BMJ Open

Impact of cancer diagnoses on the outcomes of patients with COVID-19: a systematic review and meta-analysis

Shuting Han ,[1] Qingyuan Zhuang,[2] Jianbang Chiang,[1] Sze Huey Tan,[3] Gail Wan Ying Chua,[4] Conghua Xie ,[5] Melvin L K Chua ,[4] Yu Yang Soon,[6] Valerie Shiwen Yang[1]

To cite: Han S, Zhuang Q, Chiang J, *et al*. Impact of cancer diagnoses on the outcomes of patients with COVID-19: a systematic review and meta-analysis. *BMJ Open* 2022;**0**:e044661. doi:10.1136/bmjopen-2020-044661

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2020-044661).

YYS and VSY are joint senior authors.

Received 20 September 2020
Accepted 24 December 2021

For numbered affiliations see end of article.

Correspondence to
Dr Shuting Han;
han.shuting@singhealth.com.sg

ABSTRACT

Background The COVID-19 has caused significant mortality and morbidity across the globe. Patients with cancer are especially vulnerable given their immunocompromised state. We aimed to determine the proportion of COVID-19 patients with cancer, their severity and mortality outcomes through a systematic review and meta-analysis (MA).

Methods Systematic review was performed through online databases, PubMed, Medline and Google Scholar, with keywords listed in the Methods section (1 November 2019–31 December 2020). Studies with clinical outcomes of at least 10 COVID-19 patients and at least one with a diagnosis of cancer were included. The studies for MA were assessed with PRISMA guidelines and appraised with Newcastle-Ottawa Scale. The data were pooled using a random-effects model using STATA software. The main outcomes were planned before data collection, including proportion of patients with cancer among COVID-19 populations, relative risk (RR) of severe outcomes and death of patients with cancer compared with general COVID-19 patients.

Results We identified 57 case series (63 413 patients), with 230 patients with cancer with individual patient data (IPD). We found that the pooled proportion of cancer among COVID-19 patients was 0.04 (95% CI 0.03 to 0.05, I^2=97.69%, p<0.001). The pooled RR of death was 1.44 (95% CI 1.19 to 1.76) between patients with cancer and the general population with COVID-19 infection. The pooled RR of severe outcome was 1.49 (95% CI 1.18 to 1.87) between cancer and general COVID-19 patients. The presence of lung cancer and stage IV cancer did not result in significantly increased RR of severe outcome. Among the available IPD, only age and gender were associated with severe outcomes.

Conclusion Patients with cancer were at a higher risk of severe and death outcomes from COVID-19 infection as compared with general COVID-19 populations. Limitations of this study include publication bias. A collaborative effort is required for a more complete database.

Strengths and limitations of this study

- Largest meta-analysis on cancer and COVID-19 to date.
- Specific objectives looking at proportion of patients with cancer among COVID-19 cases reported, with severity and mortality outcomes presented as relative risk against general population with COVID-19.
- Detailed cancer cohorts presented with breakdown of tumour types, recent systemic anticancer therapy and other characteristics, with analysis of patients with lung cancer versus non-lung cancer and stage IV versus non-stage IV patients.
- Limitations include publication biases and incomplete reporting of mortality outcomes by selected papers.
- Lack of stratification for age and comorbidities for specific analysis due to limited clinical data.

BACKGROUND

The COVID-19 pandemic, since its emergence in December 2019, has caused significant mortality and morbidity across the globe. In early 2021, more than 100 million people had been infected with more than 2 000 000 deaths. It has disrupted many aspects of healthcare delivery and overwhelmed many hospitals and their intensive care resources.

Patients with cancer are an at-risk population as they are generally older, immunocompromised and have multiple comorbidities. However, the outcomes of patients with cancer with COVID-19 remains conflicted despite multiple cohort studies and meta-analyses. A multicentre study of 105 patients with cancer in China suggested that patients with cancer with COVID-19 infection had higher risk of severe disease outcomes as compared with 536 age-matched non-cancer patients.[1] Another study from the Chinese Centre for Disease Control and Prevention Group reported a case fatality rate (CFR) of 2.3% (1023/44672) among confirmed COVID-19 cases and a more than double CFR of 5.6% (6/107) among the patients with cancer with COVID-19.[2] In contrast, a database report of 5688 COVID-19 positive patients from a tertiary hospital in New York found no significant difference in risk of death between

cancer and non-cancer patients (RR 1.15, 95% CI 0.84 to 1.57) although there was an increased risk of intubation among patients with cancer (RR 1.89, 95% CI 1.37 to 2.61),[3] and other cross-sectional studies also showed similar risk of morbidity and mortality as the general population[4 5] though with a small number of patients. A few meta-analyses had recently addressed this as well and found that there was increased risk of severe COVID-19 infection among patients with cancer on active oncological treatment,[6] especially chemotherapy.[7]

Hence, we aimed to review the current literature and to determine first the proportion of patients with cancer among the reported COVID-19 cases, second whether patients with cancer with COVID-19 had more severe outcomes and higher mortality compared with the general population and lastly, if there were any specific characteristics of patients with cancer that were associated with an increased risk of severe COVID-19 infection.

METHODS

Search methods and study selection

A systematic search of the literature was conducted to identify studies that include patients with cancer with COVID-19 infection. The investigators searched biomedical databases including PubMed, Medline and Google Scholar using the terms COVID-19, coronavirus, nCoV, SARS-CoV-2, characteristics, comorbidity, mortality, death, risk, oncology, cancer, malignancy, neoplasm, tumor, tumour, and carcinoma (online supplemental appendix 1). The search was conducted on 29 January 2021 for a search period from 1 November 2019 to 31 December 2020. The references of relevant meta-analysis (MA) and published reviewers were searched for additional eligible studies. The articles included met the following criteria: (1) COVID-19 diagnosis should be confirmed by real time PCR, or based on 2019 Novel COVID-19 Diagnostic criteria, if applicable (online supplemental appendix 1), (2) studies should contain clinical data of at least ten COVID-19 patients with at least one patient with a diagnosis of cancer (including haematological malignancies), (3) severity outcomes (defined as hypoxaemia, admission to intensive care unit (ICU), and/or mechanical ventilation) and/or death outcomes should be presented and (4) studies should be available in English and full text. Exclusion criteria included studies that reported only specific patient populations, that is, intensive care setting, paediatric population or single tumour type cohorts. Studies published online ahead of print and selected preprint papers were included at the discretion of the authors. For the pooled analysis on severity and death outcomes of cancer and general COVID-19 patients, we mandated that the studies included at least 10 patients with cancer.

The literature search and study selection were performed independently by three of the authors (SH, QZ and VSY), and discrepancies were resolved by consensus. The study followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (online supplemental appendix 1).

Data extraction

Two investigators (SH and VSY) independently graded the studies based on Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomised studies and discrepancies were resolved by consensus (online supplemental appendix 2). Data extraction was performed by SH, and the parameters extracted included the location (hospital and city) of the study, type of study, number of patients, demographics including median or mean age, gender, proportion of patient with comorbidities including cancer, and the clinical outcomes of severe disease and death (of patients with cancer and overall COVID-19 population) were collected for the available studies.

Statistical analysis

All statistical analyses were performed using the STATA V.15 software. MA using random-effects models was performed to analyse the pooled proportion of cancer among COVID-19 patients. The included studies were stratified into subgroups by region (within Hubei Province, China vs outside Hubei Province, including other countries), median/mean age (above or equal to vs below 60 years old) and gender (proportion of male more than or equal to 60% vs less than 60% in population). We further analysed the pooled relative risks (RR) of severe COVID-19 infection outcomes and related deaths for patients with cancer with COVID-19 versus the general population with COVID-19. The subgroup of lung cancer and stage IV patients were also evaluated for RR of severe COVID-19 infection outcomes. The results were presented as proportions (decimal) with 95% CI. Heterogeneity between studies was analysed by the I^2 statistics, where I^2 >50% was considered moderate heterogeneity and χ^2 p<0.05 was considered statistically significant. χ^2 tests were performed to look for associations between patient with cancer characteristics (age, gender, lung cancers, stage IV cancers, comorbidities and recent systemic therapy) and severe COVID-19 outcomes in the individual patient data (IPD).

Patient and public involvement

The research question was formed based on the urgent need to understand the effect of COVID-19 on patients with cancer and to address the clinical decisions that follows this understanding. No patient was directly involved in this systematic review and MA. We would like to thank the authors and also the patients that were involved in the publications that we had included in our MA.

RESULTS

Eligible studies and characteristics

We identified 3083 relevant publications after literature search and review. Additional studies were identified from the references of published meta-analyses. After screening and eligibility assessment, we included in our MA a total of 57 case series involving 63 413 patients (figure 1; online supplemental appendix 2; table 1). Studies that did not

