APPENDIX: The Association Between Underlying Conditions and Severe COVID-19:

Patients with Hematologic Malignancy and Patients with Hematologic Malignancy Receiving Hematopoietic Stem Cell Transplant/Hematopoietic Cell Transplant

Centers for Disease Control and Prevention (CDC)

National Center for Immunization and Respiratory Diseases (NCIRD)

Brief Summary of Findings on the Association Between Hematologic Malignancy and Hematopoietic Stem Cell Transplant/Hematopoietic Cell Transplant and Severe COVID-19 Outcomes

19 studies[1-19], 14 cohort studies[1,3-6,9-15,17,19], four case-control studies[2,7,8,18], and one case-series[16] reported on the association of hematologic malignancies and severe COVID-19 outcomes and were included in this analysis. Two studies[2,14] reported on the association of hematopoietic cell transplant (HCT) and hematopoietic stem cell transplant (HSCT) and COVID-19 mortality. One study[2] reported data on diagnosed hematologic malignancy and HCT, including Autologous-HCT, Allogenic-HCT, and HCT on immunosuppressive agents and ICU admission and mechanical ventilation.

The data indicate an association between hematologic malignancy and increased mortality[1,3-6,8-12,15-19], ICU admission[3,5,7,8,14-16,19], mechanical ventilation[3,7,9,15,19], and hospitalization[13,18,19] due to COVID-19 infection. Limited data from only one study is insufficient to determine if there is an association between hematologic malignancy and intubation[16] or non-invasive ventilation[15].
The data is inconsistent and inconclusive on the association between HCT[2,14] and HSCT[2,14] and COVID-19 mortality. Limited data from only one study is insufficient to determine if there is an association between HCT[2,14] and ICU admission or mechanical ventilation.

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A. Methods

The primary aim of this review was to identify and synthesize the best available evidence to answer the question "What is the association between hematologic malignancy or hematopoietic stem cell transplant/hematopoietic cell transplant and severe COVID-19 outcomes?" Due to variable reporting across studies on the use of B-cell-depleting therapies for treatment, as well as concurrent reporting on the use of B-cell-depleting therapies for other non-hematologic conditions, the appendix was separated in 2 to include studies reporting the following exposures:

1. Hematologic malignancies / hematologic stem cell transplant (with B-cell depleting therapy unspecified).
2. Treatment with B-cell-depleting medications (for example, rituximab, cyclophosphamide, and dexamethasone) for any underlying condition.

This appendix is dedicated to the primary aim of this study. It seeks to answer the question: "What is the association between hematologic malignancy, hematopoietic stem cell transplant/hematopoietic cell transplant and severe COVID-19 outcomes?"

This effort is used to update the Centers for Disease Control and Prevention (CDC) website on underlying conditions and enable the creation of a provider-specific website with more rigorous information. The methods for all underlying conditions and risk factors are outlined in the webpage, https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/systematic-review-process.html.
These methods were established in May 2021 and are standard for all conditions and risk factors on the CDC COVID-19 response underlying medical conditions page.

A.1. Literature Search

A list of search terms was developed to identify the literature most relevant to the population, exposure, comparator, and outcomes (PECO) question. Subject matter experts and library scientists were consulted to develop a robust list of search terms. These terms were then incorporated into search strategies, and these searches were performed in OVID using the COVID-19 filter for all articles from the beginning of each data base until December 1, 2021. The detailed search strategies for identifying primary literature and the search results are provided in the *Appendix*. References were included if retrieved by the literature search and reported exposures and outcomes relevant to this review.

A.2. Study Selection

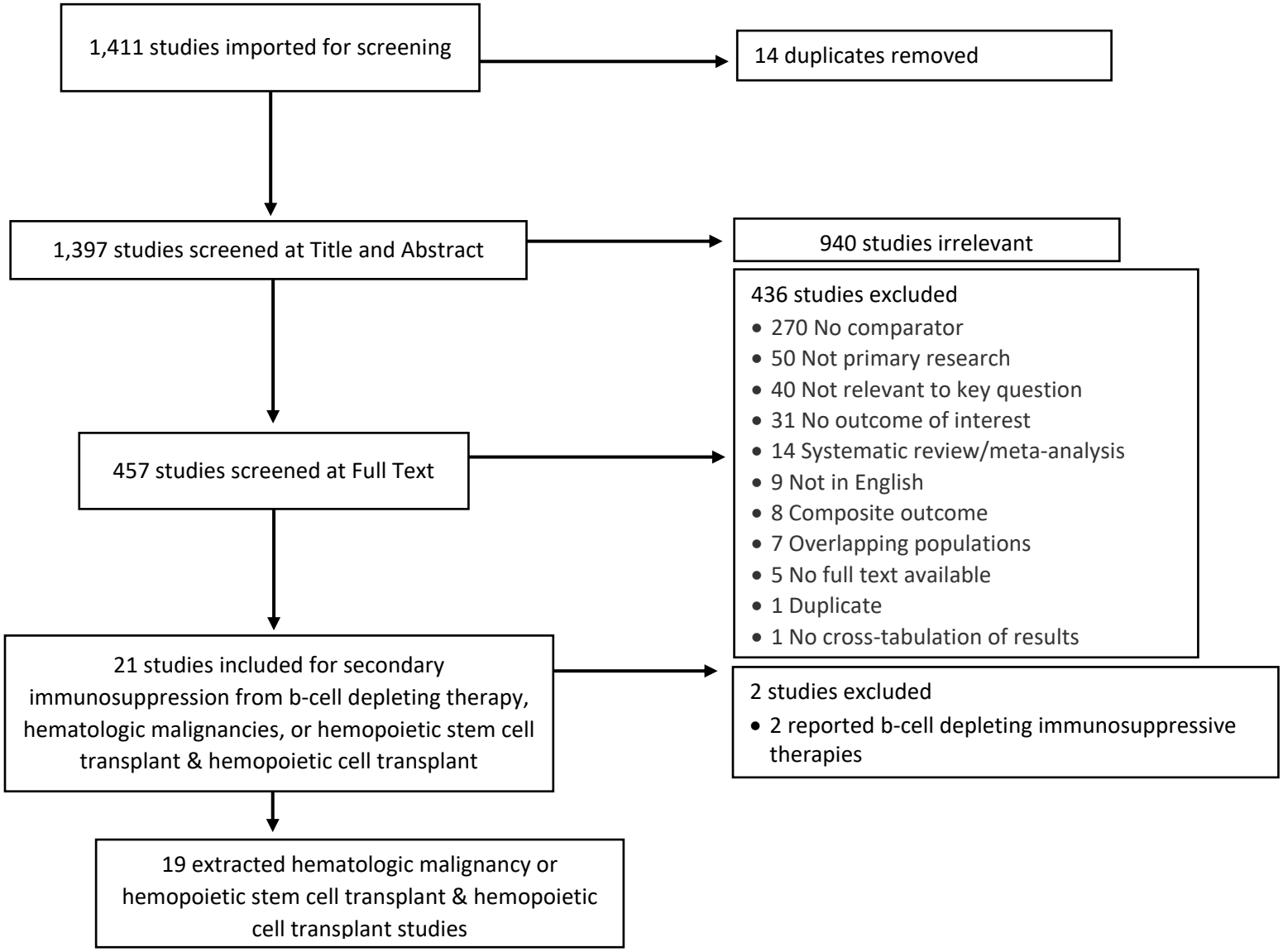
Titles and abstracts from references were screened by dual review (M.M., A.H., D.O.S., C.N.S., E.C.S., J.H., M.W., M.C., or J.K.). Full-text articles were retrieved if they were:

1. relevant to the PECO question;

2. primary research; and
3. written in English.

The *Appendix* presents the full list of exclusion criteria. The full texts of selected articles were then screened by two independent reviewers, and disagreements were resolved by discussion (M.M., A.H., D.O.S., C.N.S., E.C.S., J.H., M.W., M.C. or J.K.). The results of the study selection process are depicted in the Figure.

Figure: Results of the Study Selection Process for Hematologic Malignancy (HM) and Hematopoietic Stem Cell Transplant (HSCT)/ Hematopoietic Cell Transplant (HCT)



A.4. Data Extraction and Synthesis

Methodologic data and results of relevant outcomes from the studies meeting inclusion criteria were extracted into standardized evidence tables. Data and analyses were extracted as presented in the studies. For the purposes of this review, statistical significance was defined as $p \leq 0.05$, and a small sample size for the overall study cohort was defined as <50% of the overall median value (for example, N = 530, < 265). Extracted studies were examined to assess the risk between active HM under treatment and non-active HM, but few studies reported this comparison, and the evidence was confounded by other variables. Therefore, this comparison was excluded from analysis.

A.5. Internal Validity Assessment

The internal validity associated with each study was assessed using scales developed by the CDC's Division of Healthcare Quality Promotion and scores were recorded in the evidence tables. The *Appendix* includes the questions used to assess the quality of each study design. The strength, magnitude, precision, consistency, and applicability of results were assessed for all comparators. The overall confidence in the evidence base is reported in the aggregation tables in the *Appendix*.

A.6. Reviewing and Finalizing the Systematic Review

Draft findings, aggregation tables, and evidence tables, are presented to CDC subject matter experts for review and input. Following further revisions, the summary will be published on the CDC website.

B. Systematic Literature Review Results

B.1. Search Strategies and Results

Please note, the search strategy presented below includes terms specific to B-cell-depleting therapy. However, articles focusing on these topics which specified the immunosuppressant administered are analyzed in a separate supplementary appendix. This appendix only focused on studies that report hematologic malignancy / hematopoietic stem cell transplants in which immunosuppressant administered was not specified.

