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Prevalence and risks of severe events for cancer patients with COVID-19 infection: a systematic review and meta-analysis

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Summary

Background

The corona virus disease 2019 (COVID-19) pandemic poses a severe challenge to public health, especially to those patients with underlying diseases. In this meta-analysis, we studied the prevalence of cancer among patients with COVID-19 infection and their risks of severe events.

Methods

We searched the Pubmed, Embase and MedRxiv databases for studies between December 2019 and May 3, 2020 using the following key words and terms: sars-cov-2, covid-19, 2019-ncov, 2019 novel coronavirus, corona virus disease-2019, clinical, clinical characteristics, clinical course, epidemiologic features, epidemiology, and epidemiological characteristics. We extracted data following PICO (patient, intervention, comparison and outcome) chart. Statistical analyses were performed with R Studio (version 3.5.1) on the group-level data. We assessed the studies' risk of bias in accordance to the adjusted Joanna Briggs Institute. We estimated the prevalence or risks for severe events including admission into intensive care unit or death using meta-analysis with random effects.

Findings

Out of the 2,551 studies identified, 32 studies comprising 21,248 participants have confirmed COVID-19. The total prevalence of cancer in COVID-19 patients was 3.97% (95% CI, 3.08% to 5.12%), higher than that of the total cancer rate (0.29%) in China. Stratification analysis showed that the overall cancer prevalence of COVID-19 patients in China was 2.59% (95% CI, 1.72% to 3.90%), and the prevalence reached 3.79% in Wuhan (95% CI, 2.51% to 5.70%) and 2.31% (95% CI, 1.16% to 4.57%) in other areas outside Wuhan in China. The incidence of ICU admission in cancer patients with COVID-19 was 26.80% (95% CI, 21.65% to 32.67%) and the mortality was 24.32% (95% CI, 13.95% to 38.91%), much higher than the overall rates of COVID-19 patients in China. The fatality in COVID patients with cancer was lower than those with cardiovascular disease (OR 0.49; 95% CI, 0.34 to 0.71; p=0.39), but comparable with other comorbidities such as diabetes (OR 1.32; 95% CI, 0.42 to 4.11; p=0.19), hypertension (OR 1.27; 95% CI, 0.35 to 4.62; p=0.13), and respiratory diseases (OR 0.79; 95% CI, 0.47 to 1.33; p=0.45).

Interpretation

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This comprehensive meta-analysis on the largest number of patients to date provides solid evidence that COVID-19 infection significantly and negatively affected the disease course and prognosis of cancer patients. Awareness of this could help guide clinicians and health policy makers in combating cancer in the context of COVID-19 pandemic.

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Key words：COVID-19; Cancer; Prevalence; Fatality; Meta-analysis

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Introduction

The pandemic of severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) has caused 4,794,932 confirmed cases and 316,420 deaths globally by May 7, 2020, affecting almost all the countries in the world.[1] WHO announced COVID-19 as a public health emergency of international concern on January 30, 2020. Most COVID-19 cases experience mild to moderate respiratory symptoms or signs such as fever and cough, and will recover without special treatment. Unfortunately, the elder people, and those suffering underlying medical conditions such as cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop into more serious conditions, including multiple organ dysfunction syndrome or even death.[2-4]

Cancer is a major public health problem worldwide and is the second leading cause of death in the United States. Recent research had shown that there were about 24.5 million cancer cases worldwide and 9.6 million cancer deaths in 2017. In 2020, the number of new cancer cases and cancer related death is estimated to reach1,806,590 and 606,520 in the US, respectively.[5]Cancer patients are more susceptible to infections than those without cancer due to the systemic immunosuppression caused by the malignancy itself or anticancer treatments, such as chemo-radiation. [6-9] Therefore, it is conceivable that cancer patients are at higher risk of COVID-19 infection. Moreover, unplanned interruptions of regular anti-tumor therapies, due to the overloaded healthcare systems in the pandemic battle, expose cancer patients' adverse clinical risks of uncontrolled primary disease. Furthermore, some tumor markers such as CEA, CA-125 can be elevated and positively correlated with the pathological progression of COVID-19 infection, which may increase the cancer detection rate. [10]

The relationship between cancer and COVID-19 has drawn great attention from the beginning of the pandemic. An early study by Liang et al reported a cancer prevalence of 1.13% (95% CI, 0.61% to 1.65%) among 1,590 cases of COVID-19 in China (only 18 patients with cancer), which was higher compared with the overall cancer incidence of 0.29% in the Chinese population.[11] More importantly, cancer patients with COVID-19 had a higher risk of severe events (a composite end point defined as the percentage of patients who were admitted to the intensive care unit

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(ICU) and required invasive ventilation or who died) compared with those COVID-19 patients without cancer (39% v 8%, HR: 5.34; 95%CI, 1.80 to 16.18; P = 0.0026). A pooled meta-analysis by Aakash Desai indicated that prevalence of cancer in COVID-19 patients was 2.0% (95% CI, 2.0% to 3.0%; I2 = 83.2%), while the prevalence was 3.0% (95% CI, 1.0% to 6.0%) in studies with a sample size smaller than 100, and 2.0% (95% CI, 1.0% to 3.0%) in studies with a sample size not smaller than 100.[12] To guide clinical management and appropriate medical resources allocation, it is necessary to validate the relationship of cancer and COVID-19 in a much larger international scale. In the current study, we performed a meta-analysis of 21,248 participants in 32 clinical studies across six countries (China, Japan, Korea, Italy, France, USA)[11,13-43]to exploit the prevalence of cancer in COVID-19 patients as well as risks of severe events including ICU admission and death of these patients.