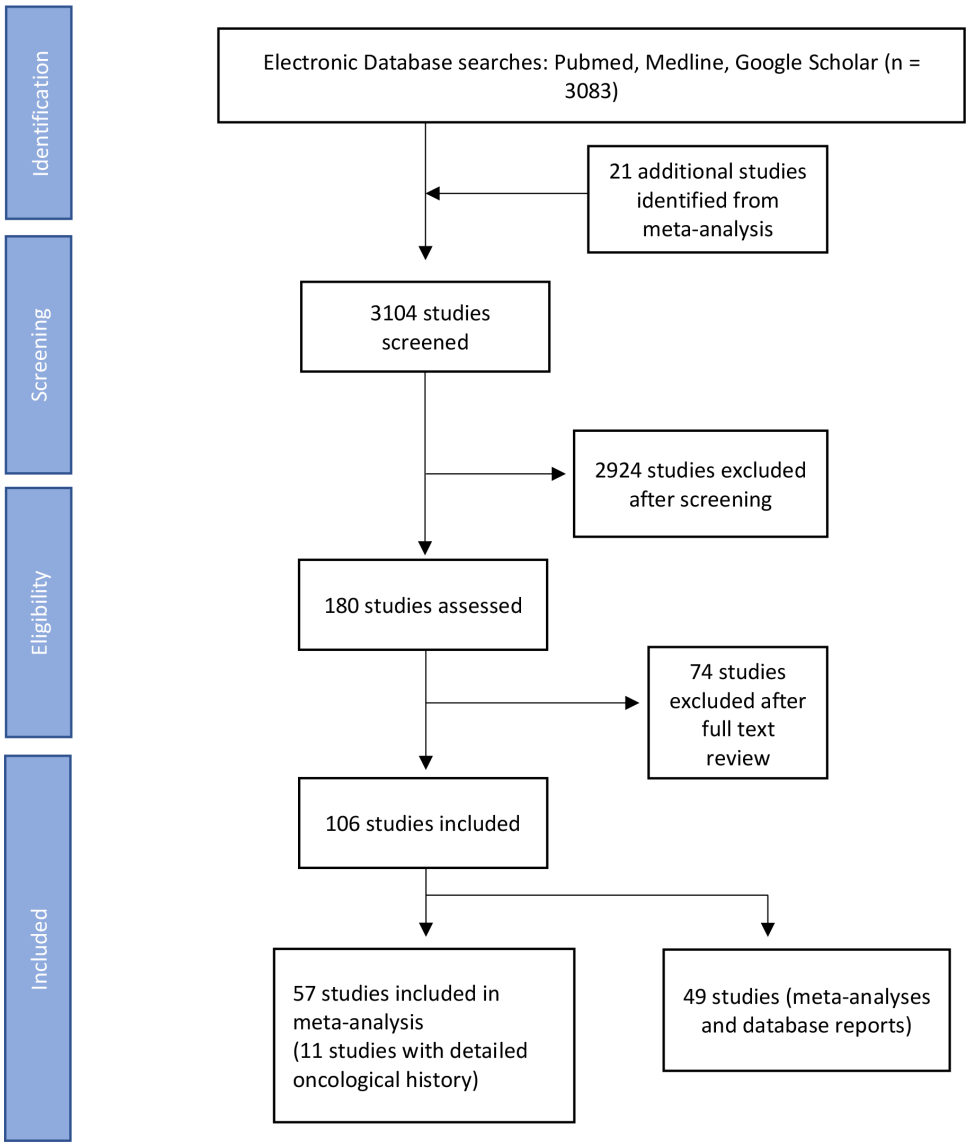

Figure 1 Flow chart of study identification and exclusion for data analysis.

meet the MA criteria were summarised in online supplemental appendix 2; table 2.

Among the 57 studies, 37 studies were from public hospitals in China (24 from Hubei province) with the rest from worldwide (USA, Canada and Spain in CCC19 study) (1), Europe (1), Korea (1), Iran (1), France (1), Spain (1), Italy (2), UK (3) and USA (9) (table 1). Most studies were retrospective cohort studies and a few observational cross-sectional studies. The quality of all the included studies ranged from 6 to 8 (out of 9) using the NOS (online supplemental table 3). Among the 57 case series, 13 contained detailed descriptions of COVID-19 patients with cancer (table 2). Only five studies provided detailed IPD (online supplemental appendix 3; table 1). Forty-seven studies were used for proportion analyses for cancer diagnoses among COVID-19 patients. For the pooled analysis on RR of severe outcomes among cancer COVID-19 patients, we identified 10 case series that contained severity data, and 7 studies that contained mortality data for analysis (studies with at least 10 patients with cancer). Five studies contained severity outcomes of lung cancer versus other patients with cancer with COVID-19 infection, and four studies contained severity outcomes of patients with stage IV vs non-stage IV cancer.

Overall, there were more males than females affected, with a median age above 60 in all case series. This median age was notably higher than the non-cancer populations reported in previous studies.[8] Severe COVID-19 disease among patients with cancer ranged from 9% to 54% in 13 eligible studies (table 2). Overall, 230 patients from five case series were identified with oncological history, stage, recent treatment history and clinical outcomes (online supplemental appendix 3; table 1). However, among these patients, there was inconsistent reporting in those on active systemic chemotherapy and some clinical data on stage of cancer were missing, limiting the usefulness of the dataset in predicting the outcomes of COVID-19 in patients with active cancer.

Table 1 Baseline characteristics, comorbidities and severity outcomes of 57 COVID-19 case series

No	Authors	Location	Definition of severity	Total	Death n (%)	Severe n (%)	Gender—male n (%)	Age	DM	HTN	Pulnomary disease	Smoking	CKD	CVS	CLD	Cancer total n (%)	Cancer—severe n (% of cancer total)	Cancer—death (% of cancer total)
1	Argenziano *et al*[31]	New York, USA	ICU, death	1000	211 (21.1)	236 (23.6)	596 (59.6)	63 (50–75	372 (37.2)	601 (60.1)	66 (6.6)	49 (4.9)	137 (13.7)	131 (13.1)	15 (1.5)	67 (6.7)	17 (25.4)	N.A
2	Assaad *et al*[32]	Lyon, France	Death	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	302	N.A	30 (9.9)
3	Benelli *et al*[33]	Crema, Italy	ICU +NIV, death	411	72 (17.5)	140 (34.1)	359 (66.6)	70.5 (1–99)	67 (16.3)	193 (47.0)	48 (11.7)	N.A	22 (5.3)	93 (22.6)	N.A	33 (8.0)	10 (30.3)	9 (27.3)
4	Cai *et al*[34]	Shenzhen, China	ICU, death	298	3 (1.0)	58 (19.5)	145 (48.7)	47.5 (33–61)	18 (6.0)	47 (15.8)	N.A	N.A	N.A	25 (8.4)	28 (9.4)	4 (1.3)	2 (50.0)	N.A
5	Cao *et al*[35]	Shanghai, China	ICU, death	198	1 (0.5)	19 (9.6)	101 (51.0)	50.1 (±16.3)	15 (7.6)	42 (21.2)	N.A	11 (5.6)	N.A	12 (6.0)	6 (3.0)	4 (2.0)	0	N.A
6	Cao *et al*[35]	Hubei, China	ICU, death	102	17 (16.7)	18 (17.6)	53 (52.0)	54 (37–67)	11 (10.8)	28 (27.5)	10 (9.8)	N.A	4 (3.9)	11 (10.8)	2 (2.0)	4 (3.9)	N.A	1 (25.0)
7	Chen *et al*[36]	Shanghai, China	ICU, death	249	2 (0.8)	22 (8.8)	126 (50.6)	51 (31–64)	25 (10.0)	N.A	5 (2.0)	N.A	N.A	55 (22.1)	N.A	1 (0.4)	N.A	N.A
8	Chen *et al*[37]	Hubei, China	ICU, death	99	11 (0.11)	23 (23.2)	67 (67.7)	55.5 (±13.1)	12 (12.1)	0	1 (1.0)	N.A	N.A	40 (40.4)	N.A	1 (1.0)	N.A	N.A
9	Colaneri *et al*[38]	Pavia, Italy	Require high FiO2	44	2 (4.5)	17 (38.6)	28 (63.6)	67.5 (10–94)	7 (15.9)	15 (34.1)	2 (4.5)	N.A	N.A	11 (25.0)	N.A	6 (13.6)	2 (4.5)	N.A
10	Dai *et al*[8]	Hubei, China	NIV and ventilation, death	641	N.A	84 (13.1)	57 (8.9)	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	105 (16.4)	20 (19.1)	12 (11.4)
11	Docherty *et al*[39]	UK	HD/ICU, death	20 133	5165 (25.7)	3001 (14.9)	12 068 (59.9)	73 (58–82)	3650 (18.1)	N.A	3128 (15.5)	852 (4.2)	2830 (14.1)	5469 (27.2)	281 (1.4)	1743 (8.7)	N.A	N.A
12	Du *et al*[40]	Hubei, China	Death	179	21 (11.7)	N.A	97 (54.1)	57.6 (±13.7)	33 (18.4)	58 (32.4)	N.A	N.A	4 (2.2)	29 (16.2)	N.A	4 (2.2)	N.A	1 (25.0)
13	Duanmu *et al*[41]	California, USA	Death	100	1 (1.0)	N.A	56 (56.0)	45 (32–65)	10 (10.0)	19 (19.0)	1 (1.0)	2 (2.0)	6 (6.0)	N.A	N.A	3 (3.0)	N.A	N.A
14	Feng *et al*[42]	Hubei, China	See below	476	38 (8.0)	124 (26.1)	271 (56.9)	53 (40–64)	17 (3.6)	40 (8.4)	14 (2.9)	44 (9.2)	2 (0.4)	26 (5.5)	N.A	12 (2.5)	7 (58.3)	N.A
15	Guan *et al*[43]	China	Composite endpoint*	1099	15 (1.4)	67 (6.1)	640 (58.2)	47 (35–58)	81 (7.4)	165 (15.0)	12 (1.1)	158 (14.4)	8 (0.7)	42 (3.8)	23 (2.1)	10 (0.9)	1 (10.0)	N.A
16	Guo *et al*[44]	Hubei, China	Mechanical ventilation	187	43 (23.0)	45 (24.1)	91 (48.7)	58.5 (±14.7)	28 (15.0)	61 (32.6)	4 (2.1)	18 (9.6)	6 (3.2)	29 (15.5)	N.A	13 (7.0)	N.A	N.A
17	Huang *et al*[45]	Hubei, China	ICU	41	6 (14.6)	13 (31.7)	30 (73.2)	49 (41–58)	8 (19.5)	6 (14.6)	1 (2.4)	3 (7.3)	N.A	6 (14.6)	1 (2.4)	1 (2.4)	0	N.A
18	Huang *et al*[46]	Hubei, China	ICU	34	N.A	8 (23.5)	14 (41.2)	56 (26–88)	4 (11.8)	8 (23.5)	3 (8.8)	N.A	N.A	6 (17.6)	1 (2.9)	3 (8.8)	N.A	N.A
19	Kim *et al*[47]	Korea	Require high FiO2	28	0	6 (24.1)	15 (53.6)	40 (20–73)	2 (7.1)	0	0	5 (17.9)	0	0	1 (3.6)	1 (3.6)	N.A	N.A
20	Kuderer *et al*[48]	Worldwide	Composite endpoint	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	928	242 (26.0)	121 (13.0)