Table 1 Secondary Immunosuppression Search Conducted December 1, 2021

Database	**Strategy**	**Records** 12/01/2021
Medline (OVID) 1946-	hematopoietic cell transplant* OR hematopoietic stem cell transplant* OR haematopoietic cell transplant* OR haematopoietic stem cell transplant* OR HCT OR hematologic malignanc* OR hematologic neoplasm* OR hematological malignanc* OR hematological neoplasm* OR hematopoietic malignanc* OR hematopoietic neoplasm* OR hematologic cancer* OR hematological cancer* OR haematologic malignanc* OR haematologic neoplasm* OR haematological malignanc* OR haematological neoplasm* OR haematopoietic malignanc* OR haematopoietic neoplasm* OR haematologic cancer* OR haematological cancer* OR chimeric antigen receptor* OR chimeric t-cell receptor* OR chimeric immunoreceptor* OR artificial t-cell receptor* OR CAR-T OR CAR-Ts OR bone marrow OR b-cell deplet* OR rituximab AND Limit COVID [use validated filter] Limit journal article	992
Embase (OVID) 1988-	(hematopoietic cell transplant* OR hematopoietic stem cell transplant* OR haematopoietic cell transplant* OR haematopoietic stem cell transplant* OR HCT OR hematologic malignanc* OR hematologic neoplasm* OR hematological malignanc* OR hematological neoplasm* OR hematopoietic malignanc* OR hematopoietic neoplasm* OR hematologic cancer* OR hematological cancer* OR haematologic malignanc* OR haematologic neoplasm* OR haematological malignanc* OR haematological neoplasm* OR haematopoietic malignanc* OR haematopoietic neoplasm* OR haematologic cancer* OR haematological cancer* OR chimeric antigen receptor* OR chimeric t cell receptor* OR chimeric immunoreceptor* OR artificial t cell receptor* OR CAR-T OR CAR-Ts OR bone marrow OR b-cell deplet* OR rituximab).ti,ab,kw. AND	877 -680 duplicates =197 unique items

Database	Strategy	**Records** 12/01/2021
	Limit COVID [use validated filter] Limit to journal article; not pubmed/medline	
Global Health	hematopoietic cell transplant* OR hematopoietic stem cell transplant* OR haematopoietic cell transplant* OR haematopoietic stem cell transplant* OR HCT OR hematologic malignanc* OR hematologic neoplasm* OR hematological malignanc* OR hematological neoplasm* OR hematopoietic malignanc* OR hematopoietic neoplasm* OR hematologic cancer* OR hematological cancer* OR haematologic malignanc* OR haematologic neoplasm* OR haematological malignanc* OR haematological neoplasm* OR haematopoietic malignanc* OR haematopoietic neoplasm* OR haematologic cancer* OR haematological cancer* OR chimeric antigen receptor* OR chimeric t cell receptor* OR chimeric immunoreceptor* OR artificial t cell receptor* OR CAR-T OR CAR-Ts OR bone marrow OR b-cell deplet* OR rituximab AND (coronavir* OR corona virus* OR corona pandemic* OR betacoronavir* OR covid19 OR covid OR nCoV OR novel CoV OR CoV 2 OR CoV2 OR sarscov2 OR sars2 OR 2019nCoV OR wuhan virus* OR NCOV19) Limit to journal article	250 -206 duplicates =44 unique items
Cochrane Library	("hematopoietic cell transplant*" OR "hematopoietic stem cell transplant*" OR "haematopoietic cell transplant*" OR "haematopoietic stem cell transplant*" OR HCT OR "hematologic malignanc*" OR "hematologic neoplasm*" OR "hematological malignanc*" OR "hematological neoplasm*" OR "hematopoietic malignanc*" OR "hematopoietic neoplasm*" OR "hematologic cancer*" OR "hematological cancer*" OR "haematologic malignanc*" OR "haematologic neoplasm*" OR "haematological malignanc*" OR "haematological neoplasm*" OR "haematopoietic malignanc*" OR "haematopoietic neoplasm*" OR "haematologic cancer*" OR "haematological cancer*" OR "chimeric antigen receptor*" OR "chimeric t cell receptor*" OR "chimeric immunoreceptor*" OR "artificial t-cell receptor*" OR CAR-T OR CAR-Ts OR "bone marrow" OR "b-cell deplet*" OR rituximab):ti,ab AND (coronavir* OR "corona virus*" OR "corona pandemic*" OR betacoronavir* OR covid19 OR covid OR nCoV OR "novel CoV" OR "CoV 2" OR CoV2 OR sarscov2 OR sars2 OR 2019nCoV OR "wuhan virus*" OR NCOV19):ti,ab	68 -7 duplicates =61 unique items
CINAHL (EbscoHost)	("hematopoietic cell transplant*" OR "hematopoietic stem cell transplant*" OR "haematopoietic cell transplant*" OR "haematopoietic stem cell transplant*" OR HCT OR "hematologic malignanc*" OR "hematologic neoplasm*" OR "hematological malignanc*" OR "hematological neoplasm*" OR	171 -84

Database	Strategy	**Records** 12/01/2021
	"hematopoietic malignanc*" OR "hematopoietic neoplasm*" OR "hematologic cancer*" OR "hematological cancer*" OR "haematologic malignanc*" OR "haematologic neoplasm*" OR "haematological malignanc*" OR "haematological neoplasm*" OR "haematopoietic malignanc*" OR "haematopoietic neoplasm*" OR "haematologic cancer*" OR "haematological cancer*" OR "chimeric antigen receptor*" OR "chimeric t cell receptor*" OR "chimeric immunoreceptor*" OR "artificial t-cell receptor*" OR CAR-T OR CAR-Ts OR "bone marrow" OR "b-cell deplet*" OR rituximab) AND (coronavir* OR "corona virus*" OR "corona pandemic*" OR betacoronavir* OR covid19 OR covid OR nCoV OR "novel CoV" OR "CoV 2" OR CoV2 OR sarscov2 OR sars2 OR 2019nCoV OR "wuhan virus*" OR NCOV19) Exclude Medline Records	duplicates =87 unique items
Scopus	TITLE-ABS-KEY("hematopoietic cell transplant*" OR "hematopoietic stem cell transplant*" OR "haematopoietic cell transplant*" OR "haematopoietic stem cell transplant*" OR HCT OR "hematologic malignanc*" OR "hematologic neoplasm*" OR "hematological malignanc*" OR "hematological neoplasm*" OR "hematopoietic malignanc*" OR "hematopoietic neoplasm*" OR "hematologic cancer*" OR "hematological cancer*" OR "haematologic malignanc*" OR "haematologic neoplasm*" OR "haematological malignanc*" OR "haematological neoplasm*" OR "haematopoietic malignanc*" OR "haematopoietic neoplasm*" OR "haematologic cancer*" OR "haematological cancer*" OR "chimeric antigen receptor*" OR "chimeric t cell receptor*" OR "chimeric immunoreceptor*" OR "artificial t-cell receptor*" OR CAR-T OR CAR-Ts OR "bone marrow" OR "b-cell deplet*" OR rituximab) AND TITLE-ABS-KEY(coronavir* OR "corona virus*" OR "corona pandemic*" OR betacoronavir* OR covid19 OR covid OR nCoV OR "novel CoV" OR "CoV 2" OR CoV2 OR sarscov2 OR sars2 OR 2019nCoV OR "wuhan virus*" OR NCOV19) AND NOT INDEX(medline) AND NOT INDEX(embase)	55 -25 duplicates =30 unique items

Notes: Duplicates were identified using EndNote automated “find duplicates” function with preference set to match on title, author, and year. There will likely be additional duplicates found that EndNote was unable to detect.

B.2. Study Inclusion and Exclusion Criteria

Inclusion Criteria: Studies were included at the title and abstract screen if they:

- were relevant to the key question "What is the association between people with hematologic malignancies, people with hematopoietic cell transplants with secondary immunosuppression, and severe COVID-19?";
    - exposures: hematologic malignancy, hematologic neoplasm; hematopoietic stem cell transplant, hematopoietic cell transplant;
    - outcomes: mortality, ICU admission, intubation (invasive ventilation, ECMO), ventilation (non-invasive ventilation, mechanical ventilation), hospitalization, and re-admission;
- were primary research;
- were written in English (can be seen as [language] in title); and
- examined humans only.

Exclusion Criteria: Studies were excluded at full text review if they:

- were not available as full-text;
- did not have data available for an analysis of interest, or had no primary comparison reported;
- were a conference abstract, poster, or reply letter;
- were narrative, mapping, or scoping review;
- were a systematic review & meta-analyses at full-text review;
- reported results examining less than 10 participants in the study population;
- reported hematologic malignancy subtypes with no main comparison;
- reported only autopsy results;
- reported on a population that overlapped with a larger study using the same data set;
- reported hematologic malignancies where the immunosuppressive therapy was specified (reported in the secondary immunosuppression appendix); and
- reported only composite outcome measures for "severe COVID-19".

B.3. Evidence Review: Hematologic Malignancy and Severe COVID-19[a]

B.3.a. Strength & Direction of Evidence

Table 2 The Association Between Hematologic Malignancies (HM) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Evidence from 15 studies[1,3-6,8-12,15-19] (N = 227,305) in patients with COVID-19 indicates that HM is associated with an increase in mortality among people with COVID-19. Five studies[5,11,16,17,19] were found to have a low threat to internal validity, and 10 studies[1,3,4,6,8-10,12,15,18] were found to have a moderate threat to internal validity. • Strength of Association: Three studies reported adjusted measures of association ranging from an adjusted odds ratio (aOR) 2.1 to an adjusted hazard ratio (aHR) 11.2 and one reported a standard mortality ratio (SMR) of 2.04. • Precision of Association: Four studies reported confidence intervals (CI): Three of the eight CIs were wide. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Summary of 14 studies: eleven cohort studies[1,3-6,9-12,17,19] (N = 84,671) and three case-control studies[8,16,18] (N = 21,475) reported measures of association[5,6,17], a SMR[11] , or proportions[1,3,4,8-10,12,16,18,19] among 106,146 individuals (4,349 had a diagnosed HM and COVID-19) suggesting an increase in mortality among individuals who had a diagnosed HM and COVID-19. • Three studies[5,6,17] (N = 103,400) reported adjusted measures of association ranging from aOR of 2.1 (95% CI: 1.9 – 2.4), p < 0.01 to aHR 11.2 (95% CI: 2.2 – 56.9), p = NR among 103,400 individuals (1,764 had a diagnosed HM and COVID-19); one study[11] reported a SMR of 2.04 (95% CI: 1.77 – 2.34), p = NR. ○ Two studies[6,17] reported wide confidence intervals. One of these studies[6] reported a low number of patients diagnosed with an HM in the study population, which may have resulted in a wide confidence. Variables included in adjusted models[5,6,17] can be found in the extractions for each study in Table 16. • Ten studies[1,3,4,8-10,12,16,18,19] (N = 24,248) reported a higher proportion of mortality among a combined 24,248 individuals (1,478 had a diagnosed HM and COVID-19), when compared to people with COVID-19 but with no HM. One of these studies[16] of 159 patients (24 who had a diagnosed HM), was propensity score matched for age,

