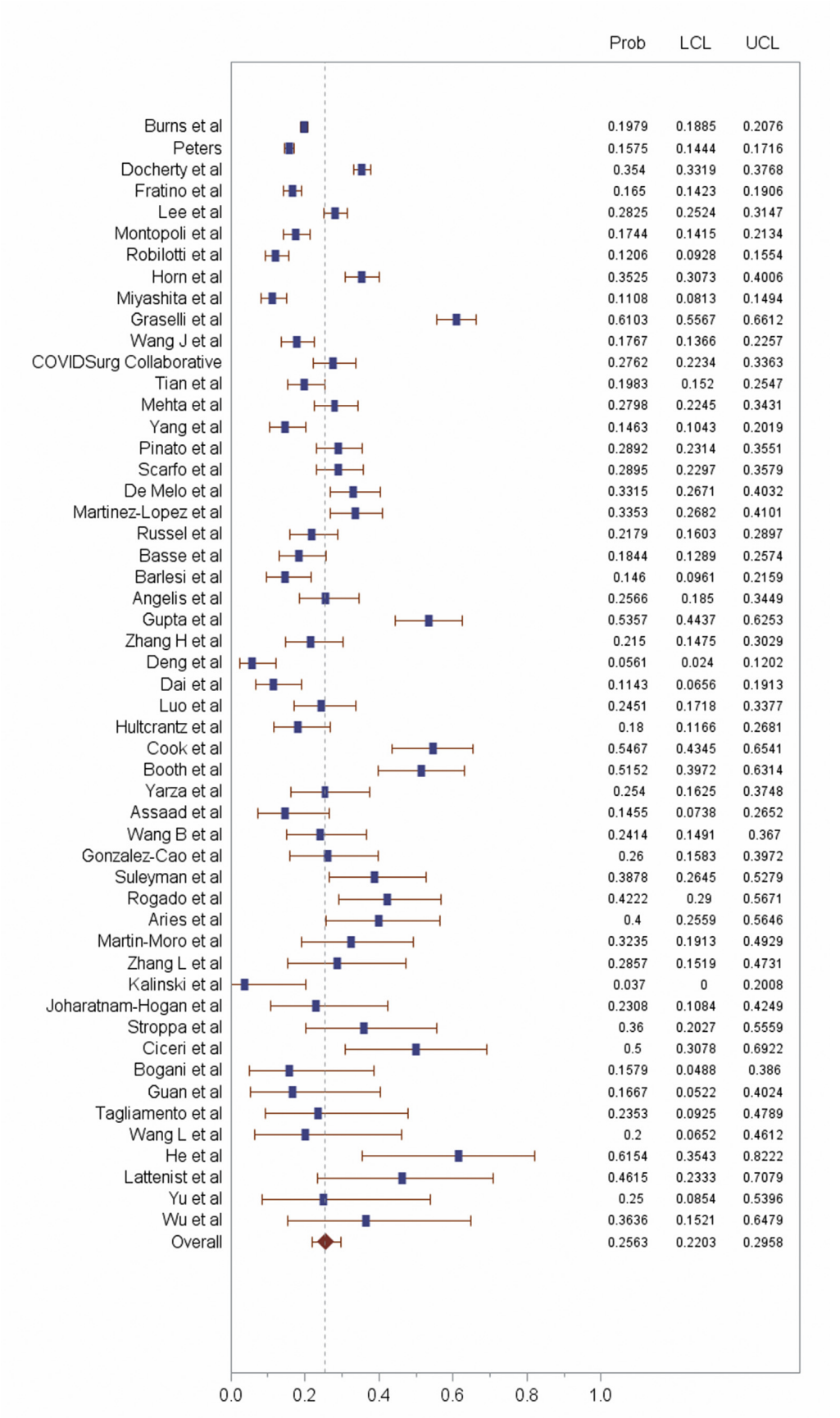

Fig. 1. Forest plot of 52 studies reporting outcomes in patients with both cancer and COVID-19. COVID-19, coronavirus disease 2019.

(inclusion of paediatric patients, duplicated results, cohorts with less than 10 patients, studies not reporting number of deaths, studies not involving patients). In total, 52 studies were included in this pooled analysis with a total of 18,650 patients with cancer and reporting 4243 deaths (Table 1).

Pooled case mortality rate among patients with cancer and COVID-19 was 25.6% (95% CI: 22.0%–29.5%; $I^2 = 48.9\%$) (Fig. 1). A sensitivity analysis excluding reports with less than 100 patients showed an $I^2 = 49.7\%$ for studies with $\geq$100 patients.

4. Discussion

The COVID-19 pandemic has had a major impact on patients with cancer [6], including a sharp reduction in cancer screening and the postponement of ongoing or planned therapy during the initial months of the pandemic, which could result in excess deaths from cancer in the future [7,8].

To restart standard cancer treatment protocols, it is important to quantify the risk of mortality among patients with both cancer and COVID-19, and data generated by large registries such as CCC-19 and Thoracic cancERs international coVid 19 cOLlaboraTion could be valuable in this regard [9,10]. Meta-analyses are also a useful tool to aggregate smaller data sets and estimate mortality risks in this vulnerable population.

The results of our pooled analysis clearly show that the mortality is high among patients with cancer and COVID-19 and should be considered as an independent risk factor, in addition to older age, male sex, black race, current smoker, other comorbidities and so on. As more data become available, it is becoming increasingly clear that within the population of patients with both cancer and COVID-19, there are subsets with greater risk, such as patients with haematological malignancies or lung cancer, which need deeper analysis.

5. Conclusions

Patients with cancer who develop COVID-19 have high probability of mortality. Appropriate and aggressive preventive measures must be taken to reduce the risk of infection with SARS-CoV-2 in patients with cancer and to optimally manage those who do contract the infection.

Author statements

Conflict of interest statement

K.S.S. reports receiving consulting fees from the European Commission outside the submitted work. M.T. reports receiving travel grants from Roche, Bristol-Myers Squibb, AstraZeneca and Takeda and receiving honoraria as a medical writer from Novartis and Amgen outside the submitted work. M.L. reports acting as a consultant for Roche and Novartis and receiving speaker honoraria from Roche, Takeda, Lilly, Novartis, Pfizer and Theramex outside the submitted work. G.C. reports receiving personal fees for consulting, advisory role and speakers' bureau from Roche/Genentech, Novartis, Pfizer, Lilly, Foundation Medicine, Samsung and Daichii-Sankyo; receiving honoraria from Ellipses Pharma; fees for travel and accommodation from Roche/Genentech and Pfizer outside the submitted work. E.d.A. reports receiving honoraria and advisory board fees from Roche/GNE, Novartis and Seattle Genetics; receiving travel grants from Roche/GNE, GSK and Novartis and receiving research grant to institution from Roche/GNE, AstraZeneca, GSK, Novartis and Servier outside the submitted work. The other authors do not report any conflicts of interest.

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Ethical approval and consent to participate

Not applicable.

Authors' contributions

K.S.S. and E.d.A. conceptualised the manuscript; all authors provided significant inputs; K.S.S. and M.T. collected the data, and R.M.N. performed the analysis. All authors wrote, reviewed, edited and approved this final manuscript.

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