Methods

Search Methods and Study Selection

We searched Pubmed, Embase and MedRxiv databases for studies according to the following key words and terms: sars-cov-2, covid-19, 2019-ncov, 2019 novel coronavirus, Corona Virus Disease-2019, clinical, clinical characteristics, clinical course, epidemiologic features, epidemiology, epidemiological characteristics. The following data from all relevant studies between December 2019 and May, 2020 were included in our meta-analysis: (1) the study subjects were patients with confirmed diagnosis of SARS-CoV-2 viral infection, based on the detection of the viral nucleic acid by reverse transcription quantitative PCR (RT-qPCR) assay; (2) the results included age, sex, epidemiology and cancer information; (3) study types include cohort studies and clinical trials; (4) restriction of language to English only. Animal studies, systematic reviews, case reports, and) small studies of fewer than 10 patients were excluded. This study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline.[44] (eTable 1)

Data extraction

The two authors (Q.S and JX.H) independently extracted the data by checking the titles, abstracts and full text. We then assessed the eligibility of the extracted studies using the PICO (patient, intervention, comparison and outcome) chart. Disagreements in the assessment were resolved via discussion with the third reviewer

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(CG.Z).[45] Finally, they extracted the following information from all eligible studies: the first author, study period, district, gender, age, diagnosis methods, the number of total patients, the number of cancer patients, serious events, death toll, the number of comorbidities, and death toll of comorbidities.

Data analysis

Statistical analyses were performed using R's META package in R Studio (version 3.5.1). We focused on the following parameters in COVID-19 patients: the cancer prevalence, the ICU admission rate, and the cancer mortality. Different subgroups of patient population with cancer were compared. The prevalence for cancer in COVID-19 patients was expressed as percentage with 95% confidence interval (95% Cis). Odds ratio (OR) was used to estimate the -risks of ICU admission and death of cancer patients with COVID-19 compared with those suffering other comorbidities including cardiovascular diseases, diabetes, hypertension or non-cancer patients with COVID-19. Heterogeneity was evaluated using the Q test and Higgin's and Thompson's I2 (I2) statistics. Defined as the percentage of variations in the effect sizes that is not the cause of sampling errors, I2 statistics is robust and not sensitive to the number of studies under analysis. We consider I2 value of over 50% as moderate to high heterogeneity. $P<0.05$ was considered statistically significant. We used random-effects model if the I^2 value was more than 50%. We also performed a multi-group subgroup analysis to explore the source of heterogeneity. Specifically, subgroup design was based on the sample size (smaller or greater than 100), and the area of the patients (China/Outside China; Japan/Korea/Italy/France/USA). The quality of the included studies was assessed by the Joanna Briggs Institute (JBI),[46]and we slightly modified the table to make it adapt with selected studies (eFigure 1). We also conducted sensitivity analysis by sequentially removing individual studies one by one, and evaluating the stability of the results. Begger test and Egger test were used to evaluate publication bias, caused by possibly missing unpublished studies of low effect sizes. Finally, we developed a funnel plot to describe the results of publication bias.

Role of the funding source

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

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publication.

Results

Eligible Studies and Characteristics

Using our searching principles, we retrieved 2,551 studies from three databases between Dec 1st, 2019 and May 3rd, 2020, among which, 32 studies comprising 21,248 patients met our selection criteria (eTable 2). 22 of the 32 studies were mutually exclusive cohorts of patients in China (Wuhan n=13; outside of Wuhan n=5; unclear n=4), 2 studies based on cohorts of other Asian countries (Korean and Japan), and 8 studies were based in Europe and USA (Italy n=1; France n=1; USA n=6). The detailed research flow chart is shown in Figure 5, characteristics of the included studies are shown in Table 1, and data on severe events in patients with COVID-19 is shown in eTable3. Among the 21,248 patients in those 32 studies, valid data including basic information, epidemiological characteristics, clinical characteristics, prevalence and mortality of cancer or other complications were extracted from COVID-19 patients. All patients presented exhibited mild to severe clinical manifestations and were confirmed of COVID-19 infection RT-qPCR.

Result of meta-analyses

Prevalence of cancer in COVID-19 patients

We first analyzed the cancer prevalence rates in COVID-19 patients. As shown in Figure 1, the total prevalence of cancer in COVID-19 patients was 3.97% (95% CI, 3.08% to 5.12%), which is higher than the total cancer rate (0.29%) in China.

When analyzing in subgroups of different sample size, the prevalence showed some variation. The prevalence of cancer was 4.16% (95% CI, 2.80% to 6.14%) in the subgroup whose sample size was ≤100, and 3.99% (95% CI, 2.96% to 5.37%) in the subgroup whose sample size was >100 (Figure 2). This observation is consistent and comparable with the analysis by Aakash Desai.[12]

We then analyzed the cancer prevalence based on patients' geographic location. The overall cancer prevalence of COVID-19 patients was 2.59% (95% CI, 1.72% to 3.90%) in China, 3.85% (95% CI, 1.45% to 9.80%) in Japan, and 3.57% (95% CI, 0.50% to 21.42%) in Korea (Figure 1). The prevalence was higher in Italy and USA, which reached 11.35% (95% CI, 10.19% to 12.61%) and 6.09% (95% CI, 5.13% to 7.21%), respectively (Figure 1). Moreover, the cancer prevalence of COVID-19 patients in Wuhan was 3.79% (95% CI, 2.51% to 5.70%), higher than the average

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level of China (Figure 3).

Our analyses clearly showed that the cancer prevalence of COVID-19 patients was higher than that of the general population. In USA and European countries, the prevalence was higher than in China and other Asian countries. In China, the prevalence in Wuhan was higher than in other areas of China (Figure1 and 3).

Risk of severe events of cancer in COVID-19 patients

In China, the incidence of ICU admission in COVID19 patients with cancer was 38.77% (95% CI, 26.04% to 53.24%) (Figure 4). In Wuhan, the incidence of ICU admission and death in COVID19 patients with cancer were 42.80 (95% CI, 23.38 % to 64.72%) and 59.61% (95% CI, 28.86% to 84.30%) respectively. The incidence of ICU admission in COVID19 patients with cancer were 23.71% (95% CI, 18.41% to 29.99%) outside China, and the fatality reached 17.45% (95% CI, 11.92% to 24.83%) in Europe. The COVID19 patients in Wuhan apparently had a worse outcome than the rest of the China. Moreover, COVID-19 patients with cancer had a significantly higher ICU admission rate than those without cancer in China (OR 2.77; 95% CI, 1.28 to 6.00; p=0.46), and had overall higher fatality irrelative with areas (OR 4.87; 95% CI, 1.52 to 15.59; p=0.74/OR 3.97; 95% CI, 1.10 to 14.32; p=0.88) (eFigure 4). This may imply the existence of complex interrelationship between COVID-19 and cancer, where cancer was able to exaggerate COVID-19 infection and vice versa.