[a] studies published since Dec 2020 were not included in the review or analysis

Outcome	Results
	sex, and underlying diseases including ischemic heart disease (IHD), diabetes mellitus (DM), and hypertension (HTN).[b] ○ Overall, seven studies[1,3,4,10,12,14,16] reported a small sample size (< 265) and seven studies[1,3,4,6,12,16] reported a low number HM in the study populations. Among the studies that reported proportions, seven studies[1,4,8,10,12,16,18] which included 588 individuals diagnosed with an HM, did not conduct statistical analyses, leaving 890 people diagnosed with an HM who were included in the proportions that reached statistical significance. Five of the studies[1,4,10,12,16] reporting proportions reported small sample sizes, decreasing confidence in the findings. One study[18] utilized a national database that included people from multiple states and could potentially overlap with other US-based studies[4,8,10,12]. • One cohort study[15] reported limited data suggesting no association between mortality and HM among patients with COVID-19. ▪ This cohort study[15] of 78 hospitalized patients with COVID-19 (10 of whom had a diagnosed HM) reported no increase in the proportion of mortality when compared to patients with no HM [20% (2/10) vs 35.9% (14/39)]. However, the study reported a low number of patients diagnosed with an HM (n = 10) in the study population and no statistical analysis was conducted for the comparison, decreasing confidence in the findings.
ICU Admission	Evidence from eight studies[3,5,7,8,14-16,19] among patients with COVID-19 (N = 96,216) indicates HM is associated with an increase in ICU admission among individuals with COVID-19. Four studies[5,7,16,19] were found to have a low threat to internal validity, and four studies[3,8,14,15] were found to have a moderate threat to internal validity. • Strength of Association: One study reported an adjusted measure of association, aOR 9.66. • Precision of Association: One study reported a wide confidence interval. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Four cohort studies[3,5,15,19] (N = 91,138) and three case-control studies[7,8,16] (N = 4,986) among 4,986 individuals with COVID-19 , including 2,266 with a diagnosis HM, reported a measure of association[7], and proportions[3,5,8,15,16,19] suggesting an increase in ICU admission among people diagnosed with an HM and COVID-19 compared to people with COVID-19 only. One case-control study[7] (N = 641) reported an adjusted measure of association among 641 patients (nine had a diagnosed HM) [aOR: 9.66 (95% CI: 2.49 – 37.36), p < 0.01]. Six additional cohort studies[3,5,8,15,16,19] (N = 95,483) of a combined 2,289

[b] See the extracted evidence in table 16 for more details

Outcome	Results
	individuals diagnosed with an HM and COVID-19 reported proportions suggesting an increase in ICU admission among individuals with a diagnosed HM and COVID-19. ○ One study[7] reported a wide confidence interval; this study reported a low number of HM in the study population (n = 9), which may have resulted in a wide confidence interval. Three studies[8,15,16] did not conduct statistical analyses, and one study[3] reported a non-significant p-value, decreasing confidence in the findings. • One cohort study[14] (N = 92) reported limited data suggesting no association between ICU admission and HM among patients with COVID-19. ▪ This study[14] reported a lower proportion of ICU admission among patients diagnosed with an HM compared to patients without HM [2.6% (1/39) vs 13.2% (7/53), p = 0.73]. However, the study reported a small sample size, decreasing confidence in the findings.
Intubation	Limited data from only one study[16] is insufficient to determine an association between HM and intubation in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[16] (N = 159) of patients with COVID-19 reported data suggesting an increase in intubation among patients diagnosed with an HM and COVID-19. ▪ This cohort study[16] reported a higher proportion of intubation among patients diagnosed with an HM compared to propensity score matched patients without HM [75.0% (18/24) vs 26.4% (28/106)]. The propensity score matching included age, sex, and underlying diseases including ischemic heart disease (IHD), diabetes mellitus (DM), and hypertension (HTN). No statistical analysis was conducted, decreasing confidence in the findings.
Mechanical Ventilation (MV)	Evidence from five studies[3,7,9,15,19] among patients with COVID-19 (N = 2,772), including 943 individuals diagnosed with an HM, indicates HM is associated with an increase in MV among people with COVID-19. Two studies[7,19] were found to have a low threat to internal validity, and three studies[3,9,15] were found to have a moderate threat to internal validity. • Strength of Association: One study reported an adjusted measure of association, aOR: 38.0. • Precision of Association: One study reported a confidence interval that was wide. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Three cohort studies[3,9,19] and one case-control study[7] (total N = 2,694)including 899 individuals with both a diagnosed HM and COVID-19, reported a measure of association[7] and proportions[3,9,19] suggesting an increase in MV among people

Outcome	Results
	diagnosed with an HM and COVID-19. One of these cohort studies[7] (N = 641) reported an adjusted measure of association, aOR: 38.0 (95% CI: 5.95 - 242.63), p < 0.01, among patients diagnosed with an HM and COVID-19. The measure of association was adjusted for age, sex, DM, HTN, smoking, and chronic obstructive pulmonary disease (COPD) at admission. Three additional cohort studies[3,9,19](N = 2,053) including a combined 992 individuals with both a diagnosed HM and COVID-19, reported an increase in the proportion of patients who received invasive mechanical ventilation (IMV). The largest of these studies[19] reported statistically significant results. ○ One study[7] (N = 641) reported a wide confidence interval; the study population included only nine patients diagnosed with an HM, which may have resulted in the wide confidence interval. Two studies[3,9] which included a combined 150 patients diagnosed with an HM reported no statistically significant difference between the proportions, decreasing confidence in the findings. • One cohort study[15] (N = 78) reported proportions suggesting no association between MV and HM among patients with COVID-19. ▪ This cohort study[15] of patients with COVID-19 reported data suggesting no difference in the proportion of MV among 78 patients (ten had a diagnosed HM), when compared to patients with no HM [30.0% (3/10) vs 28.2% (11/39), p = NR]. The study reported a low number of patients diagnosed with an HM in the study population (n = 10), and no statistical analysis was conducted, decreasing confidence in the findings.
Non-invasive Ventilation	Limited data from only one study[15] is insufficient to determine an association between HM and non-invasive ventilation in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[15] among patients with COVIC-19 (N = 78) reported proportions suggesting an increase in non-invasive ventilation among patients diagnosed with an HM and COVID-19. ▪ This cohort study[15] of hospitalized patients with COVID-19 reported a higher proportion of non-invasive ventilation among 78 patients (ten of whom had a diagnosed HM), when compared to 39 patients without cancer [40.0% (4/10) vs 10.3% (4/39), p = NR]. The study reported a small sample size, a low number of patients diagnosed with an HM in the study population (n = 10), and no statistical analysis was conducted, decreasing confidence in the findings.
Hospitalization	Evidence from three studies[13,18,19] among patients with COVID-19 (N = 117,561) indicates HM is associated with an increase in hospitalization in people with COVID-19. Two studies[13,19] were found to have a low threat to internal validity, and one study[18] was found to have a moderate threat to internal validity. • Strength of Association: One study reported an adjusted measure of association, aHR: 1.37.

Outcome	Results
	• Precision of Association: One study reported a confidence interval that was wide. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Two cohort studies[13,19] and one case-control study[18] of people with COVID-19 (total N = 117,561), which included 1,673 people diagnosed with both an HM and COVID-19, reported data suggesting an increase in hospitalization among people diagnosed with an HM and COVID-19. ▪ One cohort study[13] (N = 98,951) of people with COVID-19 reported an increase in the hazard of hospitalization among 98,951 people (which included 513 who had a diagnosed HM), when compared to people with COVID-19 in two populations: the Catalonia, Spain primary care database with no HM and the general population with no HM [database aHR: 1.37 (95% CI: 1.10 - 1.71), p = NR; general population aHR: 2.51 (95% CI: 2.12 – 2.98), p = NR]. The measure of association was adjusted for age, sex, mortality in small Spanish areas and socioeconomic and environmental inequalities (MEDEA) deprivation index, smoking status, and comorbidities including autoimmune conditions, chronic kidney disease, COPD, dementia, heart disease, hyperlipidemia, HTN, type-2 diabetes, and obesity. ▪ One case-control study[18] (N = 17,130) of people with COVID-19, including 270 with a recently diagnosed HM, reported a higher proportion of hospitalization among people who had HM compared to people with no HM [52.0% (140/270) vs 23.5% (3,960/16,860), p < 0.01]. ▪ One cohort study[19] in people with COVID-19 (N = 1,480), including 740 who had a diagnosed HM, reported a higher proportion of hospitalization among people with HM when compared to people with no HM [61.1% (452/740) vs 55.3% (409/740), p < 0.02].

Table 3 The Association Between Lymphoid Malignancies and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Evidence from seven studies[6,10,12-14,16,19] among people with COVID-19 (N = 101,752), including 841 individuals with lymphoid malignancies, suggests an increase in mortality among people with lymphoid malignancies and COVID-19. Two studies[13,16] were found to have a low threat to internal validity and five studies[6,10,12,14,19] reported a moderate threat to internal validity.

Outcome	Results
	• Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Six cohort studies[6,10,12-14,19] and one case control study[16] (total N = 2,801), among which 841 individuals had a lymphoid malignancy [including 436 individuals with diagnosed non-Hodgkin lymphoma (NHL), 86 with Hodgkin lymphoma (HL), 74 with chronic lymphocytic or lymphoblastic leukemia (CLL), 195 with multiple myeloma (MM), 33 with acute lymphoblastic or lymphocytic leukemia (ALL), and 17 with lymphoma] reported proportions suggesting an increase in mortality and COVID-19 compared to people with no HM. o One study[14] reported a small sample size (N = 92), and two studies[6,12] reported a small number of patients diagnosed with an HM (n = 11)[12] and (n = 17)[6], respectively. Four of the studies[6,10,13,19] reported proportions suggesting no difference in mortality among 101,313 people with COVID-19, of which, 60 people had the diagnosed subtype MM and 27 people had the diagnosed subtype ALL and COVID-19 when compared to people without HM. All seven studies[6,10,12-14,16,19] conducted no statistical analyses for the comparisons, decreasing confidence in the findings.
ICU Admission	Limited data from only one study[16] among patients with COVID-19 are insufficient to determine an association between lymphoid malignancies and ICU admission among patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case control study[16] (N = 159), which included 14 patients with lymphoid malignancies and COVID-19, reported proportions suggesting an increase in ICU admission among people with lymphoid malignancies and COVID-19. ▪ This case control study[16] (N = 159) of 24 patients diagnosed with an HM and COVID-19, among which, 14 had a diagnosed lymphoid malignancy, reported a higher proportion of ICU admission among patients with lymphoid malignancies, including four patients with CLL, five patients with lymphoma, two patients with MM, and three patients with ALL compared to patients with no HM [100.0% (4/4); 80.0% (4/5); 100.0% (2/2); and 66.7% (2/3) vs. 26.4% (28/106), p = NR]. The study reported a low number of patients with the diagnosed subtype CLL and MM in

Outcome	Results
	the study population, and no statistical analysis was conducted for the comparisons, decreasing confidence in the findings.
Intubation	Limited data from only one study[16] are insufficient to determine an association between lymphoid malignancies and intubation in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case control study[16] (N = 159), which included 14 patients with lymphoid malignancies and COVID-19, reported proportions suggesting an increase in intubation among people with lymphoid malignancies and COVID-19. ▪ This case control study[16] of 24 patients diagnosed with an HM and COVID-19 (including four patients with CLL, five patients with lymphoma, two patients with MM, and three patients with ALL) reported a higher proportion of intubation when compared to patients with no HM [100.0% (4/4); 80.0% (4/5); 50.0% (1/2); and 66.7% (2/3) vs. 23.6% (25/106), p = NR]. The study reported a low number of patients with the diagnosed subtype CLL, lymphoma, and MM in the study population, and no statistical analysis was conducted for the comparisons, decreasing confidence in the findings.
Hospitalization	Limited data from only one study[13] are insufficient to determine an association between lymphoid malignancies and hospitalization in people with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[13] (N = 98,951), which included 283 people with lymphoid malignancies, reported proportions suggesting an increase in hospitalization among people with lymphoid malignancies and COVID-19. ▪ This cohort study[13] (N = 98,951), including 513 people diagnosed with a HM and COVID-19, reported a higher proportion of hospitalization among 283 people diagnosed with lymphoid malignancies (including 175 people diagnosed with non-Hodgkin lymphoma, 48 people with HL, and 60 people with MM) compared to people with no HM [18.3% (32/175), 14.6% (7/48), and 13.3% (8/60) vs. 6.79% (6,116/93,558), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings.