Continued

Table 1 Continued

No	Authors	Location	Definition of severity	Total	Death n (%)	Severe n (%)	Gender —male n (%)	Age	DM	HTN	Pulnomary disease	Smoking	CKD	CVS	CLD	Cancer total n (%)	Cancer —severe n (% of cancer total)	Cancer —death (% of cancer total)
21	Lee *et al*[49]	UK	ICU, death	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	800	53 (7.0)	226 (28.3)
22	Li *et al*[50]	Hubei, China	IDSA/ATS†	548	90 (16.4)	269 (49.1)	279 (50.9)	60 (48–69)	83 (15.1)	166 (30.3)	17 (3.1)	N.A	10 (1.8)	34 (6.2)	5	24 (0.9)	14	N.A
23	Lian *et al*[51]	Zhejiang, China	Not defined	788	N.A	18 (2.3)	407 (51.6)	N.A	57 (7.2)	126 (16.0)	3	54 (6.9)	7 (0.9)	11 (1.4)	31 (3.9)	6 (0.8)	N.A	N.A
24	Liang *et al*[10]	China	Composite endpoint	1590	N.A	254 (16.0)	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	18 (1.1)	9 (50.0)	9 (50.0)
25	Liu K *et al*[52]	Hubei, China	NIV	137	16 (11.7)	34 (24.8)	61 (44.5)	57 (20–83)	14 (10.2)	13 (9.5)	2 (1.5)	N.A	N.A	10	N.A	2 (1.5)	N.A	N.A
26	Ma *et al*[53]	Hubei, China	See below‡	1380	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	37 (2.7)	20 (54.1)	5 (13.5)
27	Mehta *et al*[17]	New York, USA	Death	1308	210 (16.1)	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	218 (16.7)	N.A	61 (28.0)
28	Myers *et al*[54]	New York, USA	Intubation, death	5688	555 (9.8)	351 (6.2)	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	334 (5.9)	N.A	37 (11.1)
29	Myers *et al*[54]	California, USA	ICU	377	100 (26.5)	113 (30.0)	212 (56.2)	61 (50–73)	118 (31.3)	164 (43.5)	28 (7.4)	N.A	48 (12.7)	22 (5.8)	21 (5.6)	18 (4.8)	6 (33.3)	N.A
30	Nikpouraghdam *et al*[55]	Iran	Death	2964	239 (8.1)	N.A	1955 (66.0)	56 (46–65)	113 (3.8)	59 (2.0)	60 (2.0)	N.A	18 (0.6)	37 (1.2)	N.A	17 (0.6)	N.A	1 (5.9%)
31	Pan *et al*[56]	Hubei, China	ICU, death	204	36 (17.6)	16 (7.8)	107 (52.5)	52.9 (±16.0)	44 (21.6)	N.A	9 (4.4)	N.A	N.A	44 (21.6)	N.A	13 (6.4)	N.A	N.A
32	Paranjpe *et al*[57]	New York, USA	Death	1078	310 (28.8)	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	64 (5.9)	N.A	24 (37.5)
33	Petrilli *et al*[58]	New York, USA	ICU, death	5279	665 (12.6)	990 (18.8)	2615 (49.5)	54 (38–66)	1195 (22.6)	2256 (42.7)	786 (14.9)	288 (5.5)	647 (12.3)	704 (13.3)	N.A	403 (7.6)	138 (34.2)	N.A
34	Pinato *et al*[59]	Europe	HD/ICU, death	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	890	110 (12.4)	299 (33.6)
35	Robilotti *et al*[60]	New York, USA	Mechanical ventilation /high flow, death	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	423	87 (20.6)	51 (12.1)
36	Richardson *et al*[61]	New York, USA	ICU, death	5700	553 (9.7)	320 (5.6)	3437 (60.3)	63 (52–75)	1808 (31.7)	3026 (53.1)	287 (5.0)	2691 (47.2)	454 (8.0)	966 (16.9)	30 (0.5)	320 (5.6)	N.A	N.A
37	Shi *et al*[62]	Hubei. China	Not defined	81	N.A	N.A	42 (51.9)	49.5 (±11.0)	19 (23.5)	12 (14.8)	9 (11.1)	N.A	3 (3.7)	14 (17.3)	N.A	4 (4.9)	N.A	N.A
38	Shi *et al*[63]	Zhejiang, China	Not defined	487	0	49 (10.1)	259 (53.2)	46 (±19.0)	29 (6.0)	99 (20.3)	0	40 (8.2)	7 (1.4)	11 (2.3)	22 (4.5)	5 (1.0)	2 (40.0)	N.A
39	Tomlins *et al*[64]	UK	NIV +intubation, death	95	20 (21.1)	16 (16.8)	60 (63.2)	75 (59–82)	N.A	N.A	N.A	N.A	N.A	N.A	N.A	20 (21.1)	N.A	3 (15.0)
40	Wan *et al*[65]	Chongqing, China	Not defined	135	1 (0.7)	40 (29.6)	72 (53.3)	47 (36–55)	12 (8.9)	13 (9.6)	0	9 (6.7)	N.A	7 (5.2)	2 (1.5)	4 (3.0)	3 (75.0)	N.A

Continued

Table 1 Continued

No	Authors	Location	Definition of severity	Total	Death n (%)	Severe n (%)	Gender—male n (%)	Age	DM	HTN	Pulnomary disease	Smoking	CKD	CVS	CLD	Cancer total n (%)	Cancer—severe n (% of cancer total)	Cancer—death (% of cancer total)
41	Wang *et al*[66]	Hubei, China	ICU	138	6 (4.3)	36 (26.1)	75 (54.3)	56 (42–68)	14 (10.1)	43 (31.2)	4 (2.9)	N.A	2 (1.5)	27 (19.6)	0	10 (7.2)	4 (40.0)	N.A
42	Wang *et al*[67]	Anhui. China	ICU	125	0	19 (15.2)	71 (56.8)	38.8 (±13.8)	10 (8.0)	N.A	2 (1.6)	16 (12.8)	N.A	18 (14.4)	N.A	1 (0.8)	N.A	N.A
43	Wu *et al*[21]	Hubei, China	ARDS, death	201	44 (21.9)	84 (41.8)	N.A	51 (43–60)	22 (10.9)	39 (19.4)	5 (2.5)	N.A	2 (1.0)	8 (4.0)	7 (3.5)	1 (0.5)	N.A	N.A
44	Wu *et al*[68]	Jiangsu, China	See below	80	0	3 (37.5)	39 (48.8)	46.1 (±15.4)	5 (6.3)	N.A	0	N.A	1 (1.3)	25 (31.3)	1 (1.3)	1 (1.3)	N.A	N.A
45	Xu *et al*[69]	Guangzhou, China	Not defined	90	N.A	N.A	39 (43.3)	50 (18–86)	5 (55.6)	17 (18.9)	1 (1.1)	N.A	N.A	3 (3.3)	N.A	2 (2.2)	N.A	N.A
46	Yang *et al*[70]	Zhejiang, China	NIV	149	0	2 (1.3)	81 (54.4)	45.1 (±13.4)	9 (6.0)	0	1 (0.7)	N.A	N.A	28 (18.8)	N.A	2 (1.3)	N.A	N.A
47	Yang *et al*[71]	Hubei, China	ICU, mechanical ventilation, death	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	205	30 (14.6)	40 (19.5)
48	Yarza *et al*[72]	Spain	Respi failure	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	63	34 (54.0)	16 (25.4)
49	Yu *et al*[19]	Hubei, China	ARDS, death	1524	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	12 (0.8)	3 (25.0)	3 (25.0)
50	Zhang *et al*[13]	Hubei, China	Composite endpoint	1276	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	28 (2.2)	15 (53.6)	8 (28.6)
51	Zhang *et al*[73]	Hubei, China	IDSA/ATS	221	12 (5.4)	55 (24.9)	108 (48.9)	55 (39–66.5)	22 (10.0)	54 (24.4)	6 (2.7)	N.A	6 (2.7)	37 (16.7)	7 (3.2)	9 (4.1)	4 (44.4)	N.A
52	Zhang *et al*[74]	Hubei, China	See below	663	25 (3.8)	409 (61.7)	321 (48.4)	55.6 (44–69)	67 (10.1)	N.A	51 (7.7)	N.A	N.A	164 (24.7)	31 (4.7)	14 (2.1)	11 (78.6)	N.A
53	Zhang *et al*.§	Hubei, China	See below	1548	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A	67 (4.3)	32 (47.8)	18 (26.9)
54	Zhang *et al*¶	Hubei, China	Death	315	47 (14.9)	178 (56.5)	175 (55.6)	57 (44–66)	41 (13.0)	78 (24.8)	3 (1.0)	N.A	2 (0.6)	42 (13.3)	9 (2.9)	12 (3.8)	N.A	4 (33.3)
55	Zhao *et al*[75]	Hubei, China	Not defined	91	2 (2.2)	30 (33.0)	49 (53.8)	46 (Not stated)	3 (3.3)	18 (19.8)	1 (1.1)	N.A	1 (1.1)	N.A	N.A	3 (3.3)	2 (2.2)	N.A
56	Zhou *et al*[76]	Hubei, China	Not defined	191	54 (28.3)	119 (62.3)	119 (62.3)	56 (46–67)	36 (18.8)	58 (30.4)	6 (3.1)	11 (5.8)	2 (1.0)	15 (7.9)	0	2 (1.0)	N.A	N.A
57	Zhu *et al*[77]	Hefei, China	Not defined	32	N.A	N.A	15 (46.9)	46 (35–52)	4 (12.5)	7 (21.9)	2 (6.3)	6 (18.8)	1 (3.1)	10 (31.3)	2 (6.3)	2 (6.3)	N.A	N.A

All figures presented as n (%)—number (percentage) unless otherwise stated. Age presented as median with IQR: age (range) or as mean: age (±SD).
*Composite endpoint: severe disease composite endpoints (ICU, mechanical ventilation and/or death).
†See below: severity as defined by Chinese National Health Commission Definition of Severity (refer to online supplemental appendix 1).
‡IDSA/ATS: Infectious Diseases Society of America/American Thoracic Society Criteria for Defining Severe Community-acquired Pneumonia 2007 (online supplemental appendix 1).
§Article in press (accepted, peer-reviewed).
¶Article not peer-reviewed
ARDS, acute respiratory distress syndrome; CKD, chronic kidney disease; CLD, chronic liver disease; CVS, cardiovascular disease; DM, diabetes mellitus; FiO2, supplemental oxygen; HTN, hypertension; ICU, intensive care unit; IDSA/ATS, Infectious Disease Society of America/American Thoracic Society Guidelines; N.A, not applicable; NIV, non-invasive ventilation.