We further compared the rate of ICU admission rate and death of cancer with other underlying diseases in COVID-19 patients. As shown in eFigure 2, there was no significantly difference in the ICU admission rate of COVID 19 patients with cancer from COVID 19 patients with other comorbidities, including cardiovascular diseases (OR 0.89; 95% CI, 0.52 to 1.53; p=0.91), diabetes (OR 0.81; 95% CI, 0.48 to 1.37; p=0.85), hypertension (OR 0.88; 95% CI, 0.53 to 1.44; p=0.64), and respiratory disease (OR 0.65;95% CI, 0.37 to 1.15; p=0.45). Similarly, mortality rate of COVID 19 patients with cancer is close to COVID 19 patients with diabetes (OR 1.32; 95% CI, 0.42 to 4.11; p=0.39), hypertension (OR 1.27; 95% CI, 0.35 to 4.62; p=0.13), and respiratory diseases (OR 0.79; 95% CI, 0.47 to 1.33; p=0.45). Nevertheless, it is worth noting that COVID19 patients with cancer showed higher mortality rate than cardiovascular diseases (OR 0.49; 95% CI, 0.34 to 0.71; p=0.39) (eFigure 3).

Quality assessment and publication bias

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The quality of the included literature was satisfactory. Insufficient number of patients and incomplete coverage of the population were the main cause of low quality literature (eFigure 1), which we excluded. We performed sensitivity analysis of the included studies to assess their stability. After each study was excluded in turn, we found no significant difference in the results of the analysis (eTable 4,5). The funnel plot and Egger test results showed the risk of publication bias is low (p-value = 0.35) (eFigure 5).

The heterogeneity among our study subgroups was high. In the subgroup mortality analysis, the heterogeneity parameter I^2 were >50% in all subgroups except group IA (sample size ≤100). So, the random-effects model was deployed.

Discussion

A comprehensive analysis of cancer prevalence and severe events among patients with COVID-19 can serve as an important reference for oncology clinicians and healthcare policy makers. A few existing studies focused mainly on the prevalence analysis of cancer patients with COVID-19, lacking a comparison of the prevalence or risk for severe events among different areas. [11,12]We performed a systematic review on the prevalence of cancer and risks of severe events among patients with COVID-19 using a collection of sparse binomial data from published studies. To our knowledge, this is the largest and most comprehensive meta-analysis of the prevalence and fatality analysis of cancer among patients with COVID-19 to date.

In this study, we found that the total prevalence of cancer in COVID-19 patients was 3.97% (95% CI, 3.08% to 5.12%), which was significantly higher than that of the total cancer rate (0.29%) in China. [47]In other words, approximately 3 in 100 patients with COVID-19 had suffered from superimposed malignancy. The higher prevalence of cancer in COVID19 patients could be due to multiple factors. Firstly, caner is more common among senior patients, who are also susceptible to COVID19. Secondly, due to primary disease and the anticancer treatment, cancer patients are immune compromised, hence they are more vulnerable to viral infection. Thirdly, COVID19 infection has been shown to elevate the serum level of some cancer biomarkers such as CEA and CA19-9 etc., which may increase the cancer detection rate in this population.[10]

The cancer prevalence in COVID19 patients in the city of Wuhan was

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significantly higher than the rest of China. Meanwhile, it was significantly higher in European and American countries than in Asian countries. The geographical differences cannot be explained by factors like race or climate. It seems to be associated with overall incidence of COVID19 infection in those affected areas. Therefore, effective control of COVID19 infection, especially non-pharmaceutical interventions, could potentially reduce the cancer prevalence.[48]

In addition to the high prevalence, we found that nearly a third of cancer patients with COVID-19 experienced aggravated conditions and were admitted to ICU, which was apparently higher than total COVID-19 patients. Moreover, fatality in cancer patients with COVID-19 was about 24.32% (95% CI, 13.95% to 38.91%), also significantly higher than the rate of total patients with COVID-19 (about 3-7%).[49] Factors that affected cancer prevalence mentioned above might also explain the worse prognosis of cancer patients with COVID19. Firstly, individuals with cancer are generally older,[50] which has been shown to express higher levels of angiotensin-converting enzyme II (ACE2), a receptor for SARS-CoV-2 entry into the cell.[51] Secondly, cancer patients often suffer from immunosuppression, like lymphopenia, which often results in the impairment of the required immune response and may lead to viral propagation, tissue destruction, and progression to severe stages of the disease in ACE2-rich tissues .[52] Meanwhile, the overload in the hospitals may prevent timely and sufficient medical care for COVID19 patients with cancer, also leading to high fatality. Severe events are not only a major public health issue, but also a serious economic concern. Although health care personnel and resources were heavily allocated to ICU and treating severe cases, the outcomes were far from satisfactory. Thus, prevention of CoVID19 infection using strict quarantine and social distance measures is essential to protect cancer patients from worsening their health conditions.

The outcome of cancer patients with COVID19 was also compared with other morbidities, especially chronic diseases, which were thought as risk factors for severe event in patients with COVID-19. A meta-analysis by Yang et al showed that COVID-19 patients with hypertension, cardiovascular diseases and respiratory disease have higher risk for developing severe complications.[53] Du et al found that 61.9% patients with hypertension and 57.1% patients with cardiovascular or cerebrovascular diseases developed severe events.[54] Kang et al found that

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superimposed heart disease is the highest cause of death among all complications for COVID-19 patients. [55]From our analyses, the ICU admission rate for cancer patients with COVID19 was comparable with diabetes, hypertension, cardiovascular diseases and respiratory diseases. Meanwhile, the fatality of cancer patients with COVID19 was also similar with other chronic diseases above expect cardiovascular diseases. COVID19 patients with cardiovascular diseases showed higher mortality rate than cancer. Thus, cancer should become one of the notable superimposed comorbidities together with diabetes, cardiovascular and chronic respiratory diseases, contributing to COVID-19 infection and severe events.