Table 4 The Association Between Myeloid Malignancies and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Evidence from five studies[6,10,12,16,19] among persons with COVID-19 (N = 2,709), including 378 patients with myeloid malignancies, suggests an increase in mortality among patients with myeloid malignancies and COVID-19. Two studies[16,19] were found to have a low threat to internal validity and three studies[6,10,12] were found to have a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Four cohort studies[6,10,12,19] and one case control[16] among patients with COVID-19 (N = 2,709), including 378 individuals with myeloid malignancies and COVID-19 [55 individuals had diagnosed acute myeloid leukemia (AML), 158 had myelodysplastic syndrome (MDS), 131 had myeloproliferative neoplasms (MPN), and 34 had chronic myeloid leukemia (CML)]. Three of the five studies reported proportions suggesting an increase in mortality among people with COVID-19 and myeloid malignancies when compared to people with no HM. ○ Three studies[6,12,16] reported a low number of patients diagnosed with an HM and four studies[6,10,12,16] reported a low number of patients with myeloid malignancies (AML, MDS, and CML) in the study population. All five studies conducted no statistical analysis for the comparisons, decreasing confidence in the findings.
ICU Admission	Limited data from only one study[16] are insufficient to determine an association between myeloid malignancies and ICU admission in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case control study[16] of 159 patients with COVID-19, including ten patients with myeloid malignancies, reported proportions suggesting an increase in ICU admission among people with myeloid malignancies and COVID-19. ▪ This case control study[16] (N = 159) which included 24 patients diagnosed with an HM and COVID-19 reported a higher proportion of ICU admission among nine patients with AML and one patient with CML compared to patients with no HM [55.6% (5/9); 100.0% (1/1) vs 26.4% (28/106), p = NR]. The study only reported one patient with the diagnosed subtype CML, and no statistical analysis was conducted for the comparisons, decreasing confidence in the findings.
Intubation	Limited data from only one study[16] are insufficient to determine an association between myeloid malignancies and intubation in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study.

Outcome	Results
	• One case-control study[16] of 159 patients with COVID-19, including ten patients with myeloid malignancies, reported proportions suggesting an increase in intubation among people with myeloid malignancies and COVID-19. ▪ This case-control study[16] (N = 159) of 159 patients, which included 24 patients diagnosed with an HM and COVID-19 (nine of which had diagnosed AML and one had diagnosed CML), reported a higher proportion of intubation when compared to patients with no HM [55.6% (5/9); 100.0% (1/1) vs. 23.6% (25/106), p = NR]. The study only reported one patient with CML who was intubated. No statistical analysis was conducted for this comparison, decreasing confidence in the findings.

Table 5 The Association Between Chronic Lymphocytic or Lymphoblastic Leukemia (CLL) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Evidence from five studies [6,10,14,16,19] of people with COVID-19 (N = 2,613), including 69 people with CLL, suggests an increase in mortality among people with CLL and COVID-19. One study[16] was found to have a low threat to internal validity and four studies [6,10,14,19] reported a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Three cohort studies[10,14,19] and one case control study[16] (N = 1,949) which included 857 individuals diagnosed with an HM and COVID-19 (67 had CCL, reported proportions suggesting an increase in mortality among individuals with CLL and COVID-19. ○ One study[14] reported a low number of patients diagnosed with an HM (n = 92) and two[10,16] reported a low number of individuals with CLL in the study population, (n = 3) and (n = 4). All four studies [10,14,16,19] conducted no statistical analyses for these comparisons, decreasing confidence in the findings. • One cohort study[6] (n = 664) reported only two patients with CLL and COVID-19, which is too small to draw conclusions. ▪ This cohort study[6] (N = 664) which included 17 patients diagnosed with an HM and COVID-19 (two patients had CLL) reported a lower proportion of mortality among the two patients with CLL compared to patients with no HM [0.0% (0/2) vs 9.0% (nr/NR)]. The study reported a low number of patients diagnosed with an HM and with the

Outcome	Results
	diagnosed subtype CLL in the study population, and no statistical analysis was conducted for this comparison, decreasing confidence in the findings.
ICU Admission	Limited data from only one study[16] are insufficient to determine an association between CLL and ICU admission in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case-control study[16] (N = 159) reported four patients with CLL and COVID-19, which is too small to draw conclusions. ▪ This case-control study[16], which included 24 patients diagnosed with an HM and COVID-19, among whom four had CLL, reported a higher proportion of ICU admission when compared to patients with no HM [100.0% (4/4) vs. 26.4% (28/106), p = NR]. The study reported a low number of patients with the diagnosed subtype CLL, and no statistical analysis was conducted for this comparison, decreasing confidence in the findings.
Intubation	Limited data from only one study[16] are insufficient to determine an association between CLL and intubation in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case-control study[16] (N = 159) reported four patients with CLL and COVID-19, which is too small to draw conclusions. ▪ This case-control study[16], (N = 159) which included 24 patients diagnosed with an HM and COVID-19, among whom four had CLL, reported a higher proportion of intubation when compared to patients with no HM [100.0% (4/4) vs. 23.6% (25/106)]. The study reported a low number of patients with the diagnosed subtype CLL, and no statistical analysis was conducted for this comparison, decreasing confidence in the findings.

Table 6 The Association Between Lymphoma and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Limited evidence from two studies[14,16] among people with COVID-19 (N = 251), including 17 patients with lymphoma, suggests an increase in mortality among patients with lymphoma and COVID-19. One study[16] was found to have a low threat to internal validity and one study[14] was found to have a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals.

Outcome	Results
	• Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • One cohort study[14] and one case-control study[16] (N = 251), which included a total of 17 patients with lymphoma, reported limited data suggesting an increase in mortality among patients with lymphoma and COVID-19. ▪ One cohort study[14] (N = 92), which included 39 patients diagnosed with an HM and COVID-19 (among whom 12 had lymphoma), reported limited data suggesting a higher proportion of mortality when compared to patients with no HM [16.7% (2/12) vs 13.2% (7/53), p = NR]. The study reported a low number of HM in the study population and no statistical analysis was conducted for this comparison, decreasing confidence in the findings. ▪ One case-control study[16] (N = 159), which included 24 patients diagnosed with an HM and COVID-19, among whom five had lymphoma, reported a higher proportion of mortality when compared to patients with no HM [80.0% (4/5) vs 16.0% (17/106), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings.
ICU Admission	Limited data from only one study[16] are insufficient to determine an association between lymphoma and ICU admission in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case-control study[16] (N = 159), which included five patients with lymphoma, reported limited data suggesting an increase in ICU admission among patients with lymphoma and COVID-19. ▪ This case-control study[16] (N = 159), which included 24 patients diagnosed with an HM and COVID-19, among whom five had diagnosed lymphoma, reported a higher proportion of ICU admission when compared to patients with no HM [80.0% (4/5) vs 26.4% (28/106), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings.
Intubation	Limited data from only one study[16] are insufficient to determine an association between lymphoma and intubation in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case-control study[16] (N = 159), which included five patients with lymphoma, reported limited data suggesting an increase in intubation among patients with lymphoma and COVID-19.

Outcome	Results
	▪ This case-control study[16] (N = 159) which included 24 patients diagnosed with an HM and COVID-19 (among whom five had diagnosed lymphoma) reported a higher proportion of intubation when compared to patients with no HM [80.0% (4/5) vs 23.6% (25/106), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings.

Table 7 The Association Between Hodgkin's Lymphoma (HL) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Evidence from four studies [10,12,13,19] of people with COVID-19 (N = 100,837), including 81 individuals with HL, suggests an increase in mortality among people with HL and COVID-19. One study[13] was found to have a low threat to internal validity and three studies [10,12,19] were found to have a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Four cohort studies [10,12,13,19] (N = 100,837), which included 81 individuals with HL, reported proportions suggesting an increase in mortality among people with HL and COVID-19. ○ One study[12] reported a low number of patients diagnosed with an HM (n = 11) and one study[12] reported only one person with HL in the study population. All four studies[10,12,13,19] conducted no statistical analyses for the comparisons, decreasing confidence in the findings.
Hospitalization	Limited data from only one study[13] are insufficient to determine an association between HL and hospitalization in people with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[13](N = 98,951), which included 48 people with HL, reported proportions suggesting an increase in hospitalization among people with HL and COVID-19. ▪ This cohort study[13] (N = 98,951), which included 513 people diagnosed with an HM and COVID-19 (48 had HL) reported a higher proportion of hospitalization when compared to people with no HM [14.6% (7/48) vs. 6.79%

Outcome	Results
	(6,116/93,558), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings.

Table 8 The Association Between Non-Hodgkin's Lymphoma (NHL) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Evidence from four studies [6,10,13,19] among patients with COVID-19 (N = 101,313), including 417 individuals with NHL, suggests an increase in mortality among people with NHL and COVID-19. One study[13] was found to have a low threat to internal validity and three studies [6,10,19] reported a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Four cohort studies[6,10,13,19] (N = 101,313), which included 417 individuals with NHL, reported proportions suggesting an increase in mortality among people with NHL and COVID-19. o One study[6] reported a low number of patients with NHL (n = 4), and one study[6] reported a small number of patients diagnosed with an HM (n = 17) in the study population. All four studies [6,10,13,19] conducted no statistical analyses for the comparisons, decreasing confidence in the findings.
Hospitalization	Limited data from only one study[13] are insufficient to determine an association between NHL and hospitalization in people with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One cohort study[13] (N = 98,951) which included 175 people with NHL reported proportions suggesting an increase in hospitalization among people with NHL and COVID-19. ▪ This cohort study[13] (N = 98,951) which included 513 people diagnosed with an HM and COVID-19 (175 had NHL) reported a higher proportion of hospitalization when compared to people with no HM [18.3% (32/175) vs. 6.79%

Outcome	Results
	(6,116/93,558), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings.