Table 2 Baseline characteristics of patients with cancer with COVID-19 infections from 13 case series

Characteristics	Zhang *et al*[13] 2020 (n=28) n (%) or median (range)		Yu *et al*[19] 2020 (n=12) n (%) or median (range)		Liang *et al*[10] 2020 (n=18) n (%) or median (range)		Ma *et al*[53] 2020 (n=37) n (%) or median (range)		Dai *et al*[8] 2020 (n=105) n (%) or median (range)		Zhang *et al*[73] 2020 (n=67) n (%) or median (range)	
Age	65.0 (56.0–70.0)		66 (48–78)		63.1 (51–75)		62 (59–70)		64 (50–78)		66 (37–98)	
Gender												
Male	17 (60.7)		10 (83.3)		12 (66.7)		20 (54.1)		57 (54.7)		41 (61.2)	
Female	11 (39.3)		2 (16.7)		6 (33.3)		17 (45.9)		48 (45.3)		26 (38.8)	
Stage												
I-III	18 (64.3)		5 (41.7)		13 (72.2)		N.A		88 (83.8)		N.A	
IV	10 (35.7)		6 (50.0)		4 (22.2)		N.A		17 (16.2)		N.A	
Unknown	N.A		1 (8.3)		1 (5.6)		N.A		N.A		N.A	
Smoking history												
Yes	N.A		N.A		4 (22.2)		N.A		36 (34.3)		9 (13.4)	
No	N.A		N.A		N.A		N.A		69 (65.7)		N.A	
Unknown	N.A		N.A		N.A		N.A		N.A		N,A	
	Lung ca	7 (25.0)	Lung ca	7 (58.3)	Lung ca	5 (27.8)	CRC	11 (29.7)	Lung ca	22 (20.1)	Lung ca	15 (22.4)
	Oesophageal ca	4 (14.3)	Rectal ca	1 (8.3)	CRC	4 (22.2)	Lung ca	8 (21.6)	GI ca	13 (12.4)	CRC	11 (16.4)
	Breast ca	3 (10.7)	Colon ca	1 (8.3)	Breast ca	3 (16.7)	Breast ca	7 (18.9)	Breast ca	11 (10.5)	Thyroid ca	8 (11.9)
	Laryngoca	2 (7.1)	Pancreatic ca	1 (8.3)	Bladder ca	2 (11.1)	Gynae ca	5 (13.5)	Thyroid ca	11 (10.5)	Urinary system	8 (11.9)
	Liver ca	2 (7.1)	Breast ca	1 (8.3)	Lymphoma	1 (0.56)	Other ca	6 (16.2)	Blood ca	9 (8.6)	Breast & gynae	7 (10.4)
	Prostatic ca	2 (7.1)	Urothelial ca	1 (8.3)	Thyroid ca	1 (0.56)			Cervix ca	6 (5.7)	Head and Neck	5 (7.5)
	Cervical ca	1 (3.6)			Adrenal ca	1 (0.56)			Oesophageal ca	6 (5.7)	CNS tumour	4 (5.9)
	Gastric ca	1 (3.6)			RCC	1 (0.56)					Haematological	3 (4.5)
	Colon ca	1 (3.6)									Gastric ca	3 (4.5)
	Rectum ca	1 (3.6)									Oesophageal ca	2 (3.0)
	NPC	1 (3.6)									HCC	1 (1.15)
	Endometrial ca	1 (3.6)										
	Ovarian ca	1 (3.6)										
	Ca of testis	1 (3.6)										
Baseline treatment	ChemoRT	25 (89.3)	BSC	4 (33.3)	Surveillance	12 (75.0)	Antitumour therapy	13 (35.1)	Chemotherapy	17 (16.2)	Follow-up	44 (65.7)
	Operation	21 (75.0)	Chemo-immuno Therapy	2 (16.7)	Chemo and surgery within 1 month	4 (25.0)			RT	13 (12.4)	On treatment	23 (34.3)
	Targeted therapy/ immunotherapy	6 (21.4)	Surveillance	2 (16.7)					Surgery	8 (7.6)		
	Chemo (<14 d)	3 (10.7)	Targeted Therapy/RT	1 (8.3)					Immunotherapy	6 (5.7)		
	Targeted Therapy	2 (7.1)	Chemo/RT	1 (8.3)					Targeted Therapy	4 (3.8)		
	RT (<14 d)	1 (3.6)	Adjuvant RT	1 (8.3)								

Continued

Table 2 Continued

Characteristics	Zhang *et al*[13] 2020 (n=28) n (%) or median (range)	Yu *et al*[19] 2020 (n=12) n (%) or median (range)	Liang *et al*[10] 2020 (n=18) n (%) or median (range)	Ma *et al*[53] 2020 (n=37) n (%) or median (range)	Dai *et al*[8] 2020 (n=105) n (%) or median (range)	Zhang *et al*[73] 2020 (n=67) n (%) or median (range)
	Immunotherapy (<14 d) 1 (3.6)	Not started 1 (8.3)				
Severe disease	Severe 15 (53.6) 8/15 Non-invasive ventilation 2/15 Invasive ventilation	Severe 3 (25.0)	Severe 9 (50.0)	Severe 20 (54.1)	Severe 40 (38.0) ICU 20 (19.1)	Severe 32 (47.8) Mechanical ventilation 28 (41.8)
ARDS	8 (28.6)	N.A	N.A	N.A	N.A	14 (20.9)
Death	8 (28.6)	3 (25.0)	9 (50.0)	5 (13.5)	12 (11.4)	18 (26.9)

Characteristics	Kuderer *et al*[48] (CCC19) (n=928) n (%) or median (range)	Lee LY *et al*[49] (UKCCMP) (n=800) n (%) or median (range)	Robilotti *et al*[60] (MSKCC) (n=423) n (%) or median (range)	Pinato *et al*[59] (n=890) n (%) or median (range)	Assaad *et al*[32] (n=302) n (%) or median (range)	Yang *et al*[70] (n=205) n (%) or median (range)	Yarza *et al*[72] (n=63) n (%) or median (range)
Age	66 (57–76)	69 (59–76)	N.A	Mean: 68.0±12.8	Mean: 58.2±1.1	63 (56–70)	66 (63–69)
Gender							
Male	468 (50)	449 (56)	212 (50.1)	503 (56.5)	144 (47.7)	96 (46.8)	34 (54)
Female	459 (49)	349 (44)	211 (49.9)	387 (43.5)	158 (52.3)	109 (53.2)	29 (46)
Stage							
I-III	N.A	227 (29)	N.A	539 (60.6)	N.A	N.A	52 (82.5)
IV	N.A	347 (43)	238 (56.3)	351 (39.4)	161 (53.3)	N.A	11 (17.5)
Unknown	N.A	205 (25)	N.A	0	N.A	N.A	N.A
Smoking history							
Yes	369 (40)	N.A	167 (39.5)	380 (42.7)	N.A	N.A	34 (54.0)
No	469 (51)	N.A	249 (58.9)	343 (38.5)	N.A	N.A	29 (46.0)
Unknown	90 (10)	N.A	7 (1.7)	167 (18.8)	N.A	N.A	0
	Haematological ca 204 (22.0)	Digestive organs 150 (18.8)	Others 137 (32.4)	Breast 162 (18.2)	Solid tumour 234 (77.5)	Solid tumour 183 (89.3)	Lung 17 (27.0)
	Breast ca 191 (20.6)	Other haematological 109 (13.6)	Breast 86 (20.3)	Haematological 137 (15.4)	Haematological 68 (22.5)	Breast 40 (19.5)	
	Prostate ca 152 (16.4)	Breast 102 (12.8)	Lymphoma 48 (11.3)	Genito-Urinary 132 (14.8)	Lung 42 (13.9)	Colorectal 28 (13.6)	
	Gastrointestinal ca 108 (11.6)	Respiratory and intrathoracic organs 90 (11.3)	Colorectal ca 37 (8.7)	Lung 119 (13.4)		Lung 24 (11.7)	
	Lung ca 91 (9.8)	Male genital organs 78 (9.8)	Lung 35 (8.3)	Gastrointestinal 105 (11.8)		Haematological 22 (10.7)	
	Gynaecological ca 49 (5.3)	Lymphoma 60 (7.5)	Leukaemia 32 (7.6)	Gynaecological 41 (4.6)		Thyroid 16 (7.8)	
	RCC 45 (4.8)	Female genital organs 45 (5.6)	Prostate 26 (6.1)	Gastro-oesophageal 40 (4.5)		Stomach 12 (5.9)	
	Endocrine ca 39 (4.2)	Urinary tract 50 (6.3)	Melanoma 22 (5.2)	Hepatobiliary 45 (5.1)		Cervical 9 (4.4)	
	Melanoma 38 (4.1)	Other or unspecified 47 (5.9)		Head and Neck 29 (3.3)		Lymphoma 7 (3.4)	