Our findings are of values to both cancer patients and oncology clinicians in COVID-19 outbreak countries and territories. Future studies should rely on more detailed analyses. For example, the prevalence and risks of severe events can vary with different cancer types. A recent cohort study by Dai et al. indicated that COVID-19 patients in Wuhan with hematologic cancer had the highest frequency of severe events, which was followed by lung cancer, and patients with metastatic cancer hade much higher incidence of severe events than those with non-metastatic cancers. Moreover, cancer patients who had received surgery tended to have higher risks of severe events than other treatments except immunotherapy. [56] We anticipate further investigations on these issues in broader geographic and clinical settings.

Limitations

Our meta-analysis studied the cancer prevalence and risks of severe events in COVID-19 patients by accommodating fully reported and censored data from diverse literature. But this meta-analysis has limitations. Small-study effects were observed when studies with smaller sample sizes had different incidences and wider CIs for fatality in patients with COVID-19 and cancer. Although the forest plots showed no asymmetry favoring cancer fatality studies, this meta-analysis is subject to publication bias given that all of our analyses were based on publications. In addition, this study is subject to any biases or errors of the original investigators, and the results are generalizable only to patient groups with COVID-19. Meanwhile, it currently cannot summarize the prevalence or risk of severe events of different types of cancer in COVID-19 patients due to the lack of enough data.

Conclusions:

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In summary, using the largest dataset to date, our meta-analysis has clearly demonstrated that (1) there is higher prevalence of COVID19 infection in cancer patients, (2) when COVID19 infection occur in a patient with cancer, the patient is more likely to develop severe clinical events. Patients with chronic health conditions require more stringent preventive measures and more delicate therapeutic strategies during the COVID19 pandemic.

Author contributions

QS, JXH and EC. Z had access to all the data included in the study and are responsible for the completeness of the data and the accuracy of our analysis. JXH, HSL and ZZ helped to design the study. QS, DYW, and BWC contributed to the statistical analysis and the revision of this manuscript. ZHG and CGZ approved the final manuscript.

Declaration of interests

All other authors declare no competing interests.

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Reference

1. http://coronavirusstatistics.org/. .
2. Guan W, Liang W, Zhao Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J* 2020; **55**(5).
3. Jordan R, Adab P, Cheng K. Covid-19: risk factors for severe disease and death. *BMJ* 2020; **368**: m1198.
4. Chen R, Liang W, Jiang M, et al. Risk Factors of Fatal Outcome in Hospitalized Subjects With Coronavirus Disease 2019 From a Nationwide Analysis in China. *Chest* 2020.
5. Siegel R, Miller K, Jemal A. Cancer statistics, 2020. *CA: a cancer journal for clinicians* 2020; **70**(1): 7-30.
6. Kamboj M, Sepkowitz K. Nosocomial infections in patients with cancer. *The Lancet Oncology* 2009; **10**(6): 589-97.
7. Li J, Duan X, Wang L, et al. Selective depletion of regulatory T cell subsets by docetaxel treatment in patients with nonsmall cell lung cancer. *Journal of immunology research* 2014; **2014**: 286170.
8. Longbottom E, Torrance H, Owen H, et al. Features of Postoperative Immune Suppression Are Reversible With Interferon Gamma and Independent of Interleukin-6 Pathways. *Annals of surgery* 2016; **264**(2): 370-7.
9. Sica A, Massarotti M. Myeloid suppressor cells in cancer and autoimmunity. *Journal of autoimmunity* 2017; **85**: 117-25.

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10. Wei X, Su J, Yang K, et al. Elevations of serum cancer biomarkers correlate with severity of COVID-19. *Journal of medical virology* 2020.

11. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *The Lancet Oncology* 2020; **21**(3): 335-7.

12. Desai A, Sachdeva S, Parekh T, Desai R. COVID-19 and Cancer: Lessons From a Pooled Meta-Analysis. *JCO global oncology* 2020; **6**: 557-9.

13. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 2020; **395**(10223): 497-506.

14. 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. *The Lancet* 2020; **395**(10223): 507-13.

15. 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**(11): 1061-9.

16. 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 Medicine Infectious Disease* 2020: 101606.

17. Zhang J, Dong X, Cao Y, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy* 2020.

18. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine*
2020.

19. Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infectious Diseases* 2020.

20. 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. *The Lancet* 2020.

21. Chen L, H L, W L. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. *Chin J Tuberc Respir Dis* 2020; **43**(3): 203-8.

22. 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 Internal Medicine* 2020.

23. Liu W, Tao Z, Lei W, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. *Chinese Medical Journal* 2020: 1.

24. 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. *Annals of Oncology* 2020.

25. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *Bmj* 2020; **368**.

26. Liu K, Fang Y-Y, Deng Y, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chinese medical journal* 2020.

27. Wang J, Song Q, Chen Y, et al. Systematic investigations of COVID-19 in 283 cancer patients. *https://wwwmedrxivorg/* 2020.

28. Zhu W, Xie K, Lu H, Xu L, Zhou S, Fang S. Initial clinical features of suspected Coronavirus Disease 2019 in two emergency departments outside of Hubei, China. *Journal of Medical Virology* 2020.

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29. 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. *Journal of Infection* 2020.

30. Wu J, Liu J, Zhao X, et al. Clinical Characteristics of Imported Cases of COVID-19 in Jiangsu Province: A Multicenter Descriptive Study. *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America* 2020.

31. Xu X, Yu C, Qu J, et al. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2. *European journal of nuclear medicine molecular imaging* 2020: 1-6.

32. Leung KS-S, Ng TT-L, Wu AK-L, et al. A territory-wide study of early COVID-19 outbreak in Hong Kong community: A clinical, epidemiological and phylogenomic investigation. *https://wwwmedrxivorg/* 2020.

33. Guan W-j, Ni Z-y, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *New England journal of medicine* 2020; **382**(18): 1708-20.

34. 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. *Journal of Korean medical science* 2020; **35**(13).

