

Abstract

The coronavirus disease 2019 (COVID-19) is a relatively new but concerning virus that affects cancer patients in excess and with more severe complications compared to the general population. Despite the disproportionate incidence and adverse effects of COVID-19 on cancer patients, clinical trials rarely investigate treatment outcomes in patients with both conditions. This study investigated the eligibility of cancer-related terms in 7203 COVID-19 clinical trial study reports collected from clinicaltrials.gov (MeSH ID D000086382) and found such terms to be excluded from clinical trials at an overwhelming rate (84.2%). Chemotherapy, carcinomas, and tumors were the most frequently excluded cancer-related terms in COVID-19 clinical trials. Cancer treatments (chemotherapy and radiation therapy) elicited the greatest volume of terms included and excluded from clinical trials. Despite a smaller overall sample, lymphomas and melanomas were also excluded disproportionately. The exclusion of cancer-related terms from COVID-19 clinical trials was statistically significant by t-test paired for two sample means ($p < .01$). These data indicate a pressing demand for COVID-19 clinical trials that include cancer patients.

Background

The coronavirus disease 2019 (COVID-19) emerged as a major virus with flu-like symptoms and other cardiorespiratory complications. This virus shares some pathophysiological similarities with various cancers, and thus increases the incidence and prognostic severity in cancer patients (Zong et al., 2021, 1-19). COVID-19 has even elicited an increased mortality rate in lung cancer patients (Yang et al., 2021, 298). While COVID-19 may increase the incidence of cancer in general, treatment outcomes aren't affected equally in all cancer types. For example, hematologic, nasopharyngeal, brain, digestive, and lung tumors are all considered high-risk cancers with higher mortality rates when combined with COVID-19, though this trend was not found in genitourinary cancers (Chai et al., 2021, 1244-1256). Collectively, research indicates a clear relationship between cancer and COVID-19 incidence and exacerbated effects of COVID-19 in some cancer types.

Methods

This study investigated the eligibility criteria of COVID-19 clinical trial study reports to assess the historical inclusion and exclusion of comorbid cancer within COVID-19 clinical trials. Data were collected via the national clinical trial repository, clinicaltrials.gov. Clinical trials selected were completed interventional trials dated between 1990 and 2022. Researchers used Python 3.9.10 to search these study reports for terms related to cancer and tally instances of these terms in both the inclusion and exclusion sections of the eligibility criteria..I. Search terms were only counted once per clinical trial inclusion or exclusion section. Synonymous terms were merged so that the presence of any variant signaled the presence of that merged term once for a given study. Clinical trials that lacked explicit inclusion and exclusion sections, as well as those that mentioned the same search term in both the inclusion and exclusion sections were manually inspected to determine the correct term assignment. The resulting dataset was organized using

the tidyverse (1.3.2) in R (4.2.2) and Excel was used to generate the table. Figures were created using ggplot2 (3.4.0) and BioVenn (1.1.3) in R. Statistical analyses were performed using the R 'stats' package.