Continued

Table 2 Continued

Characteristics	Kuderer *et al*[48] (CCC19) (n=928) n (%) or median (range)		Lee LY *et al*[49] (UKCCMP) (n=800) n (%) or median (range)		Robilotti *et al*[60] (MSKCC) (n=423) n (%) or median (range)		Pinato *et al*[59] (n=890) n (%) or median (range)		Assaad *et al*[32] (n=302) n (%) or median (range)		Yang *et al*[70] (n=205) n (%) or median (range)		Yarza *et al*[72] (n=63) n (%) or median (range)	
	Head and neck ca	30 (3.2)	Lip, oral cavity, and pharynx	27 (3.4)			Skin	28 (3.1)			Acute lymphoblastic leukaemia	5 (2.4)		
	Sarcoma	24 (2.6)	Melanoma (skin)	27 (3.4)			Other	52 (5.8)			Chronic lymphoblastic leukaemia	4 (2.0)		
	CNS	12 (1.3)	CNS	15 (1.9)							Multiple myeloma	3 (1.5)		
	Solid tumour, not otherwise specified	43 (4.6)									Acute myelogenous leukaemia	2 (1.0)		
											MDS	1 (<1)		
Baseline treatment	None	553 (59.6)	Chemotherapy	281 (35.1)	Chemo in last 30 days	191 (45.2)	Chemotherapy	164 (69.8)	Any cancer treatment	194 (64.2)	All	54/182 (29.7)	Chemotherapy	36 (57.1)
	Chemotherapy	160 (17.2)	None	272 (34.0)	Surgery in last 30 days	31 (7.3)	Ongoing anticancer therapy at COVID-19 diagnosis	479 (53.8)	Cytotoxics	137 (45.4)	Chemotherapy	31/182 (17.0)	Endocrine therapy	10 (15.9)
	Endocrine	85 (9.2)	RT	76 (9.5)	ICI	31 (7.3)	Surgery	417 (46.8)	No cancer treatment	108 (35.8)	Targeted therapy	12/182 (6.6)	Immunotherapy	8 (12.7)
	Targeted therapy	75 (8.1)	Targeted treatment	72 (9)			Adjuvant /Neoadjuvant chemotherapy	210 (23.6)	Immunotherapy	26 (8.6)	Others	10/182 (5.5)	Targeted therapy	7 (11.1)
	Immunotherapy	38 (4.1)	Hormone therapy	64 (8.0)			Endocrine Therapy	48 (20.4)	Antiangiogenic	18 (6.0)	RT	9/182 (5.0)	No active tx	2 (3.2)
	RT	12 (1.3)	Other	60 (7.5)			Target Therapy	41 (17.4)	Anti-CD20	14 (4.6)	Surgery	4/182 (2.2)		
			Immunotherapy	44 (5.5)			Immunotherapy	38 (16.2)	Anti-HER2	12 (4.0)	Immunotherapy	4/182 (2.2)		
			Surgery	29 (3.6)					Antiproteasomes	8 (2.6)				
			No information	10 (1.3)					Everolimus (mTORi)	4 (1.3)				
Severe disease	Severe (composite) 242 (26.1) ICU 132 (14.2) Mechanical ventilation 116 (12.5)		Severe/critical 360 (45) ICU 53 (6.6)		Mechanical ventilation 40 (9.5) High flow 47 (11.1)		Admission to ICU /sub-intensive 110/760 (14.5)		N.A		ICU 30 (14.6) Mechanical ventilation 21 (10.2)		Respi failure 34 (54.0)	
ARDS	NA		NA		NA		127 (22.5)		N.A		23 (11.2)		23 (36.5)	
Death	121 (13.0)		226 (28.3)		51 (12.1)		299 (33.6)		30 (9.9)		40 (19.5)		16 (25.4)	

ARDS, acute respiratory distress syndrome; BSC, best supportive care; Ca, carcinoma; CNS, central nervous system; CRC, colorectal cancer; GI, gastrointestinal; ICU, intensive care unit; ICU, intensive care unit; MDS, myelodysplastic syndrome; MSKCC, Memorial Sloan Kettering Cancer Center; N.A, not applicable; NPC, nasopharyngeal cancer; RCC, renal cell carcinoma; RT, radiotherapy; UKCCMP, Coronavirus Cancer Monitoring Project UK.

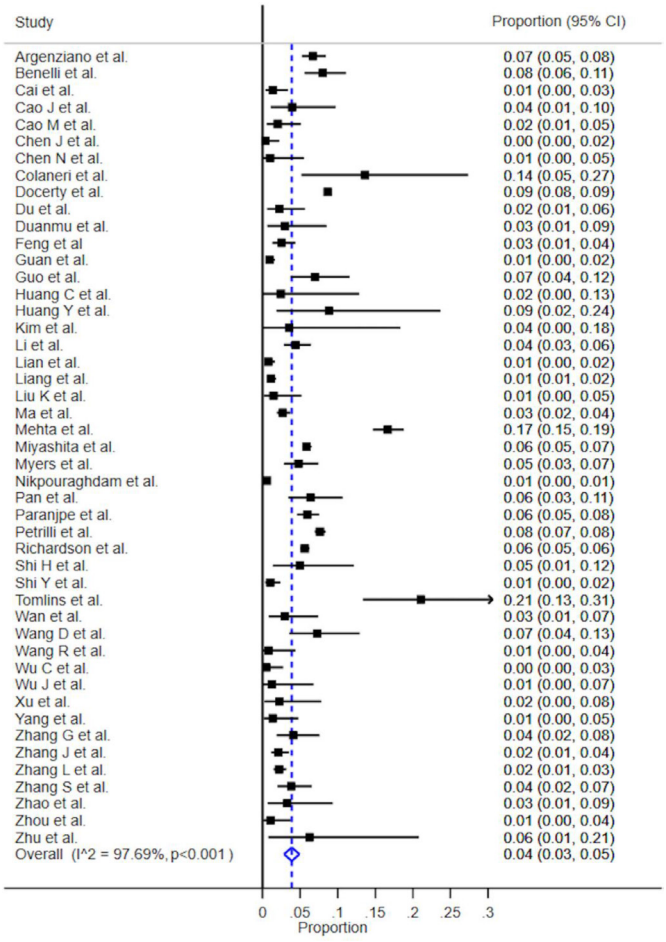

Figure 2 Random effects pooled proportion of patients with cancer among patients diagnosed with COVID-19. 10 papers were excluded in the proportion calculations (did not represent overall COVID-19 populations).

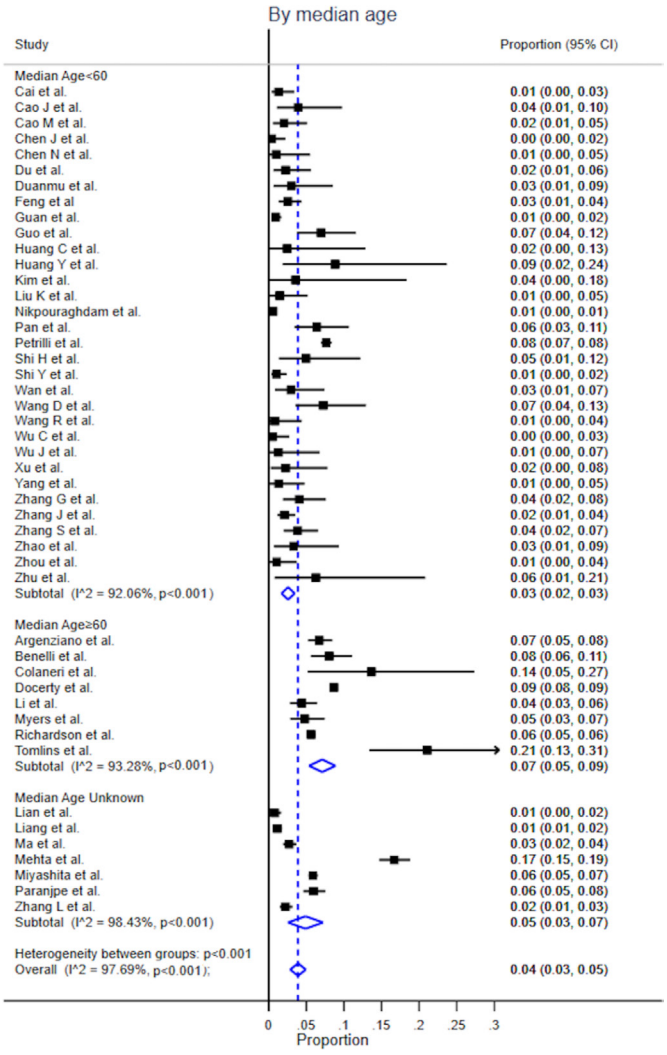

Figure 3 Random effects pooled proportion of patients with cancer among total patients diagnosed with COVID-19 (subgroup by median/mean age ≥60 vs <60 years).

Proportion of cancer diagnoses

The overall pooled proportion of cancer diagnoses among COVID-19 patients from 47 studies was 0.04 (95% CI 0.03 to 0.05) with significant heterogeneity among the included studies, I^2=97.69%, $\chi 2$ p≤0.001 (figure 2). The proportion of patients with cancer was significantly lower in the studies with median or mean age less than 60 years, at 0.03 (95% CI 0.02 to 0.03) compared with 0.07 (95% CI 0.05 to 0.09) for studies with median or mean age above or equal 60 years (figure 3). The proportion of cancer was higher in the studies with male predominance (more than or at least 60% population being male), at 0.05 (95% CI 0.02 to 0.07) than studies with less than 60% population being male, at 0.03 (95% CI 0.02 to 0.05; figure 4). The proportion of cancer in Hubei province was 0.03 (95% CI 0.02 to 0.05) and outside Hubei province 0.04 (95% CI 0.02 to 0.04; online supplemental appendix 3; figure 1).

Mortality outcomes of patients with cancer with COVID-19

Overall, the mortality rates of patients with cancer with COVID-19 infection ranged widely from 5.9% to 50% across 20 studies (table 3). The pooled RR of death was significantly higher in cancer patients with COVID-19 infection than in the general population with COVID-19 infection based on seven studies as shown in table 3 (RR 1.41; 95% CI 1.15 to 1.73), I^2=26.2%, χ^2 p=0.229 (figure 5A). The pooled mortality rate was estimated at 0.22 (95% CI 0.21 to 0.33) among patients with cancer with COVID-19, which was significantly higher than that of the overall COVID-19 patients, at 0.09 (95% CI 0.07 to 0.11; online supplemental appendix 3; figure 2A–C).