35. Tabata S, Imai K, Kawano S, et al. The clinical characteristics of COVID-19: a retrospective analysis of 104 patients from the outbreak on board the Diamond Princess cruise ship in Japan. *https://wwwmedrxivorg/* 2020.

36. Rossi PG, Marino M, Formisano D, et al. Characteristics and outcomes of a cohort of SARS-CoV-2 patients in the Province of Reggio Emilia, Italy. *https://wwwmedrxivorg/* 2020.

37. Basse C, Diakite S, Servois V, Frelaut M, Noret A. Characteristics and outcome of SARS-CoV-2 infection in cancer patients. *https://wwwmedrxivorg/* 2020.

38. McMichael TM, Currie DW, Clark S, et al. Epidemiology of Covid-19 in a long-term care facility in King County, Washington. *New England Journal of Medicine* 2020.

39. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospitalization and critical illness among 4,103 patients with COVID-19 disease in New York City. *https://wwwmedrxivorg/* 2020.

40. Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *https://wwwmedrxivorg/* 2020.

41. Paranjpe I, Russak A, De Freitas JK, et al. Clinical Characteristics of Hospitalized Covid-19 Patients in New York City. *https://wwwmedrxivorg/* 2020.

42. Argenziano MG, Bruce SL, Slater CL, et al. Characterization and Clinical Course of 1000 Patients with COVID-19 in New York: retrospective case series. *https://wwwmedrxivorg/* 2020.

43. 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.

44. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS medicine* 2009; **6**(7): e1000097.

45. Huang X, Lin J, Demner-Fushman D. Evaluation of PICO as a knowledge representation for clinical questions. AMIA annual symposium proceedings; 2006: American Medical Informatics Association; 2006. p. 359.

46. Institute TJB. Joanna Briggs Institute Reviewers' manual. *Australia : The Joanna Briggs Institute* 2016.

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47. Zheng R, Sun K, Zhang S, et al. Report of cancer epidemiology in China, 2015. *Zhonghua Zhong Liu Za Zhi* 2019; **41**(1): 19-28.

48. Lai S, Ruktanonchai NW, Zhou L, et al. Effect of non-pharmaceutical interventions for containing the COVID-19 outbreak in China. *https://wwwmedrxivorg/* 2020.

49. Brown P, Rai K, Vecchia CL, Rodriguez PS, Qu K, Brown MG. Mortality from COVID-19 in 12 countries and 6 states of the United States. *https://wwwmedrxivorg/* 2020.

50. E. NsSaERp. Age and cancer risk. . *Available from: https://wwwcancergov/about-cancer/causes-prevention/risk/age*.

51. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell* 2020; **181**(2): 271-80.e8.

52. Zheng M, Gao Y, Wang G, et al. Functional exhaustion of antiviral lymphocytes in COVID-19 patients. *Cellular molecular immunology* 2020; **17**(5): 533-5.

53. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. *International Journal of Infectious Diseases* 2020.

54. Du RH, Liang LR, Yang CQ, 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**(5).

55. Kang Y, Chen T, Mui D, et al. Cardiovascular manifestations and treatment considerations in covid-19. *Heart* 2020.

56. 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 discovery* 2020; **10**(6): 783-91.

Table 1. List of the 32 Studies Included in This Meta-Analysis

Study	Year	District	Diagnosis methods	Total patients	Cancer patients	Cancer-related Death	Death toll
Huang C[13]	12-6,19 1-2,20	Wuhan, CHN	RT-PCR and NGS	41	1	NA	6
Chen N[14]	1-1,20 1-20,20	Wuhan, CHN	RT-PCR	99	1	NA	11
Wang D[15]	1-1,20 1-28,20	Wuhan, CHN	bron-choalveolar lavage fluid	138	10	NA	6
Huang Y[16]	12-21,2019 1-28,2020	Wuhan, CHN	unclear	34	3	NA	0
Zhang J[17]	1-16,2020 1-3,2020	Wuhan, CHN	RT-PCR	140	6	NA	NA
Yang X[18]	12，2019 1-26,2020	Wuhan, CHN	RT-PCR	52	2	NA	32
Shi H[19]	12-20,2019 1-23,2020	Wuhan, CHN	RT-PCR and NGS	81	4	NA	3

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Zhou F[20]	12-29,2019 1-31,2020	Wuhan, CHN	unclear	191	2	NA	54
Chen L[21]	12,2019 2-3,2020	Wuhan, CHN	RT-PCR	29	2	1	2
Wu C[22]	12-30,2019 1-15,2020	Wuhan, CHN	RT-PCR	201	1	NA	44
Liu W[23]	12-30,2019 1-15,2020	Wuhan, CHN	RT-PCR	78	4	NA	2
Zhang L[24]	1-13,2020 2-26,2020	Wuhan, CHN	RT-PCR	28	28	8	8
Chen T[25]	1-13,2020 2-12,2020	Wuhan, CHN	RT-PCR	274	7	5	113
Liu K[26]	12-30,2019 1-24,2020	NA, CHN	RT-PCR	137	2	NA	16
Wang J[27]	12-17,2019 3-18,2020	NA, CHN	RT-PCR	283	283	50	50

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Zhu W[28]	1-24,2020 2-20,2020	outside of WH,CHN	RT-PCR	32	2	NA	NA
Yang W[29]	1-17,2020 2-10,2020	outside of WH,CHN	unclear	149	2	NA	0
Wu J[30]	1-22,2020 2-14,2020	outside of WH,CHN	RT-PCR	80	1	NA	0
Xu X[31]	1-23,2020 2-4,2020	outside of WH,CHN	RT-PCR	90	2	NA	NA
Leung KS-S[32]	1-26,2020 2-28,2020	outside of WH,CHN	RT-PCR	50	1	NA	NA
Guan W[33]	12,2019 1 29,2020	NA, CHN	RT-PCR	1099	10	NA	15
Liang W[11]	12,2019 1 31,2020	NA, CHN	unclear	1590	18	NA	NA
Kim ES[34]	12,2019 2,2020	Korea	unclear	28	1	NA	0