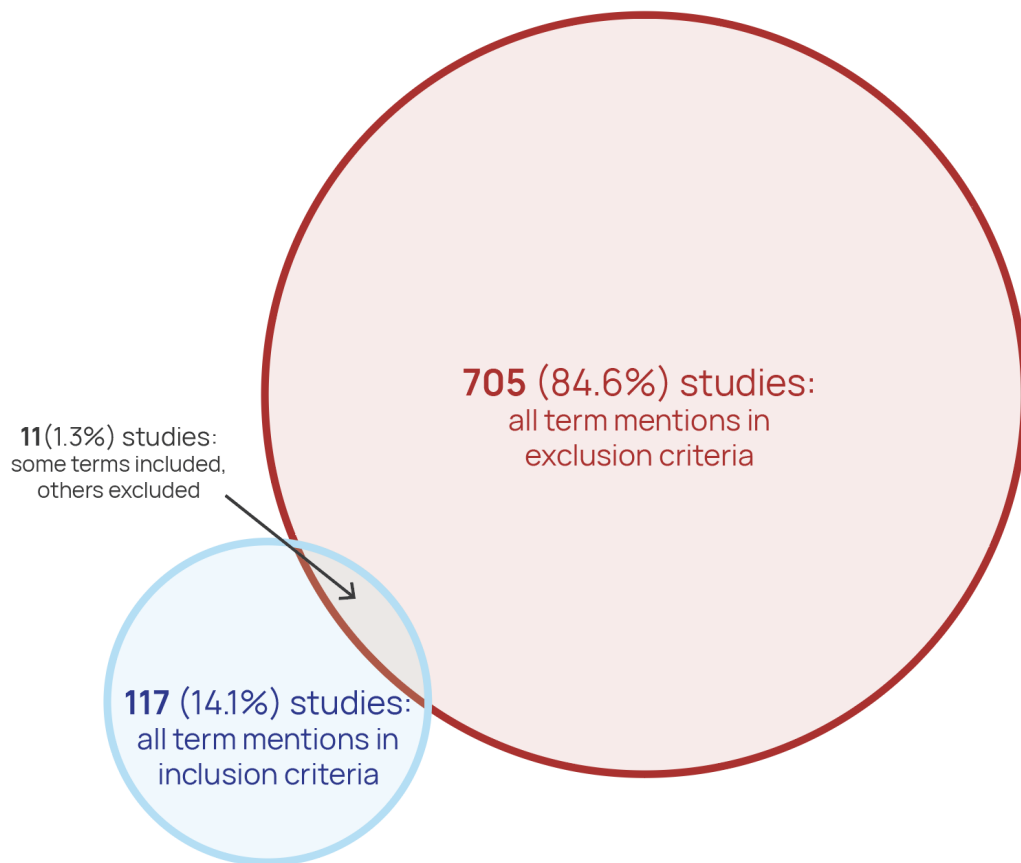


Figure 1. Proportional Venn diagram of COVID-19 clinical trials that exclusively contained instances of cancer-related search terms in their inclusion versus exclusion criteria (and those that mentioned different search terms in both sections).

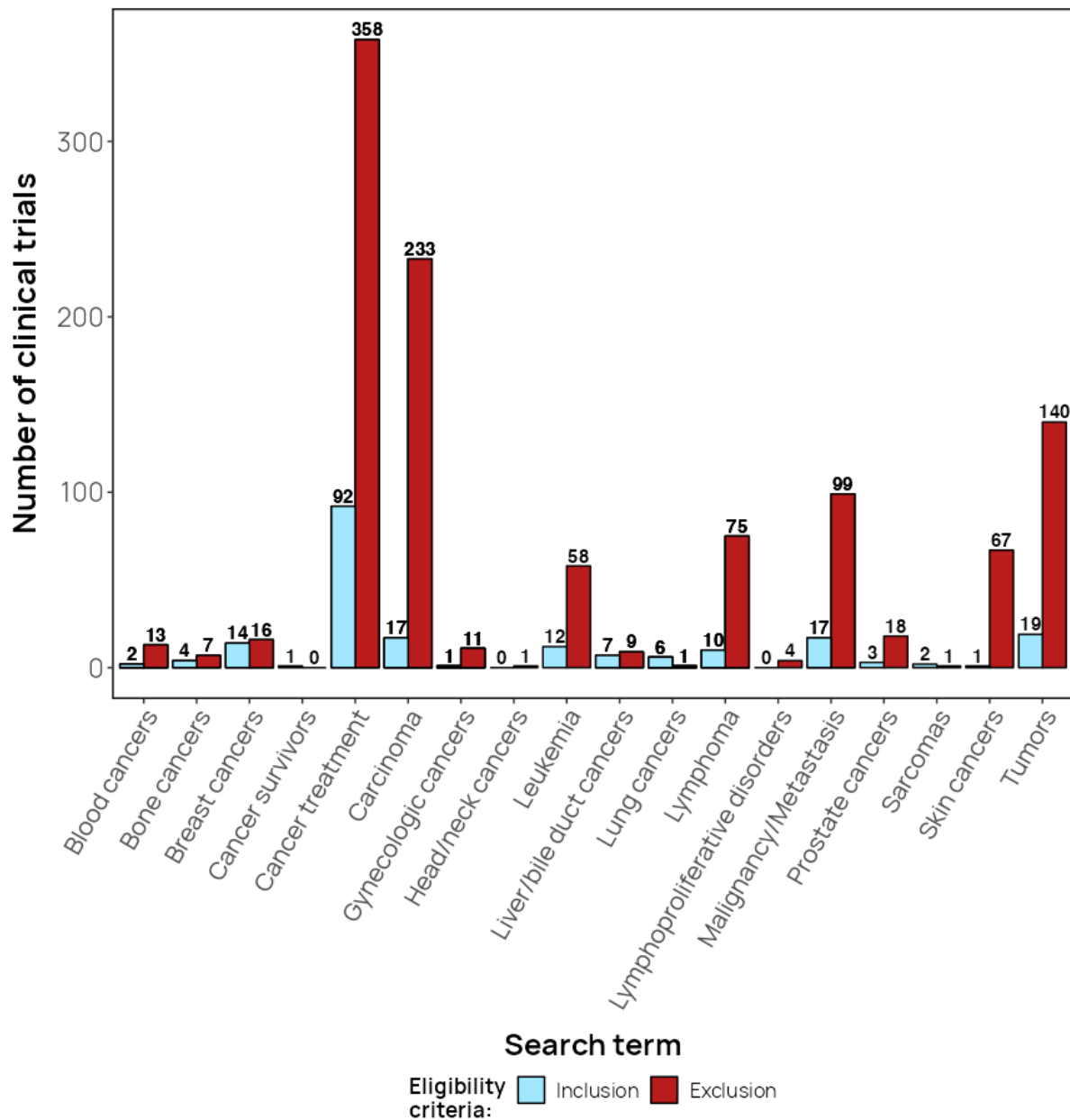
Table 1. Inclusion and exclusion frequencies of cancer-related terms in COVID-19 clinical trials.