Severity outcomes of patients with cancer with COVID-19

Further analyses were conducted for the 10 case series with available severity outcomes for both cancer and general COVID-19 patient cohorts. We found that patients with cancer had higher risk of severe COVID-19 outcomes compared with the general COVID-19 population, with a pooled RR of 1.49 (95% CI 1.18 to 1.87) and substantial heterogeneity, I^2=66.7%, χ^2 p=0.001 (figure 5B). Also, we noted that the pooled proportion of severe outcomes in patients with cancer was 0.42 (95% CI 0.30 to 0.54), which was higher than the proportion of severe cases of all COVID-19 patients at 0.27 (95% CI 0.21

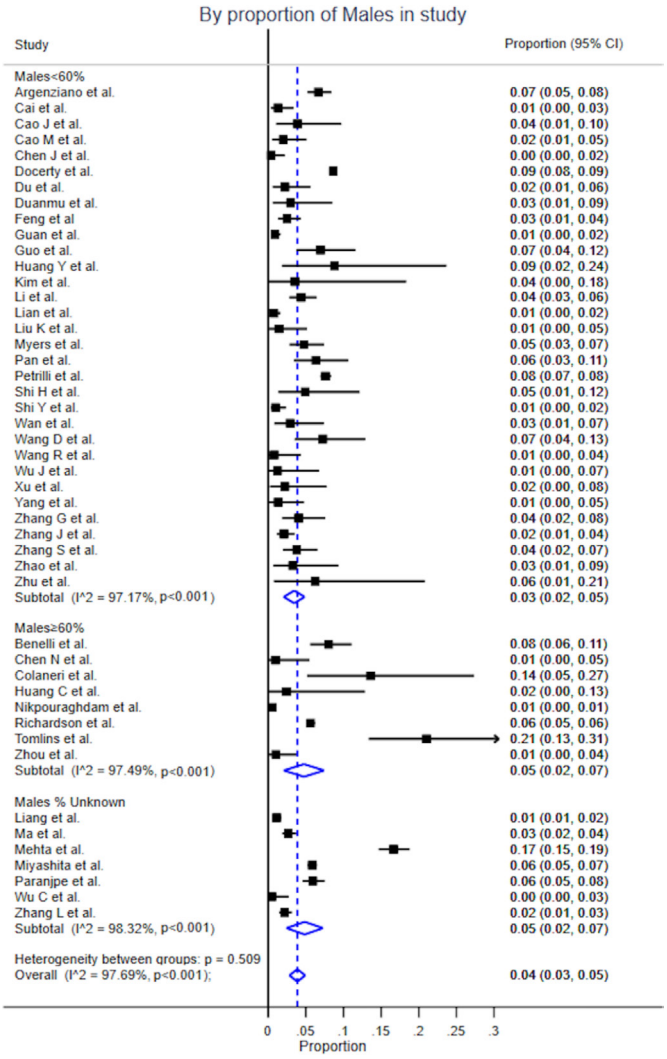

Figure 4 Random effects pooled proportion of patients with cancer among total patients diagnosed with COVID-19 (subgroup by male ≥60% or <60%).

to 0.33; online supplemental appendix 3; figure 3A–C). There was no statistically significant difference in RR of severe outcomes between those patients (available data from five studies identified) with lung cancers vs non lung cancers (RR at 1.46; 95% CI 1.84 to 2.52, I^2=48.1%, χ^2 p=0.7; figure 6A). There was no statistically significant difference in RR of severe outcomes between stage IV vs non stage IV cancers from four studies identified (RR 1.48; 95% CI 0.89 to 2.47; figure 6B, online supplemental figure 4).

The severe outcomes of COVID-19 in patients with cancer was also analysed from the available 230 IPD and summarised in online supplemental table 1. Only patient age and gender appeared to be significantly associated with severity outcomes by χ^2 test (online supplemental table 2).

DISCUSSION

We performed a systematic review and MA to elucidate the proportion of cancer diagnoses among COVID-19 patients, and whether patients with cancer had more severe outcomes compared with the general population. We also looked at the patient characteristics that may be associated with severe clinical outcomes among these patients. To our knowledge, this is the largest MA that directly addresses the clinical outcomes of COVID-19 patients with cancer, including the RR of severity and death as compared with general COVID-19 patients.

First, we found that the pooled proportion of patients with cancer among COVID-19 cases was 4%. This result was similar to the proportion rate from an earlier MA[9] of 11 studies with a proportion of 2%, but higher than the 0.2% described by the Chinese Centre for Disease Control and Prevention Group.[2] We found that the cancer proportion was higher among older patients and in male patients with COVID-19. In the subsequent IPD analysis, it was also advanced age and male gender that were significantly associated with severity of COVID-19 infection. We also noted that the cancer proportion among the COVID-19 case series from Hubei province was 3% (online supplemental appendix 3; figure 1), which was higher than the estimated cancer prevalence of 0.45% in the region.[10] However, cancer proportion can vary across geographical locations and specialist medical centres.

We have shown that COVID-19 patients with cancer had significantly more severe outcomes compared with the general COVID-19 patients, with a pooled RR of 1.49 (95% CI 1.18 to 1.87, p=0.001). The pooled estimated proportion of severe COVID-19 outcomes was higher among patients with cancer in our MA compared with the largest cancer cohort data (CCC19).[11] Overall, the proportion of patients with cancer with severe COVID-19 outcomes varied across studies but remained high, highlighting the vulnerability of patients with cancer to SARS-CoV-2 infection.

We also observed that lung cancer was the most common cancer among those affected by COVID-19 in Chinese studies (table 2) and this may be due to the fact that lung cancer is the most common cancer in China, rather than a direct relation to the risk of COVID-19 infection.[12] A few case series noted that patients with lung cancers had significantly worse outcomes compared with non-lung cancer cohorts,[8 13] which was also supported by data from TERAVOLT,[14] an international database of thoracic cancers (not included in our MA as it is a single tumour registry). TERAVOLT demonstrated 33% mortality and high morbidity among patients with thoracic malignancies, but with low ICU admission rates, presumably partly due to resource allocations and patient prognosis. However, in our MA, we did not find the RR of severity to be significant for lung cancers (vs other tumour types) or stage IV cancers (vs stage I–III) across four studies. This was also echoed by our IPD analysis, where lung cancer and the stage of cancer were not significantly associated with severe outcomes. This could reflect that lung cancer or stage IV cancer did not necessarily confer a higher risk of severe COVID-19 infection, but given the small number of included studies for this part of the analysis, this conclusion should be cautiously interpreted.

Separately, haematological cancers also showed severe outcomes with high mortality rates in multiple cohort

Table 3 Mortality rate among patients with cancer diagnosed with COVID-19 infection*

Case series	Death/cancer population	Mortality rate in cancer cohorts (%)	Death/total COVID-19 population	Mortality rate in general COVID-19 cohorts (%)	Relative risk of death (95% CI)
Liang *et al*[10]	9/18	50.0	N.A	N.A.	N.A
Zhang *et al*[13]	8/28	28.6	N.A	N.A	N.A
Yu *et al*[19]	3/12	25	N.A	N.A	N.A
Ma *et al*[53]	5/37	13.5	N.A	N.A.	N.A
Zhang *et al*[73]	18/67	26.9	N.A	N.A	N.A
Dai *et al*[8]	12/105	11.4	N.A	N.A	N.A
Kuderer *et al*[11]	121/928	13.0	N.A	N.A	N.A
Lee *et al*[16]	226/800	28.3	N.A	N.A	N.A
Robilotti *et al*[60]	51/423	12.1	N.A	N.A	N.A
Assaad *et al*[32]	30/302	9.9	N.A	N.A	N.A
Pinato *et al*[59]	299/890	33.6	N.A	N.A	N.A
Yang *et al*[70]	40/205	19.5	N.A	N.A	N.A
Yarza *et al*[72]	16/63	25.4	N.A	N.A	N.A
Benelli *et al*[33]	9/33	27.3	72/411	17.5	1.56 (0.86 to 2.82)
Mehta *et al*[17]	61/218	28.0	210/1308	16.1	1.74 (1.36 to 2.23)
Miyashita *et al*[3]	37/334	11.1	555/5688	9.8	1.14 (0.83 to 1.55)
Nikpouraghdam *et al*[55]	1/17	5.9	239/2964	8.1	0.73 (0.11 to 4.90)
Paranjpe *et al*[57]	24/64	37.5	310/1078	28.8	1.30 (0.94 to 1.81)
Tomlins *et al*[64]	3/20	15.0	20/95	21.1	0.71 (0.23 to 2.17)
Zhang *et al*[74]	4/12	33.3	47/315	14.9	2.23 (0.96 to 5.19)

*Only papers with at least 10 patients with cancer were included.
N.A, not available.

studies.[8 15] The available individual data in our study were not large enough to analyse the influence of modality of systemic treatment (targeted therapy, immunotherapy or chemotherapy), surgery or radiotherapy on the outcome of COVID-19 infections. Recent studies did not consistently find active systemic therapy to be associated with risk of severe COVID-19 infection[16] though some studies suggest that patients on recent chemotherapy[10] or immunotherapy[8] were at higher risk. These questions remain unanswered and require further collaborative efforts to identify risk factors of severe COVID-19 infection among patients with cancer. One suggestion is to have standardised reporting format for cancer COVID-19 cohorts including specific tumour type, stage, date of last chemotherapy or systemic treatment, comorbidities, active versus past cancer diagnosis and also the severity and mortality data for each subgroup.

Overall, the pooled RR of death among the patients with cancer was 1.41 (95% CI 1.15 to 1.73), compared with general COVID-19 patients. However, pooled mortality risk of patients with cancer with COVID-19 should be interpreted with caution due to the limited sample size. Some case series also had patients who remained hospitalised or with incomplete patient outcome at the time of reporting. CFR were lower at 5.6% among cancer COVID-19 patients in a large Chinese report[2] and 11.1% from a tertiary centre in New York, USA.[3] Notably, among selected COVID-19 mortality reports from Italy and USA, around 20%–30% of deaths had a history of cancer.[17 18] We would encourage mortality data to be taken from database reports instead of small case series from single centres.

In light of the severity of COVID-19 in patients with cancer-patients with cancer, efforts should be undertaken to reduce nosocomial exposure in patients with cancer, as nosocomial infections may contribute to incidence of COVID-19 in oncology patients.[19] The decision to attend clinics and continue non-urgent systemic therapy should be made judiciously, especially in regions with high burden of disease transmission. This has been echoed by various oncology bodies, including American Society of Clinical Oncology and European Society of Medical Oncology.[20] Given the higher risk of severe outcomes and mortality among patients with cancer, it is important that patients with cancer with COVID-19 infection should be monitored closely and decisions for ICU support discussed early. ICU outcomes should also be an important question for future retrospective studies in view of the ethical and clinical considerations of putting patients with advanced cancer on mechanical ventilation, especially in countries with significant outbreak and limited ICU resources. In light of the recent advances in COVID-19 vaccine efforts, another area of active discussion is that of the risk and benefit of vaccination for patients with cancer, especially those who are deemed to be significantly immunocompromised. Our data shows that there is risk of severe COVID-19 infection and risk of death among patients with cancer compared with general population. Hence, this factor should be strongly considered in the individualised decision for vaccination.