Table 9 The Association Between Acute Lymphocytic or Lymphoblastic Leukemia (ALL) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Limited evidence from four studies[6,10,16,19] among patients with COVID-19 (N = 2,521), including 27 individuals with ALL, suggests no difference in mortality among people with ALL and COVID-19. One study[16] was found to have a low threat to internal validity and three studies[6,10,19] were found to have a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Three cohort studies[6,10,19] and one case-control study[16] (N = 2,680), which included 27 individuals with ALL, reported proportions suggesting no difference in mortality among people with ALL and COVID-19. o One study[6] reported a low number of individuals diagnosed with an HM in the study population (n = 17). Three studies[16] [6,10] reported a low number of individuals with the diagnosed subtype ALL in the study population (n = 3), (n = 2), (n = 4), respectively. All four studies[6,10,16,19] conducted no statistical analyses for the comparisons, decreasing confidence in the findings.
ICU Admission	Limited data from only one study[16] are insufficient to determine an association between ALL and ICU admission in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case control study[16] (N = 159) examined three patients with ALL and COVID-19, which is too small to draw conclusions. ▪ This case control study[16] (N = 159), which included 24 patients diagnosed with an HM and COVID-19 (three patients had ALL) reported a higher proportion of ICU admission when compared to patients with no HM [66.7% (2/3) vs

Outcome	Results
	26.4% (28/106), p = NR]. The study reported a low number of patients with the diagnosed subtype ALL, and no statistical analysis was conducted for this comparison, decreasing confidence in the findings.
Intubation	Limited data from only one study[16] are insufficient to determine an association between ALL and intubation in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case control study [16] (N = 159) included three patients with ALL and COVID-19, which is too small to draw conclusions. ▪ This case control study[16] (N = 159), including 24 patients diagnosed with an HM and COVID-19 (three had ALL) reported a higher proportion of intubation when compared to patients with no HM [66.7% (2/3) vs 23.6% (25/106), p = NR]. The study reported a low number of patients with the diagnosed subtype ALL, and no statistical analysis was conducted for this comparison, decreasing confidence in the findings.

Table 10 The Association Between Multiple Myeloma (MM) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Evidence from seven studies[6,10,12-14,16,19] among patients with COVID-19 (N = 101,752), including 176 patients with MM and COVID-19, is inconsistent on the association between mortality and MM. Two studies[13,16] were found to have a low threat to internal validity and five studies[6,10,12,14,19] reported a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals. • Consistency of Association: The evidence is inconsistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Five cohort studies[6,10,12,14,19] and one case-control study[16] (N = 2,801), which included 116 individuals with MM, reported proportions suggesting an increase in mortality among people with MM and COVID-19. ○ Two studies[6,12] (N = 852) reported a low number of patients diagnosed with an HM (n = 11 and n = 17, respectively) and one[16] reported a low number of individuals with MM in the study population (n = 2). All six studies[6,10,12,14,16,19] (N = 2,801) conducted no statistical analyses for the comparisons, decreasing confidence in the findings. • One cohort study[13] (N = 98,951) reported proportions suggesting no difference in mortality among people with MM and COVID-19.

Outcome	Results
	▪ This cohort study[13] (N = 98,951) included 513 people diagnosed with an HM and COVID-19 (60 had MM) reported a lower proportion of mortality when compared to people with no HM [0.0% (0/60) vs. 3.37% (2,631/93,558), p = NR]. The study also reported a lower proportion of mortality among hospitalized patients with MM, compared to people with no HM [2/60 (3.33%) vs. 1,522/11,428 (15.71%), p = NR].
ICU Admission	Limited data from only one study[16] are insufficient to determine an association between MM and ICU admission in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case-control study[16] (N = 159) reported limited data on two patients with MM and COVID-19, which is insufficient to draw conclusions. ▪ This case-control study[16] (N = 159), including 24 patients diagnosed with an HM and COVID-19, reported two patients with MM who were admitted to the ICU, compared to patients with no HM [100.0% (2/2) vs. 26.4% (28/106), p = NR]. The study reported a low number of people with the diagnosed subtype MM, and no statistical analysis was conducted for this comparison, decreasing confidence in the findings.
Intubation	Limited data from only one study[16] are insufficient to determine an association between MM and intubation in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case-control study[16] (N = 159) reported limited data on two patients with MM and COVID-19, which is insufficient to draw conclusions. ▪ This case-control study[16] (N = 159), which included 24 patients diagnosed with an HM and COVID-19 (two patients had MM), reported one patient with MM who was intubated when compared to patients with no HM [50.0% (1/2) vs. 23.6% (25/106), p = NR]. The study reported a low number of people with the diagnosed subtype MM in the study population, and no statistical analysis was conducted for this comparison, decreasing confidence in the findings.
Hospitalization	Limited data from only one study[13] are insufficient to determine an association between MM and hospitalization in people with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study.

Outcome	Results
	• One cohort study[13](N = 98,951) reported proportions suggesting an increase in hospitalization among people with MM and COVID-19 ▪ This cohort study[13] (N = 98,951), including 513 people diagnosed with an HM and COVID-19 (60 patients had MM), reported a higher proportion of hospitalization when compared to people with no HM [13.3% (8/60) vs. 6.79% (6,116/93,558), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings.

Table 11 The Association Between Acute Myeloid Leukemia (AML) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Evidence from four studies[6,10,16,19] among patients with COVID-19 (N = 2,521), which included 52 individuals with AML, suggests an increase in mortality among people with AML and COVID-19. One study[16] was found to have a low threat to internal validity and three studies[6,10,19] were found to have a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Two cohort studies[6,19] and one case-control study[16] which included 51 individuals with AML reported proportions suggesting an increase in mortality among individuals with AML and COVID-19. ▪ One cohort study[19] (N = 1,480), which included 740 people diagnosed with an HM and COVID-19 (40 patients had AML), reported a higher proportion of mortality when compared to people with no HM [20.0% (8/40) vs 6.8% (50/740), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings. ▪ One case-control study[16] (N = 159), which included 24 patients diagnosed with an HM and COVID-19 (nine patients had AML), reported a higher proportion of mortality when compared to patients with no HM [55.6% (5/9) vs. 16.0% (17/106), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings. ▪ One cohort study[6] (N = 664) which included 17 patients diagnosed with an HM and COVID-19 (two patients had AML), reported limited data suggesting a higher proportion of mortality when compared to patients with no HM

Outcome	Results
	[50.0% (1/2) vs 9.0% (nr/NR), p = NR]. The study reported a low number of patients with the diagnosed subtype AML, a low number of patients diagnosed with an HM in the study population, and no statistical analysis was conducted for this comparison, decreasing confidence in the findings. • One cohort study[10] included only one person with AML and COVID-19, which is too small to draw conclusions. ▪ This cohort study[10] (N = 664), which included 54 patients diagnosed with an HM and COVID-19 (only one patient had AML), reported no mortality when compared to the greater NYC region with no HM [0.0% (0/1) vs. 13.7% (149/1090), p = NR]. The study only reported one patient with the diagnosed subtype AML and no statistical analysis was conducted for this comparison, decreasing confidence in the findings.
ICU Admission	Limited data from only one study[16] are insufficient to determine an association between AML and ICU admission in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case-control study[16] (N = 159), which included nine patients with AML, reported proportions suggesting an increase in ICU admission among patients with AML and COVID-19. ▪ This case-control study[16] (N = 159), which included 24 patients diagnosed with an HM and COVID-19 (nine patients had AML), reported a higher proportion of ICU admission when compared to patients with no HM [55.6% (5/9) vs 26.4% (28/106), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings.
Intubation	Limited data from only one study[16] are insufficient to determine an association between AML and intubation in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case-control study[16] (N = 159) which included nine patients with AML reported proportions suggesting an increase in intubation among patients with AML and COVID-19. ▪ This case-control study[16] (N = 159) of 24 patients diagnosed with an HM and COVID-19, among whom nine had AML, reported a higher proportion of intubation when compared to patients with no HM [55.6% (5/9) vs. 23.6% (25/106), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings.

Table 12 The Association Between Myelodysplastic Syndromes (MDS) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Evidence from three studies[6,10,19] among patients with COVID-19 (N = 2,362), including 152 individuals with MDS, suggests an increase in mortality among people with MDS and COVID-19. All three studies[6,10,19] were found to have a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Two cohort studies[10,19], which included 151 individuals with MDS, reported proportions suggesting an increase in mortality among people with MDS and COVID-19. ▪ One cohort study[19] (N = 1,480), which included 740 people diagnosed with an HM and COVID-19 (among whom 146 had MDS), reported a higher proportion of mortality when compared to people with no HM [15.0% (22/146) vs. 6.8% (50/740), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings. ▪ One cohort study [10] (N = 664), which included 54 patients diagnosed with an HM and COVID-19, among whom five had MDS, reported a greater proportion of mortality when compared to the greater NYC region with no HM [60.0% (3/5) vs 13.7% (149/1,090), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings. • One cohort study[6] reported only one patient with MDS and COVID-19, which is insufficient to draw conclusions. ▪ This cohort study[6] (N = 664), which included 17 patients diagnosed with an HM and COVID-19, reported only one patient with MDS compared to patients with no HM [0.0% (0/1) vs. 9.0% (nr/NR)]. The study reported a low number of patients diagnosed with an HM in the study population, only one patient with MDS, and with and no statistical analysis was conducted for this comparison, decreasing confidence in the findings.

Table 13 The Association Between Myeloproliferative Neoplasms (MPN) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Evidence from two studies[10,19] among patients with COVID-19 (N = 1,698), which included 124 individuals with MPN, suggests an increase in mortality among people with MPN and COVID-19. Both studies[10,19] were found to have a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable. Summary of Evidence: • Two cohort studies[10,19], which included 124 individuals with MPN, reported proportions suggesting an increase in mortality among people with MPN and COVID-19. ▪ One cohort study[19] (N = 1,480), including 740 people diagnosed with an HM and COVID-19 (among whom 116 had MPN), reported a slightly higher proportion of mortality when compared to people with no HM [8.6% (10/116) vs. 6.8% (50/740), p = NR]. No statistical analysis was conducted for this comparison, decreasing confidence in the findings. ▪ One cohort study[10] (N = 664) which included 54 patients diagnosed with an HM and COVID-19, among whom seven had MPN, reported a higher proportion of mortality when compared to the greater NYC region with no HM [29.0% (2/7) vs. 13.7% (149/1090)]. The study reported a low number of people with the diagnosed subtype MPN, and no statistical analysis was conducted for this comparison, decreasing confidence in the findings.

Table 14 The Association Between Chronic Myeloid Leukemia (CML) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Limited evidence from four studies among patients with COVID-19 (N = 2,045), which included individuals with CML, is insufficient to determine an association between mortality and CML among people with COVID-19. One study[16] was found to have a low threat to internal validity and three studies[10,12,19] reported a moderate threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals. • Consistency of Association: The evidence is consistent. • Applicability of Association: Settings and populations were applicable.