Search Term	Inclusion criteria	Exclusion criteria	Term groups
Haematological malignancies	0	3	Blood cancers
Multiple myeloma	1	10	
Neoplasms plasma cell	1	0	
Myelodysplastic syndrome MDS	4	4	Bone diseases/cancers
Myeloproliferative disorders	0	3	

Breast cancer	13	15	Breast cancers
Metastatic breast cancer	1	1	
Cancer survivors	1	0	Cancer survivors
Chemotherapy	69	287	Cancer treatment
Radiotherapy	23	71	
Carcinoma	14	158	Carcinoma
Carcinoma squamous cell	0	3	
Carcinoma in situ	3	72	
Cervical intraepithelial neoplasia	0	3	
Endometrial cancer	0	6	Gynecologic cancers
Leiomyoma	1	0	
Ovarian cancer	0	2	
Head and neck cancer	0	1	Head/neck cancers
Leukemia	12	58	Leukemia
Hepatocellular carcinoma	3	7	Liver/bile duct cancers
Liver cancer	4	2	
Lung cancers	0	1	
Mesothelioma	2	0	Lung cancers
Non small cell lung cancer	2	0	
Small cell lung cancer sclc	2	0	
Hodgkin lymphoma	0	2	
Lymphoma	9	73	Lymphoma
Small lymphocytic lymphoma	1	0	
Lymphoproliferative disorders	0	4	Lymphoproliferative disorders
Malignancies	16	87	Malignancy/Metastasis
Metastasis	1	12	
Prostate cancer	3	18	Prostate cancers
Sarcoma	2	1	Sarcomas
Melanoma	1	67	Skin cancers
Tumors	19	140	Tumors
TOTAL:		208 (15.8%)	1111 (84.2%)

Search Terms in COVID-19 Clinical Trial Eligibility Criteria:

(Based on interventional trials initiated between 2000 and 2022.)



(Source: www.clinicaltrials.gov)

Figure 2. Comparison of inclusion and exclusion frequencies of cancer-related terms in COVID-19 clinical trials. Individual search terms have been grouped according to Table 1.

Results and Discussion

This study analyzed 7203 COVID-19 clinical trials and found 833 trials that recorded cancer-related terms within the eligibility section. Of those, 128 (15.4%) trials were found with cancer-related terms within the inclusion criteria compared to 716 (86.0%) with terms in the exclusion criteria (Figure 1). Studies that included an identical term in their inclusion and exclusion or studies that failed to discern between the inclusion and exclusion criteria were manually inspected to determine the correct assignment of each term (24 studies). Overall, 35 cancer-related terms were identified (Table 1) and recorded a total frequency of 1319. Of these instances, 1111 (84.2%) were identified in the exclusion criteria compared to 208 (15.8%) in the inclusion criteria. Chemotherapy, carcinomas, and tumors were excluded the most frequently while melanoma and lymphoma yielded disproportionate inclusion rates with 1.46% and 11.76%, respectively (Figure 2). Collectively, cancer treatments (chemotherapy and radiation therapy) were included and excluded the most voluminously of all grouped terms. Subsequent data analysis identified statistically significant differences between the inclusion and exclusion of cancer-related terms in COVID-19 clinical trials by a t-test paired for two sample means ($p=0.018$).

Based on the results above, COVID-19 clinical trials have failed to consistently investigate co-treatment in patients with comorbid cancer. Clinical trial administrators have avoided the inclusion of cancer patients with tumors or under chemotherapy, despite the increased incidence of COVID-19 among this vulnerable group. Considering the evidence suggesting cancer-specific COVID-19 treatment outcomes, it's important for clinical trials to more actively include cancer patients in future COVID-19 clinical trials.

References

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