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Tabata S[35]	2-11,2020 2-25,2020	Japan	RT-PCR	104	4	NA	0
Rossi PG[36]	2-27,2020 4-2,2020	Italy	PCR	2653	301	44	217
Basse C[37]	3,2020 5,2020	France	RT-PCR	141	141	30	30
McMichael TM[38]	2-28,2020 3-18,2020	King County, Washington, US	RT-PCR	167	15	NA	34
Petrilli CM[39]	3-1,2020 4-2,2020	New York, US	RT-PCR	4103	185	NA	176
Cummings MJ[40]	3-2,2020 4-1,2020	New York, US	RT-PCR	257	18	NA	86
Paranjpe I[41]	2-27,2020 4-2,2020	New York, US	RT-PCR	2199	151	NA	310
Argenziano MG[42]	3-1,2020 4-15,2020	New York, US	RT-PCR	1000	66	NA	172

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Richardson S[43]	3-1,2020	4-4,2020	New York, US	RT-PCR	5700	320	NA	553

Note :RT-PCR and NGS :Real-time RT-PCR and next-generation sequencing; NA: Not available; NA, CHN: The patients were from China, but was not sure whether from Wuhan or outside of Wuhan

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Figure legends

Figure 1. Prevalence of cancer in COVID-19 patients in China and outside China.

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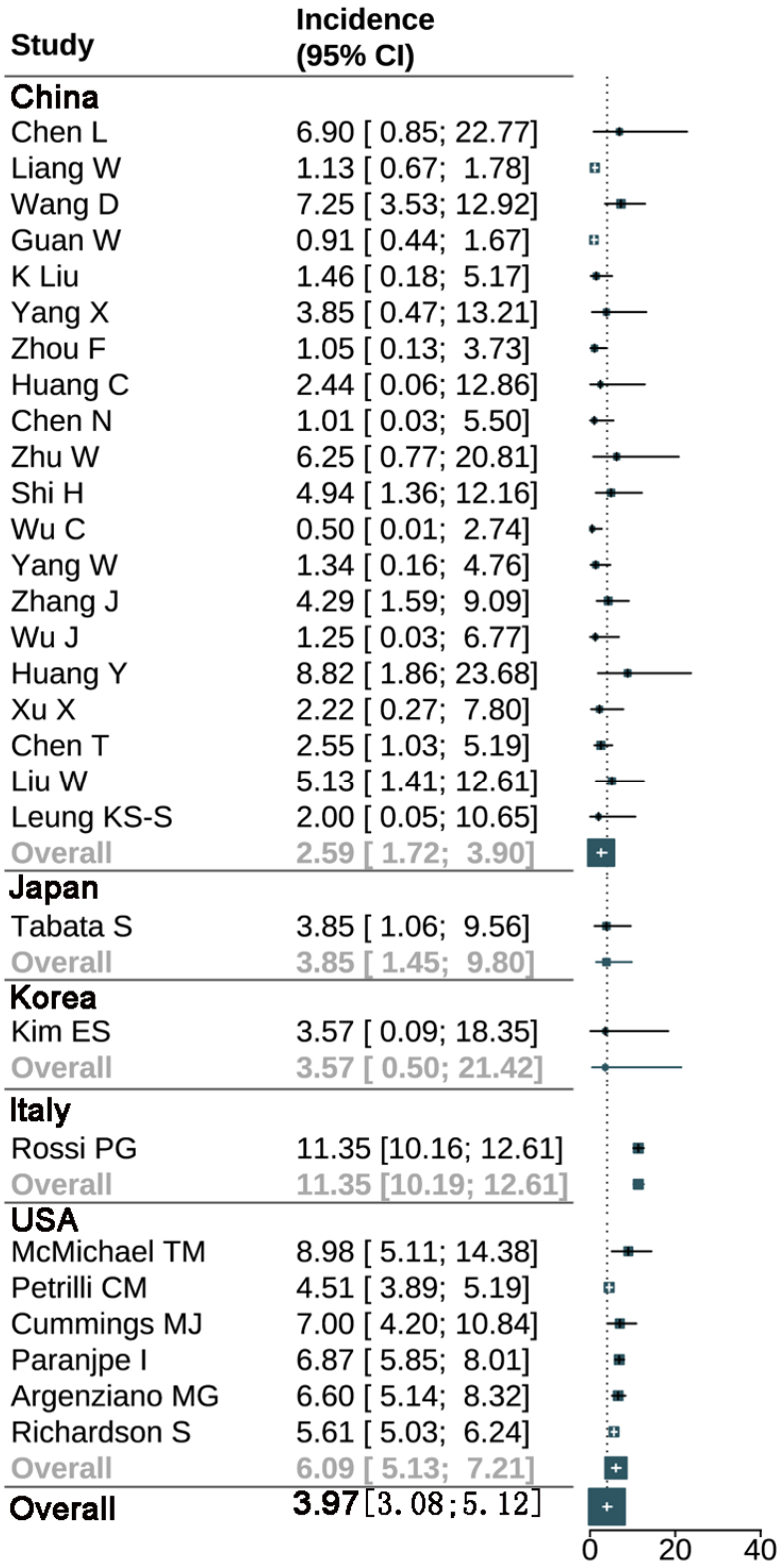

Figure 2. Prevalence of cancer in COVID-19 patients in subgroups based on sample size over or not over 100.