Outcome	Results
	Summary of Evidence: • Three cohort studies[10,12,19] and one case control study[16] (N = 2,045), which included 829 individuals diagnosed with an HM (among whom 33 had CML), reported proportions suggesting an increase in mortality among people with CML and COVID-19. ○ Three studies[10,12,16] (N = 565) only reported one patient with CML (n = 3), which is insufficient to draw conclusions. All four studies[10,12,16,19] conducted no statistical analyses for the comparisons, decreasing confidence in the findings.
ICU Admission	Limited data from only one study[16] are insufficient to determine an association between CML and ICU admission in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case-control study[16] among patients with COVID-19 (N = 159) reported only one patient with CML, which is insufficient to draw conclusions. ▪ This case-control study[16] (N = 159), including 24 patients diagnosed with an HM and COVID-19, reported one patient with CML compared to patients with no HM [100.0% (1/1) vs. 26.4% (28/106)]. The study only reported one patient with the diagnosed subtype CML, and no statistical analysis was conducted for this comparison, decreasing confidence in the findings.
Intubation	Limited data from only one study[16] is insufficient to determine an association between CML and intubation in patients with COVID-19. The study was found to have a low threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case-control study[16] (N = 159) included only one patient with CML which is insufficient to draw conclusions. ▪ This case-control study[16], which included of 24 patients diagnosed with an HM and COVID-19, included one patient with CML who was intubated compared to patients with no HM [100.0% (1/1) vs. 23.6% (25/106)]. The study only reported one patient with the diagnosed subtype CML, and no statistical analysis was conducted for this comparison, decreasing confidence in the findings.

Table 15 The Association Between Hematologic Malignancy (HM) with Hematopoietic Cell Transplant (HCT) or Hematopoietic Stem Cell Transplant (HSCT) Treatment and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Limited evidence from two studies[2,14] among patients with COVID-19 (N = 1,086), which included 36 patients diagnosed with an HM who underwent HCT or HSCT, is inconsistent and inconclusive on the association between HCT and mortality. One study[14] was found to have a moderate threat to internal validity and one study[2] was found to have a high threat to internal validity. • Strength of Association: No studies reported measures of association. • Precision of Association: No studies reported confidence intervals. • Consistency of Association: The evidence is inconsistent. • Applicability of Association: Settings and populations were applicable. Summary of evidence: • One study[2] (N = 994), which included 32 patients diagnosed with an HM who underwent a HCT, reported proportions suggesting an increase in mortality among patients with COVID-19 and HM who underwent HCT. ▪ This case-control study[2] reported statistically significant higher rates of mortality among patients diagnosed with an HM who underwent HCT when compared to patients without cancer who were matched on age and comorbid status [15.6% (5/32) vs. 5.6% (28/497), p = 0.001]. When comparing groups of cancer patients, the difference was more marked. The study also reported a higher CFR among HCT recipients on immunosuppressive therapy at the time of COVID-19 diagnosis compared to HCT recipients not taking an immunosuppressive medication at the time of COVID-19 diagnosis [33.0% vs 11.5%, p = NR]. The study reported a low number of patients that underwent HCT, a low number of events, did not report statistical methods used, and did not report analysis results, decreasing confidence in the findings. • One cohort study[14] (N = 92), which included 39 patients diagnosed with an HM and COVID-19, reported limited data among four patients diagnosed with an HM who underwent HSCT, which is insufficient to draw conclusions. ▪ This cohort study[14] of patients with COVID-19 reported no mortality among four patients diagnosed with an HM who underwent an autologous or allogenic cell transplant compared to seven deaths among patients with no HM [autologous: 0% (0/3) and allogenic: 0% (0/1) vs 13.2% (7/53), p = NR]. No statistical analysis was conducted for this comparison, the study reported a small sample size, and a low number of patients underwent HSCT, decreasing confidence in the findings.
ICU Admission	Limited data from only one study[2] among patient with COVID-19 (N = 994) is insufficient to determine an association between HCT and ICU admission in patients with COVID-19. The study was found to have a high threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case-control study[2] (N = 994) reported proportions suggesting an increase in ICU admission among patients diagnosed with an HM who received HCT and COVID-19.

Outcome	Results
	▪ This case-control study[2] reported a higher rate of ICU admission among 32 patients diagnosed with an HM who underwent HCT compared to patients without cancer who were matched by age and comorbid status [21.9% (7/32) vs 11.3% (56/497), p = NR]. The study reported a low number of patients that underwent HCT, did not report statistical methods used, reported no p-value for the comparison and did not report analysis results, decreasing confidence in the findings.
Mechanical Ventilation (MV)	Limited data from only one study[2] among patients with COVID-19 are insufficient to determine an association between HCT and MV in patients with COVID-19. The study was found to have a high threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. • One case-control study[2] (N = 994) reported proportions suggesting an increase in MV among patients diagnosed with an HM who receive HCT and COVID-19. ▪ This case-control study[2] reported a higher rate of MV among 32 patients diagnosed with an HM who underwent HCT compared to patients without cancer who were matched by age and comorbid status [15.6% (5/32) vs 7.2% (36/465), p = NR]. The study reported a low number of patients that underwent HCT, did not report statistical methods used, reported no p-value for the comparison, and did not report analysis results, decreasing confidence in the findings.

B.3.b. Extracted Evidence

Table 16 Extracted Studies Reporting the Association Between HM and Severe COVID-19 Outcomes

Study	Population and Setting	Exposure	Definitions	Results
Author: Al-Mozaini[1] **Year:** 2021 **Data Extractor:** MM **Reviewer:** AJ **Study Design:** Cohort	**Population:** N = 184 COVID-19+ **Setting:** Hospital **Data Source:** Case-report and EHR **Location:** Saudi Arabia & Bangladesh	**Medical Condition, n/N (%):** Cancers: 64/184 (34.8%) • Hematologic malignancy: 3/64 (4.7%) **Control/Comparison Group, n/N (%):** No Cancer: 120/184 (65.2%)	**Medical Condition(s):** *Active cancer:* patients undergoing anticancer treatment with curative, radical, adjuvant, or neoadjuvant therapy or treated in the last 12 months with radiotherapy, surgery, and chemotherapy **Severity Measure(s):** NR **Clinical Marker:** NR	**Severe COVID-19:** *Mortality, n/N (%), or median (IQR):* • Hematologic malignancy: 3/3 (100%) • No cancer: 9/120 (7.5%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR

Study	Population and Setting	Exposure	Definitions	Results
Study Objective: To illustrate the clinical characteristics and outcome of patients with and without cancer and presented evidence of the effects of SARS-CoV-2 viral loads among patients with and without cancer. **IVA Score:** 21 (Moderate)	**Study Dates:** June 30—August 7, 2020 **Inclusion Criteria:** Cancer confirmed with COVID-19 who were admitted to the hospitals during the study dates, and COVID-19- positive noncancer adult patients admitted by the same hospitals and same time period were included as a control group. **Exclusion Criteria:** Patients who displayed radiological or clinical diagnosis of COVID-19 but without a positive RT-PCR result.		**Outcome Definitions:** *Mortality:* patients admitted to the hospitals with COVID-19-related symptoms who died during their hospital stay *ICU admission:* Severe COVID-19 *Intubation:* NR *Ventilation:* Mechanical, Severe COVID-19 *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** High SARS-CoV-2 viral loads (high: Ct value <21; medium: Ct value 21–26; and low: Ct value >26) may play a significant role in the overall mortality and severity of COVID-19-positive cancer patients.	**Long-term Sequelae:** NR Non-elective readmissions: NR
Author: Altuntas[2] **Year:** 2021 **Data Extractor:** MM **Reviewer:** AH **Study Design:** Case-Control **Study Objective:** To report the outcome of COVID-19 in hemopoietic cell transplant (HCT) recipients.	**Population:** N = 994 COVID-19+ **Setting:** Hospital **Data Source:** National Ministry of Health database **Location:** Turkey **Study Dates:** March 11—May 29, 2020 **Inclusion Criteria:** People hospitalized for COVID1-9 with a hematological disease that were or were not	**Medical Condition, n/N (%):** Hematological malignancy: 465/994 (46.8%) **Control/Comparison Group, n/N (%):** No Cancer: 497/994 (50.0%)	**Medical Condition(s):** *Hematological malignancy:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* ND *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None.	**Severe COVID-19:** *CFR: Case fatality rate* *Mortality (CFR), n/N (%):* • HM + HCT: 5/32 (15.6%) • HM alone: 55/465 (11.8%) • No Cancer: 28/497 (5.6%) • p = 0.001 *CFR post-hoc analysis:* • *CFR in patients with HM was higher than in patients without cancer, but there was no statistical difference between patients with HM and HCT recipients* *ICU admission, n/N (%):* • HM + HCT: 7/32 (21.9%) • HM alone: 98/465 (21.1%) • No Cancer: 56/497 (11.3%)

Study	Population and Setting	Exposure	Definitions	Results
IVA Score: 17 (High)	recipients of HCT, and COVID-19 patients without cancer. **Exclusion Criteria:** NR			• p = 0.001 *ICU admission post-hoc analysis:* • *Rate of ICU admission in patients with HM was higher than the patients without cancer, but there was no significant difference between patients with HM and HCT recipients* *Duration of ICU admission:* Recipients of a HCT remained in ICU for 12 days, while those that did not undergo an HCT, with either a hematologic malignancy or no cancer, remained in ICU for 6 or 7 days, respectively (p = 0.25). *Mechanical ventilation (MV), n/N (%):* • HM + HCT: 5/32 (15.6%) • HM alone: 70/465 (16.8%) • No Cancer: 36/465 (7.2%) • p = 0.001 *MV post-hoc analysis:* • *MV in patients with HM was significantly higher than the patients without cancer,but there was no statistical difference between patients with HM and HCT recipients* *Duration of Hospitalization, Median (IQR):* Recipients of a HCT remained in the hospital for 13 days, while those that did not undergo an HCT, with either a hematologic malignancy or no cancer, remained hospitalized for 10 days, (p = 0.2). **Severity of Condition:** *Type of HCT:* *Mortality: CFR* • Auto-HCT recipients vs. allo-HCT recipients: p = 0.9 *ICU admission* • Auto-HCT recipients vs. allo-HCT recipients: p = 0.6 *MV support* • Auto-HCT recipients vs. allo-HCT recipients: p = 0.4

Study	Population and Setting	Exposure	Definitions	Results
				Receiving immunosuppressive therapy *Mortality, CFR, n/N (%)* • *HCT+HM +IST: 2/6 (33.3%)* • *HCT+HM – IST: 3/26 (11.5%)* **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Arcani[3] **Year:** 2021 **Data Extractor:** AH **Reviewer:** MM **Study Design:** Cohort **Study Objective:** To compare patients with hematologic malignancies to patients without malignancies, matched by sex and age and hospitalized for COVID-19 at the same time and in the same center.	**Population:** N = 50 COVID-19+ **Setting:** Hospital **Data Source:** Medical records **Location:** France **Study Dates:** September – November 2020 **Inclusion Criteria:** All consecutive adult patients (aged ≥ 18 years) admitted to the hospital between the study dates with WHO-defined hematologic malignancy and laboratory confirmed	**Medical Condition, n/N (%):** Hematological malignancy: 25/50 (50.0%) **Control/Comparison Group, n/N (%):** No hematologic malignancy: 25/50 (50.0%)	**Medical Condition(s):** *Hematologic malignancy:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* 28-day mortality rate *ICU admission:* ICU due to SARS-CoV-2 infection *Intubation:* NR *Ventilation:* Mechanical ventilation due to acute respiratory distress (ARDS) *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%), or Median (IQR):* 28-day mortality rate • Hematologic malignancy: 10/25 (40.0%) • No hematologic malignancy: 1/25 (4.0%) • P < 0.001 *ICU admission, n/N (%), or Median (IQR):* • Hematologic malignancy: 9/25 (36.0%) • No hematologic malignancy: 6/25 (24.0%) • p = NS *Mechanical ventilation, n/N (%), or Median (IQR):* • Hematologic malignancy: 5/25 (20.0%) • No hematologic malignancy: 1/25 (4.0%) • p = NS **Severity of Condition:** NR **Duration of Condition:** NR