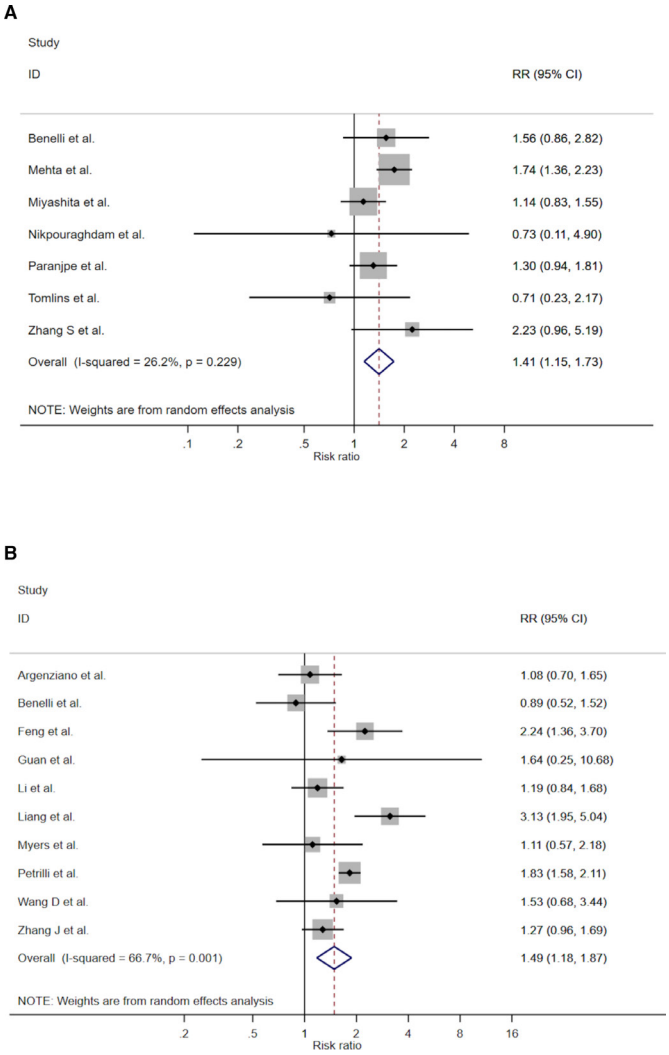

Figure 5 (A) Random effects pooled relative risk (RR) of death for cancer COVID-19 patients versus total population of COVID-19 patients. (B) Random effects pooled RR for severe outcome of cancer COVID-19 patients versus total population of COVID-19 patients.

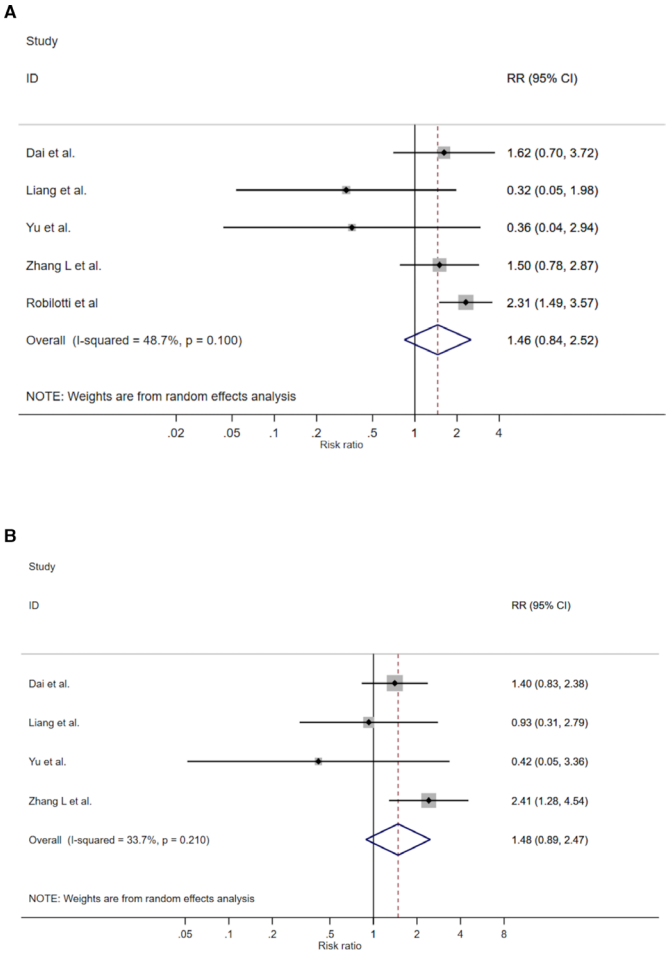

Figure 6 (A) Random effects pooled relative risk (RR) for severe outcome of lung cancer versus other patients with cancer infected with COVID-19. (B) Random effects pooled RR for severe outcome of patients with stage IV cancer vs non-stage IV cancer infected with COVID-19.

The limitations of this MA include the heterogeneity and retrospective nature of the case studies, including reporting and selection biases. A few studies were reported from the same hospitals and hence there may be overlapping patients although efforts were taken to reduce this. During screening of papers by the authors, we have ensured that the analysed studies were not reported from the same hospital during the same period of admission (online supplemental appendix 2; table 1). The small numbers and incomplete death outcomes at the time of reporting also restricted our mortality analysis. Due to the limited clinical data, we could not adjust for co-morbidities and other characteristics that may contribute to severe disease. It should also be noted that severity outcomes were defined inconsistently across some studies but efforts were taken to indicate the different definitions in table 1. Of note, some earlier studies also included clinically diagnosed COVID-19 cases.

While we acknowledge other risk factors such as age,[21–23] gender,[24] cardiovascular risk factors[23 25 26] including diabetes mellitus[27 28] and hypertension[29] remain important in COVID-19 infection, this is the largest MA to show that malignancy is also a significant risk factor for severe disease and mortality. However, we did not identify other tumour or treatment-related factors associated with severe outcomes among patients with cancer with COVID-19. We also did not stratify for gender, age and comorbidities in our analysis due to limited available data for pooled analysis on severity and mortality. As more data becomes available in the literature, further analyses may be performed to discern the clinical outcomes of patients with cancer with COVID-19 infection, with specific attention to underlying lung cancers, haematological cancers and the effects of various systemic therapies or other treatment modalities. CCC19, UKCCMP (Coronavirus Cancer Monitoring Project UK) and TERAVOLT are some examples of collaborative efforts on the outcomes of patients with cancer with COVID-19 infection, though a limitation is that there is a lack of comparison against general population. Information on COVID-19 patients with cancer should also be collected in more detail and with consistency across studies, to allow further meta-analyses to ascertain the outcomes of patients with cancer with COVID-19 infection.

CONCLUSION

Given that COVID-19 may persist in the foreseeable future, it is imperative to continue active research and data collection on the effect of SARS-CoV-2 on oncology patients. Due to the clinical burden of their disease, oncology patients will continue to require systemic chemotherapy and urgent care at medical centres.[30] As such, treating physicians need to be able to make more discerning decisions on the choice of systemic treatment and escalation of care.

Overall, we found through MA that the severity and mortality rates of COVID-19 in patients with cancer were higher than that in the general population. However, the dataset remains small and should be interpreted with caution. We hope that with collaborative efforts, comprehensive patient outcomes of COVID-19 patients, and specifically, of patients with cancer, can be collated to better understand the disease trajectory and outcomes of COVID-19.

Author affiliations
[1]Division of Medical Oncology, National Cancer Centre Singapore, Singapore
[2]Division of Supportive and Palliative Care, National Cancer Centre Singapore, Singapore
[3]Biostatistics and Epidemiology Unit, National Cancer Centre Singapore, Singapore
[4]Division of Radiation Oncology, National Cancer Centre Singapore, Singapore
[5]Department of Radiation and Medical Oncology, Wuhan University Zhongnan Hospital, Wuhan, Hubei, China
[6]Department of Radiation Oncology, National University Cancer Institute, Singapore

Twitter Melvin L K Chua @DrMLChua

Contributors SH and VSY conceived the idea of the study. SH, VSY and QZ contributed to data collection. SHT, SH and YYS contributed to data analysis. SH, QZ, JC, GWYC and VSY contributed to the manuscript writing. MLKC and CX contributed to clinical data. MLKC, YYS and VSY provided guidance. YYS and VSY are joint last authors. SH is responsible for the overall content as the guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as online supplemental information. Data are available in a public, open access repository.

ORCID iDs
Shuting Han http://orcid.org/0000-0002-0217-7956
Conghua Xie http://orcid.org/0000-0001-6623-9864
Melvin L K Chua http://orcid.org/0000-0002-1648-1473

REFERENCES

1 Dai M, Liu D, Liu M, *et al*. Patients with cancer appear more vulnerable to SARS-CoV-2: a multicenter study during the COVID-19 outbreak. *Cancer Discov* 2020;10:783–91.
2 Wu Z, McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020;323:1239–42.
3 Miyashita H, Mikami T, Chopra N, *et al*. Do patients with cancer have a poorer prognosis of COVID-19? an experience in New York City. *Ann Oncol* 2020;31:1088–9.
4 Joharatnam-Hogan N, Hochhauser D, Shiu K-K, *et al*. Outcomes of the 2019 novel coronavirus in patients with or without a history of cancer: a multi-centre North London experience. *Ther Adv Med Oncol* 2020;12:1758835920956803.
5 Jee J, Foote MB, Lumish M, *et al*. Chemotherapy and COVID-19 outcomes in patients with cancer. *J Clin Oncol* 2020;38:3538–46.
6 Park R, Lee SA, Kim SY, *et al*. Association of active oncologic treatment and risk of death in cancer patients with COVID-19: a systematic review and meta-analysis of patient data. *Acta Oncol* 2021;60:13–19.
7 Yekedüz E, Utkan G, Ürün Y. A systematic review and meta-analysis: the effect of active cancer treatment on severity of COVID-19. *Eur J Cancer* 2020;141:92–104.
8 Dai M, Liu D, Liu M, *et al*. Patients with cancer appear more vulnerable to SARS-CoV-2: a multicenter study during the COVID-19 outbreak. *SSRN Electron J* 2020
9 Desai A, Sachdeva S, Parekh T, *et al*. Covid-19 and cancer: lessons from a pooled meta-analysis. *JCO Glob Oncol* 2020;6:557–9.
10 Liang W, Guan W, Chen R, *et al*. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol* 2020;21:335–7.
11 Kuderer NM, Choueiri TK, Shah DP, *et al*. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet* 2020;6736:1–13.
12 Cao M, Chen W. Epidemiology of lung cancer in China. *Thorac Cancer* 2019;10:3–7.
13 Zhang L, Zhu F, Xie L, *et al*. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Ann Oncol* 2020;31:894–901.
14 Garassino MC, Whisenant JG, Huang L-C, *et al*. COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. *Lancet Oncol* 2020;21:914–22.
15 He W, Chen L, Chen L, *et al*. COVID-19 in persons with haematological cancers. *Leukemia* 2020;34:1637–45.
16 Lee LYW, Cazier JB, Starkey T. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments : a prospective cohort study. *Lancet* 2020;395:P1919–26.
17 Mehta V, Goel S, Kabarriti R, *et al*. Case fatality rate of cancer patients with COVID-19 in a new York hospital system. *Cancer Discov* 2020;10:935–41.
18 Onder G, Rezza G, Brusaferro S. Case-Fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA* 2020;323:1775–6.
19 Yu J, Ouyang W, Chua MLK, *et al*. SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China. *JAMA Oncol* 2020;6:1108.
20 Banna G, Curioni-Fontecedro A, Friedlaender A, *et al*. How we treat patients with lung cancer during the SARS-CoV-2 pandemic: *primum non nocere*. *ESMO Open* 2020;5:e000765.
21 Wu C, Chen X, Cai Y, *et al*. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med* 2020;180:934–43.
22 Centers for Disease Control and Prevention. People who are at higher risk for severe illness | CDC. *Centers Dis Control Prev* 2020.
23 Yang J, Zheng Y, Gou X. Prevalence of comorbidities and its effects in coronavirus disease 2019 patients: a systematic review and meta-analysis. *Int J Infect Dis* 2020;94:91–5.
24 Cai H. Sex difference and smoking predisposition in patients with COVID-19. *Lancet Respir Med* 2020;8:e20.
25 CDC COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019 - United States, February 12-March 28, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:382–6.
26 Li B, Yang J, Zhao F, *et al*. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol* 2020;109:531–8.
27 Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia

– a systematic review, meta-analysis, and meta-regression. *Diabetes Metab Syndr* 2020;14:395–403.
28 Hu Y, Sun J, Dai Z, *et al*. Prevalence and severity of corona virus disease 2019 (COVID-19): a systematic review and meta-analysis. *J Clin Virol* 2020;127:104371.
29 Li L-Q, Huang T, Wang Y-Q, *et al*. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. *J Med Virol* 2020;92:577–83.
30 Xu Y, Liu H, Hu K, *et al*. [Clinical management of lung cancer patients during the outbreak of 2019 novel coronavirus disease (Covid-19). *Zhongguo Fei Ai Za Zhi* 2020;23:136–41.
31 Argenziano MG, Bruce SL, Slater CL, *et al*. Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: retrospective case series. *BMJ* 2020;34:m1996.
32 Assaad S, Avrillon V, Fournier M-L, *et al*. High mortality rate in cancer patients with symptoms of COVID-19 with or without detectable SARS-COV-2 on RT-PCR. *Eur J Cancer* 2020;135:251–9.
33 Benelli G, Buscarini E, Canetta C. SARS-COV-2 comorbidity network and outcome in hospitalized patients in Crema, Italy. *PLoS One* 2020;16:e0248498.
34 Cai Q, Huang D, Ou P, *et al*. COVID-19 in a designated infectious diseases hospital outside Hubei Province, China. *Allergy* 2020;75:1742–52.
35 Cao J, Tu W-J, Cheng W, *et al*. Clinical features and short-term outcomes of 102 patients with coronavirus disease 2019 in Wuhan, China. *Clin Infect Dis* 2020;71:748–55.
36 Chen J, Qi T, Liu L, *et al*. Clinical progression of patients with COVID-19 in Shanghai, China. *J Infect* 2020;80:e1–6.
37 Chen N, Zhou M, Dong X, *et al*. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507–13.
38 Colaneri M, Sacchi P, Zuccaro V, *et al*. Clinical characteristics of coronavirus disease (COVID-19) early findings from a teaching hospital in Pavia, North Italy, 21 to 28 February 2020. *Euro Surveill* 2020;25.
39 Docherty AB, Harrison EM, Green CA, *et al*. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ* 2020;369:m1985.
40 Du R-H, Liang L-R, Yang C-Q, *et al*. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. *Eur Respir J* 2020;55:2000524.
41 Duanmu Y, Brown IP, Gibb WR, *et al*. Characteristics of emergency department patients with COVID-19 at a single site in northern California: clinical observations and public health implications. *Acad Emerg Med* 2020;27:505–9.
42 Feng Y, Ling Y, Bai T, *et al*. COVID-19 with different severities: a multicenter study of clinical features. *Am J Respir Crit Care Med* 2020;201:1380–8.
43 Guan W-J, Ni Z-Y, Hu Y, *et al*. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020;382:1708–20.
44 Guo T, Fan Y, Chen M, *et al*. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020;5:811.
45 Huang C, Wang Y, Li X, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497–506.
46 Huang Y, Tu M, Wang S, *et al*. Clinical characteristics of laboratory confirmed positive cases of SARS-CoV-2 infection in Wuhan, China: a retrospective single center analysis. *Travel Med Infect Dis* 2020;36:101606.
47 Kim ES, Chin BS, Kang CK, *et al*. Clinical course and outcomes of patients with severe acute respiratory syndrome coronavirus 2 infection: a preliminary report of the first 28 patients from the Korean cohort study on COVID-19. *J Korean Med Sci* 2020;35:e142.
48 Kuderer NM, Choueiri TK, Shah DP, *et al*. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet* 2020;395:1907–18.
49 Lee LYW, Cazier J-B, Starkey T, *et al*. COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study. *Lancet Oncol* 2020;21:1309–16.
50 Li X, Xu S, Yu M, *et al*. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *J Allergy Clin Immunol* 2020;146:110–8.
51 Lian J, Jin X, Hao S, *et al*. Analysis of epidemiological and clinical features in older patients with coronavirus disease 2019 (COVID-19) outside Wuhan. *Clin Infect Dis* 2020;71:740–7.
52 Liu K, Fang Y-Y, Deng Y, *et al*. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chin Med J* 2020;133:1025–31.
53 Ma J, Yin J, Qian Y, *et al*. Clinical characteristics and prognosis in cancer patients with COVID-19: a single center's retrospective study. *J Infect* 2020;81:318–56.
54 Myers LC, Parodi SM, Escobar GJ, *et al*. Characteristics of hospitalized adults with COVID-19 in an integrated health care system in California. *JAMA* 2020;323:2195.
55 Nikpouraghdam M, Jalali Farahani A, Alishiri G, *et al*. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in Iran: a single center study. *J Clin Virol* 2020;127:104378.
56 Pan L, Mu M, Yang P, *et al*. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. *Am J Gastroenterol* 2020;115:766–73.
57 Paranjpe I, Russak A, De FJK. Clinical characteristics of hospitalized Covid-19 patients in New York City. *medRxiv* 2020.
58 Petrilli CM, Jones SA, Yang J, *et al*. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ* 2020;369:m1966.
59 Pinato DJ, Zambelli A, Aguilar-Company J, *et al*. Clinical portrait of the SARS-CoV-2 epidemic in European patients with cancer. *Cancer Discov* 2020;10:1465–74.
60 Robilotti EV, Babady NE, Mead PA, *et al*. Determinants of COVID-19 disease severity in patients with cancer. *Nat Med* 2020;26:1218–23.
61 Richardson S, Hirsch JS, Narasimhan M, *et al*. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the new York City area. *JAMA* 2020;323:2052–9.
62 Shi H, Han X, Jiang N, *et al*. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis* 2020;20:425–34.
63 Shi Y, Yu X, Zhao H, *et al*. Host susceptibility to severe COVID-19 and establishment of a host risk score: findings of 487 cases outside Wuhan. *Crit Care* 2020;24:108.
64 Tomlins J, Hamilton F, Gunning S, *et al*. Clinical features of 95 sequential hospitalised patients with novel coronavirus 2019 disease (COVID-19), the first UK cohort. *J Infect* 2020;81:e59–61.
65 Wan S, Xiang Y, Fang W, *et al*. Clinical features and treatment of COVID-19 patients in northeast Chongqing. *J Med Virol* 2020;92:797–806.
66 Wang D, Hu B, Hu C, *et al*. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020;323:1061–9.
67 Wang R, Pan M, Zhang X, *et al*. Epidemiological and clinical features of 125 hospitalized patients with COVID-19 in Fuyang, Anhui, China. *Int J Infect Dis* 2020;95:421–8.
68 Wu J, Liu J, Zhao X, *et al*. Clinical characteristics of imported cases of coronavirus disease 2019 (COVID-19) in Jiangsu Province: a multicenter descriptive study. *Clin Infect Dis* 2020;71:706–12.
69 Xu X, Yu C, Qu J, *et al*. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2. *Eur J Nucl Med Mol Imaging* 2020;47:1275–80.
70 Yang W, Cao Q, Qin L, *et al*. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19):A multi-center study in Wenzhou city, Zhejiang, China. *J Infect* 2020;80:388–93.
71 Yang K, Sheng Y, Huang C, *et al*. Clinical characteristics, outcomes, and risk factors for mortality in patients with cancer and COVID-19 in Hubei, China: a multicentre, retrospective, cohort study. *Lancet Oncol* 2020;21:904–13.
72 Yarza R, Bover M, Paredes D, *et al*. SARS-CoV-2 infection in cancer patients undergoing active treatment: analysis of clinical features and predictive factors for severe respiratory failure and death. *Eur J Cancer* 2020;135:242–50.
73 Zhang G-qin, Hu C, Luo L-jie, *et al*. Clinical features and treatment of 221 patients with COVID-19 in Wuhan, China. *SSRN Journal* 2020.
74 Zhang J, Wang X, Jia X, *et al*. Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China. *Clin Microbiol Infect* 2020;26:767–72.
75 Zhao X-Y, Xu X-X, Yin H-S, *et al*. Clinical characteristics of patients with 2019 coronavirus disease in a non-Wuhan area of Hubei Province, China: a retrospective study. *BMC Infect Dis* 2020;20.
76 Zhou F, Yu T, Du R, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054–62.
77 Zhu W, Xie K, Lu H, *et al*. Initial clinical features of suspected coronavirus disease 2019 in two emergency departments outside of Hubei, China. *J Med Virol* 2020;92:1525–32.