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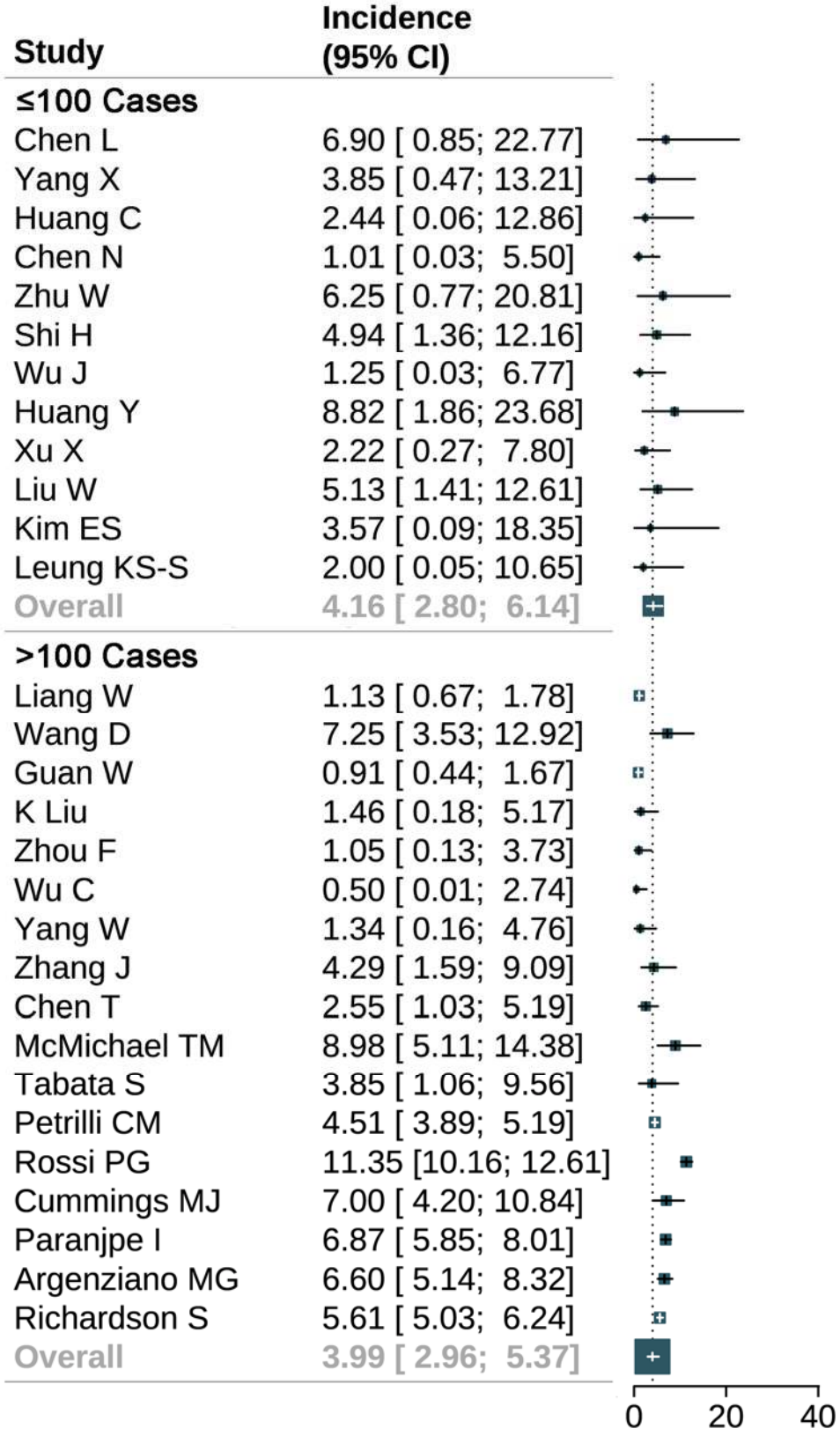

Figure 3. Prevalence of cancer in COVID-19 patients based on areas.

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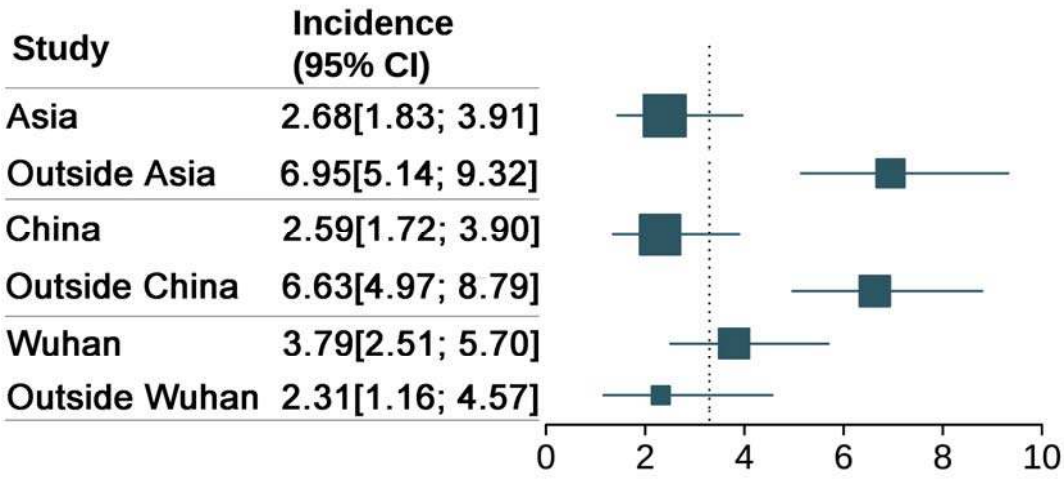