Study	Population and Setting	Exposure	Definitions	Results
IVA Score: 24 (Moderate)	SARS-CoV-2 infection. A control cohort consisted of a 1:1 sex- and age-matched randomized patients with symptomatic and laboratory confirmed but without hematologic malignancy admitted into the same hospital. Laboratory confirmed SARS-CoV-2 infection was assessed by RT-PCR on nasopharyngeal samples. **Exclusion Criteria:** NR			**Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Bange[4] **Year:** 2021 **Data Extractor:** AH **Reviewer:** MM **Study Design:** Cohort **Study Objective:** To understand the immunologic determinants of COVID-19 mortality in cancer. **IVA Score:** 24 (Moderate)	**Population:** • MESSI Cohort: N = 130 COVID-19+ **Setting:** Hospital **Data Source:** Electronic medical record **Location:** USA **Study Dates:** April 28 – September 15, 2020 **Inclusion Criteria:** Adult patients with a current or prior diagnosis of cancer and hospitalized with a probable or confirmed diagnosis of COVID-19, as defined by the WHO criteria within	**Medical Condition, n/N (%):** MESSI cohort Cancer: 22/130 (17.0%) • Hematological malignancy: 7/22 (31.8%) **Control/Comparison Group, n/N (%):** MESSI cohort No cancer: 108/130 (83.0%)	**Medical Condition(s):** *Cancer:* hematological malignancy or solid tumor **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* mortality due to COVID-19 *ICU admission:* ICU due to respiratory distress *Intubation:* intubation due to COVID-19 *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** This study included three cohorts from hospitals within the University of	**Severe COVID-19:** *Mortality, n/N (%), or Median (IQR):* MESSI cohort, 28-day mortality • Hematological malignancy: 2/7 (28.6%) • No cancer: 12/108 (11.1%) • Active cancer: 8/22 (36.4%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR

Study	Population and Setting	Exposure	Definitions	Results
	the University of Pennsylvania Health System (UPHS) during the study dates. **Exclusion Criteria:** Patients with low suspicion for COVID-19 infection, or benign tumor diagnosis.		Pennsylvania Health System (UPHS)	
Author: Bernard[5] **Year:** 2021 **Data Extractor:** AH **Reviewer:** AJ **Study Design:** Cohort **Study Objective:** To compare patients hospitalized for COVID-19 with cancer to those without cancer using national data and to study the effect of cancer on the risk of hospital death and intensive care unit (ICU) admission. **IVA Score:** 27 (Low)	**Population:** N = 89,530 COVID-19+ **Setting:** Hospital **Data Source:** French national administrative database **Location:** France **Study Dates:** Series 1: March 1—April 30, 2020 Series 2**:** March 14—April 30, 2020 **Inclusion Criteria:** All patients hospitalized for or with COVID-19 during the study dates, regardless of age. **Exclusion Criteria:** Patients with 2 tumor subtypes.	**Medical Condition, n/N (%):** Cancer: 5,722/89,530 (6.4%) Hematological Cancer: 1,389/89,530 (1.6%) **Control/Comparison Group, n/N (%):** Without Cancer: 83,329/89,530 (93.1%)	**Medical Condition(s):** *Hematological Cancer*: ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* In-hospital death due to COVID-19 *ICU admission:* Intensive care support due to COVID-19 *Intubation: NR* *Ventilation: NR* *Hospitalization:* All patients were hospitalized due to COVID-19 complications *Non-elective readmissions*: NR **Comments:** Stage 1 of the COVID-19 epidemic was declared on 23 February, Stage 2 on 29 February, and Stage 3 on 14 March 2020. During stages 1 and 2, all patients with COVID-19 had to be hospitalized regardless of clinical presentation, while only those requiring hospital care for their	**Severe COVID-19:** *aOR_1: Adjusted odds ratio, hierarchical model using hospitals as the 2nd level model model variables include: sex, dementia, heart failure, chronic respiratory disease, cirrhosis, diabetes, deficiency anemia and pulmonary* *aOR_2: Adjusted odds ratio, hierarchical model using geographical unit as the 2nd level model variables include: sex, dementia, heart failure, chronic respiratory disease, cirrhosis, diabetes, deficiency anemia and pulmonary* *Mortality, n/N (%), or Median (IQR):* <u>Series 1</u> Hematological cancer • aOR_1: 2.2 (95% CI: 2.0 – 2.5), p < 0.01 • aOR_2: 2.8 (95%CI: 2.5 – 3.1), p < 0.01 • Without cancer: reference • Hematological cancer: 470/1,389 (33.8%) • Without cancer: 13,057/83,329 (15.7%) • p < 0.01 *ICU admission, n/N (%), or Median (IQR):* • Hematological cancer: 345/1,389 (24.8%) • Without cancer: 13,655/83,329 (16.4%) • p < 0.01 *Mortality, n/N (%), or Median (IQR):* <u>Series 2</u> Hematological cancer

Study	Population and Setting	Exposure	Definitions	Results
			clinical condition were admitted to hospital during Stage 3.	• aOR_1: 2.7 (95% CI: 2.4 – 3.0), p < 0.01 • aOR_2: 2.1 (95%CI: 1.9 – 2.4), p < 0.01 • Without cancer: reference • Hematological cancer: 428/1,389 (31.0%) • Without cancer: 12,251/83,329 (15.0%) • p < 0.01 *ICU admission, n/N (%), or Median (IQR):* • Hematological cancer: 320/1,389 (23.0%) • Without cancer: 12,888/83,329 (15.5%) • p < 0.01 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *ICU admission, n/N (%), or Median (IQR):* <u>Series 1</u> Age <40 • Hematological cancer: aOR: 10.4 (95% CI: 5.5 – 19.9), p = NR • Without cancer: ref 41-50 • Hematological cancer: aOR: 3.7 (95% CI: 2.0 – 6.7), p = NR • Without cancer: ref 51-80 • Hematological cancer: aOR: 1.5 (95% CI: 1.3 – 1.8), p = NR • Without cancer: ref 81-90 • Hematological cancer: aOR: 1.0 (95% CI: 0.7 – 1.5), p = NR • Without cancer: ref

Study	Population and Setting	Exposure	Definitions	Results
				>90 • Hematological cancer: aOR: 0.5 (95% CI: 0.1 – 3.4), p = NR • Without cancer: ref <u>Series 2</u> *ICU admission, n/N (%), or Median (IQR):* Age <40 • Hematological cancer: aOR: 10.6 (95% CI: 5.5 – 20.3), p = NR • Without cancer: ref 41-50 • Hematological cancer: aOR: 3.3 (95% CI: 1.8 – 6.2), p = NR • Without cancer: ref 51-80 • Hematological cancer: aOR: 1.5 (95% CI: 1.3 – 1.8), p = NR • Without cancer: ref 81-90 • Hematological cancer: aOR: 1.1 (95% CI: 0.7 – 1.6), p = NR • Without cancer: ref >90 • Hematological cancer: aOR: 0.6 (95% CI: 0.1 – 4.3), p = NR • Without cancer: ref **Long-term Sequelae:** Non-elective readmissions: NR
Author: Chai[6] **Year:** 2021 **Data Extractor:** MM **Reviewer:** AH **Study Design:** Cohort	**Population:** N = 664 COVID-19+ **Setting:** 4 hospitals **Data Source:** EHR **Location:** China **Study Dates:** January 1—March 18, 2020	**Medical Condition, n/N (%):** Cancer: 166/664 (25.0%) Hematologic malignancy: 17/166 (10%) • Lymphoid malignancy: 14/166 (8.0%) ○ Multiple myeloma: 6/166 (4.0%)	**Medical Condition(s):** *COVID-19 disease severity:* defined according to World Health Organization (WHO) guidelines *Primary tumor subtypes:* classified by the WHO Classification of Tumors series **Severity Measure(s):**	**Severe COVID-19:** *aHR: Adjusted Hazard Ratio; Cox proportional hazards ratio; included model variables: age, sex* *HR: Hazard Ratio* *Mortality, n/N (%), or Median (IQR):* *Hematologic malignancy:* • HR: 9.01 (95% CI: 4.65 - 17.49), p < 0.001 • aHR: 11.2 (2.2 - 56.9), p = NR • 8/17 (47.0%)

Study	Population and Setting	Exposure	Definitions	Results
Study Objective: To generate a representative sample of cancer patients with COVID-19 from four hospitals. **IVA Score:** 24 (Moderate)	**Inclusion Criteria:** Cancer patients admitted to the four hospitals with laboratory confirmation of SARS-CoV-2 virus infection by RT-PCR test and active cancer during the study dates. **Exclusion Criteria:** At the 1-year follow-up, 56 cancer COVID-19 patients were excluded because 49 patients died and seven patients could not be reached, and 70 COVID-19 patients were excluded because 44 patients died, and 26 patients lost contact.	○ Non-Hodgkin lymphoma: 4/166 (2.0%) ○ Chronic lymphoblastic leukemia: 2/166 (1.0%) ○ Acute lymphoblastic leukemia: 2/166 (1.0%) • Myeloid malignancy: 3/166 (2.0%) ○ Acute myelogenous leukemia: 2/166 (1.0%) ○ Myelodysplastic syndrome: 1/166 (1.0%) **Control/Comparison Group, n/N (%):** No cancer: 498/664 (75.0%)	**Clinical Marker:** **Outcome Definitions:** *Mortality:* death from COVID-19, and 1-year all-cause mortality *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** Compared with the COVID-19 no cancer cohort, COVID-19 patients with hematologic, brain, nasopharyngeal, digestive system, and lung malignancies showed a significantly high risk of mortality (44% vs 9%, P < .001). The 1-year all-cause mortality was highest among patients with hematologic malignancies (59.0%) compared to nasopharyngeal, brain, and skin tumors (45.0%), digestive system neoplasm (43.0%), lung cancers (32.0%), genitourinary (14.0%), female genital (13.0%), breast (11.0%), and thyroid tumors (0.0%).	*1-year all-cause mortality, n/N (%), or Median (IQR):* • Hematologic malignancy: 11/17 (65.0%) • No HM: NR/NR (9.0%) • p < 0.001 **Severity of Condition:** *Mortality, n/N (%), or Median (IQR):* Lymphoid malignancy: 7/14 (50.0%) • Multiple myeloma: 4/6 (67%.0) • Non-Hodgkin lymphoma: 1/4 (25.0%) • Chronic lymphoblastic leukemia: 0/2 (0.0%) • Acute lymphoblastic leukemia: 2/2 (100.0%) Myeloid malignancy: 1/3 (33.3%) • Acute myelogenous leukemia: 1/2 (50.0%) • Myelodysplastic syndrome: 0/1 (0.0%) *1-year all-cause mortality, n/N (%), or Median (IQR):* Lymphoid malignancy: 9/14 (64.0%) • Multiple myeloma: 5/6 (83%.0) • Non-Hodgkin lymphoma: 2/4 (50.0%) • Chronic lymphoblastic leukemia: 0/2 (0.0%) • Acute lymphoblastic leukemia: 2/2 (100.0%) Myeloid malignancy: 2/3 (67.0%) • Acute myelogenous leukemia: 2/2 (100.0%) • Myelodysplastic syndrome: 0/1 (0.0%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR