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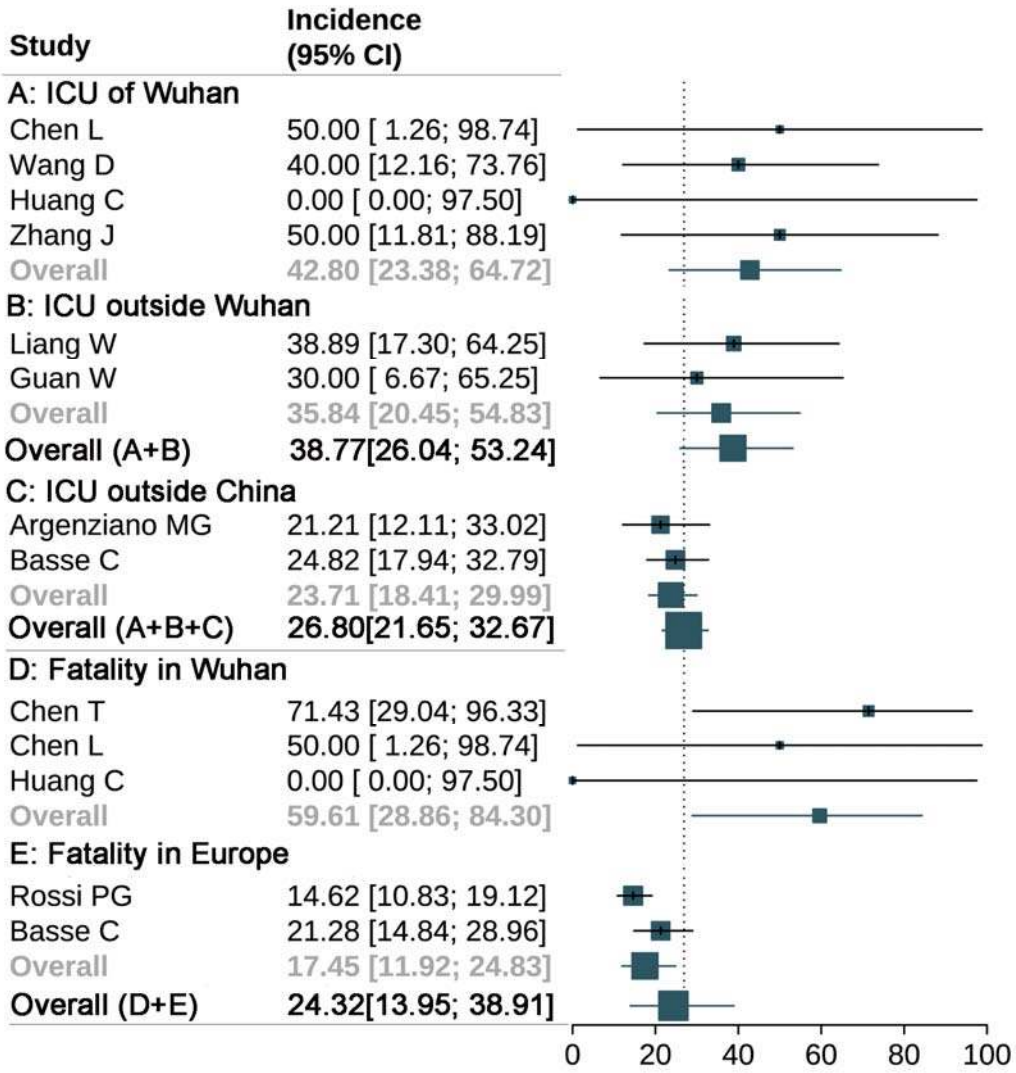
Figure 4. The incidence of ICU admission and fatality of cancer patients with COVID-19 in different areas.



A:ICU admission incidence of cancer patients with COVID-19 in Wuhan, **B**:ICU admission incidence of cancer patients with COVID-19 outside Wuhan, **C**:ICU admission incidence of cancer patients with COVID-19 outside China, **A+B**:ICU admission incidence of cancer patients with COVID-19 in China, **A+B+C**:ICU admission incidence of cancer patients with COVID-19 in all areas(all available statistics), **D**:Fatality of cancer patients with COVID-19 in Wuhan; **E**:Fatality of cancer patients with COVID-19 in Europe; **D+E**: Fatality of cancer patients with COVID-19 in all areas(all available statistics)

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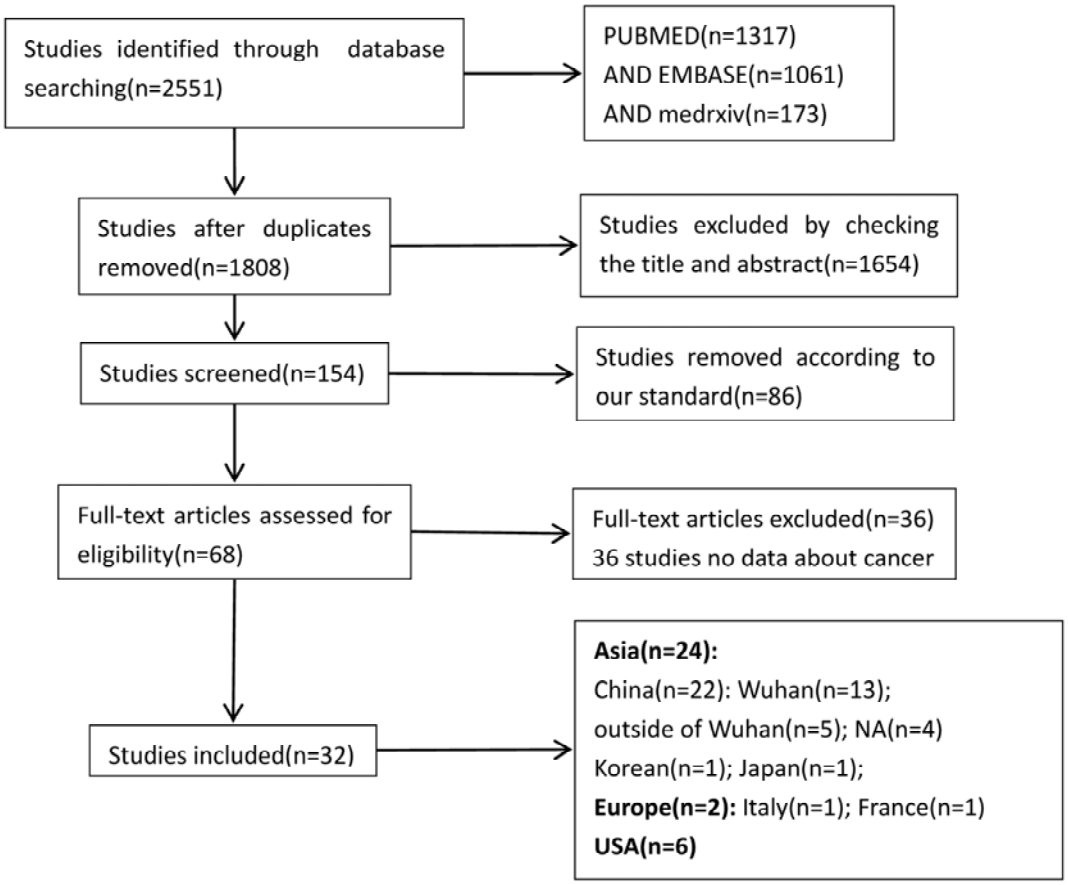
Figure 5. Flowchart depicting the studies selection process.