Study	Population and Setting	Exposure	Definitions	Results
				Long-term Sequelae: Non-elective readmissions: • OR: 5 (95% CI: 1.95-12.76) • Cirrhosis (& COVID-19): 13/29 (44.8%) • No cirrhosis (& COVID-19): 13/93 (14.0%) • p=0.002
Author: Dai[7] **Year:** 2020 **Data Extractor:** MM **Reviewer:** AJ **Study Design:** Cohort **Study Objective:** **IVA Score:** 26 (Low)	**Population:** N = 641 COVID-19+ **Setting:** 14 hospitals **Data Source:** Medical records **Location:** China **Study Dates:** January 1—February 24, 2020 **Inclusion Criteria:** COVID-19 patients with cancer from 14 hospitals and COVID-19 patients without cancer (matched by the same hospital, hospitalization time, and age) were randomly selected as the control group. **Exclusion Criteria:** Younger COVID-19 patients without cancer.	**Medical Condition, n/N (%):** Cancer: 105/641 (16.4%) • Blood cancer: 9/105 (8.57%) **Control/Comparison Group, n/N (%):** No Cancer: 536/641 (83.6%)	**Medical Condition(s):** *Hematologic cancer:* including leukemia, lymphoma, and myeloma **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* ND *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aOR: Multivariable logistic regression; included model variables: age, sex, diabetes, hypertension, smoking, and COPD at admission* *Mortality, n/N (%), or Median (IQR):* *Blood cancer vs no cancer* • aOR: 9.07 (95% CI: 2.16 - 38.18), p < 0.01 • Blood cancer: 3/9 (33.33%) *ICU Admission, n/N (%), or Median (IQR):* *Blood cancer vs no cancer* • aOR: 9.66 (95% CI: 2.49 – 37.36), p < 0.01 • Blood cancer: 4/9 (44.44%) *Invasive mechanical ventilation, n/N (%), or Median (IQR):* *Blood cancer vs no cancer* • aOR: 38 (95% CI: 5.95 - 242.63), p < 0 .01 • Blood cancer: 2/9 (22.22%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR

Study	Population and Setting	Exposure	Definitions	Results
Author: Fu[8] **Year:** 2021 **Data Extractor:** AH **Reviewer:** MM **Study Design:** Case-control **Study Objective:** To study the risk factors associated with severe outcomes in hospitalized coronavirus disease 2019 (COVID-19) patients with cancer. **IVA Score:** 25 (Moderate)	**Population:** N = 4,186 COVID-19+ **Setting:** Hospital **Data Source:** Medical records **Location:** New York, USA **Study Dates:** March 1 - May 15, 2020 **Inclusion Criteria:** Patients 18+ years old positive for SARS-CoV-2 that were admitted to 1 of the hospitals during the study. Sars-CoV-2 was tested by reverse transcription polymerase chain reaction. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Active cancer: 233/4,186 (5.6%) • Hematologic cancer: 69/233 (29.6%) **Control/Comparison Group, n/N (%):** No Cancer: 3,460/4,186 (82.7%) Not-active cancer: 492/4,186 (11.8%)	**Medical Condition(s):** *Active cancer:* new diagnosis of cancer on or after March 1, 2019 (1 year before data collection), or ongoing cancer-directed therapy on or after March 1, 2019 *Solid tumor:* those originating from the following organs: lung, prostate, breasts, liver, skin, gastrointestinal tract, and hepatobiliary system *Hematologic cancer:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%), or Median (IQR):* • Hematologic cancer: 33/69 (47.8%) • No cancer: 683/3,460 (19.7%) *ICU admission, n/N (%), or Median (IQR):* • Hematologic cancer: NR/69 (27.4%) • No cancer: 402/3,460 (11.6%) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Kalicinska[9] **Year:** 2021 **Data Extractor:** MM **Reviewer:** AH **Study Design:** Cohort	**Population:** N = 523 COVID-19+ **Setting:** Hospital **Data Source:** NR **Location:** Poland **Study Dates:** March 2020—March 2021	**Medical Condition, n/N (%):** Hematologic cancer: 125/523 (24.0%) **Control/Comparison Group, n/N (%):** No Hematologic cancer: 398/523 (76.1%)	**Medical Condition(s):** *Hematologic cancer:* ND **Severity Measure(s):** **Clinical Marker:** *Endothelial activation and stress index (EASIX):* calculated by the formula LDH (U/L) × Creatinine (mg/dL)/platelet count (109/L), and applied as a tool to assess the outcome of acute graft-	**Severe COVID-19:** *HR: Hazard ratio* *Mortality, n/N (%), or Median (IQR):* • Hematologic malignancy: 46/125 (37.0%) • No hematologic malignancy: 90/398 (23.0%) • $p < 0.01$ *Mechanical ventilation, n/N (%), or Median (IQR):* • Hematologic malignancy: 24/125 (19.2%) • No hematologic malignancy: 50/398 (12.7%)

Study	Population and Setting	Exposure	Definitions	Results
Study Objective: To evaluate the EASIX index in the context of clinical outcome and survival in both hematological and non-hematological COVID-19 patients. **IVA Score:** 24 (Moderate)	**Inclusion Criteria:** Patients hospitalized at the 7 medical centers with COVID-19. Sars-CoV-2 infection underwent molecular confirmation molecular confirmation (defined by a positive real-time reverse-transcriptase J. Clin. Med. 2021, 10, 4373 3 of 16 polymerase chain reaction (RT-PCR) assay using nasal and pharyngeal swab specimens). **Exclusion Criteria:** NR		versus-host disease after allogeneic stem cell transplantation, as well as prognosis in patients with lower-risk myelodysplastic syndromes who are not candidates for allogeneic stem cell transplantation **Outcome Definitions:** *Mortality:* In-hospital mortality *ICU admission:* ND *Intubation:* NR *Ventilation:* Mechanical ventilation *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** EASIX was the strongest predictor of intensive care unit (ICU) admission and in-hospital mortality.	• p = 0.07 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Mehta[10] **Year:** 2020 **Data Extractor:** AH **Reviewer:** AJ **Study Design:** Cohort **Study Objective:** To investigate the risk posed by COVID-19 to the cancer population with more	**Population:** N = 218 COVID-19+ **Setting:** Community **Data Source:** Electronic medical records **Location:** Ny, USA **Study Dates:** March 18 – April 8, 2020 **Inclusion Criteria:** NR **Exclusion Criteria:** Cases identified as having benign neoplasms.	**Medical Condition, n/N (%):** Hematologic malignancies (HM): 54/218 (25.0%) • Non-Hodgkin lymphoma (NHL): 15/54 (28.0%%) • Myelodysplastic syndromes (MDS): 5/54 (9.3%) • Myeloproliferative neoplasm (MPN): 7/54 (13.0%) • Acute lymphoblastic leukemia (ALL): 4/54 (7.4%) • Acute myeloid leukemia (AML): 1/54 (1.9%)	**Medical Condition(s):** *Hematologic malignancies:* ND *Myeloid malignancy:* ND *Lymphoid malignancy:* ND **Severity Measure(s):** *Non-Hodgkin lymphoma (NHL):* ND *Myelodysplastic syndromes (MDS):* ND *Myeloproliferative neoplasm (MPN):* ND *Acute lymphoblastic leukemia (ALL)*: ND *Acute myeloid leukemia (AML):* ND *Multiple myeloma (MM):* ND *Chronic myeloid leukemia (CML):* ND	**Severe COVID-19:** *Mortality, n/N (%), or Median (IQR):* • HM: 20/54 (37.0%) • Greater NYC region: 149/1090 (13.7%) **Severity of Condition:** *Mortality, n/N (%), or Median (IQR):* • Myeloid malignancy: 6/14 (43.0%) • Lymphoid malignancy: 14/40 (35.0%) • NHL: 5/15 (33.3%) • MDS: 3/5 (60.0%) • MPN: 2/7 (29.0%) • ALL: 0/4 (0.0%) • AML: 0/1 (0.0%) • MM: 5/13 (38.5%) • CML: 1/1 (100.0%) • HL: 3/5 (60.0%)

Study	Population and Setting	Exposure	Definitions	Results
granular data regarding cancer type and active treatment, and identify factors that placed patients with cancer at highest risk of fatality from COVID-19. **IVA Score:** 24 (Moderate)		• Multiple myeloma (MM): 13/54 (24.1%) • Chronic myeloid leukemia (CML): 1/54 (%1.9) • Hodgkin lymphoma (HL): 5/54 (9.3%) • Chronic lymphoid leukemia (CLL): 3/54 (5.6%) Myeloid malignancy: 14/218 (6.4%) Lymphoid malignancy: 40/218 (18.3%) **Control/Comparison Group, n/N (%):** Greater NYC region (age- and sex-matched control): 1,090/NR	*Hodgkin lymphoma (HL):* ND *Chronic lymphoid leukemia (CLL):* ND **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* death due to COVID-19 *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	• CLL: 1/3 (33.3%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Passamonti[11] **Year:** 2020 **Data Extractor:** AJ **Reviewer:** AH **Study Design:** Cohort **Study Objective:** To collect and analyze data from adult patients with hematological malignancies who required	**Population:** N = 536 COVID-19+ **Setting:** Hospital (in- and out- patient) **Data Source:** EMR or clinical charts **Location:** Italy **Study Dates:** Feb 25 - June 22, 2020 **Inclusion Criteria:** Consecutive adult patients (aged ≥18 years) with any comorbidity who were admitted between Feb	**Medical Condition, n/N (%):** Hematologic malignancy: 536/582 (92.1%) • Myeloid neoplasms: 175/536 (33%) • Myeloproliferative neoplasms: 83/536 (15%) • Myelodysplastic syndromes: 41/536 (8%) • Acute myeloid leukemias: 51/536 (10%) • Acute lymphoblastic leukemias: 16/536 (3%) • Hodgkin lymphoma: 17/536 (3%)	**Medical Condition(s):** *Hematological malignancy:* ND **Severity Measure(s):** NR *Myeloid neoplasms:* ND *Myeloproliferative neoplasms:* ND *Myelodysplastic syndromes:* ND *Acute myeloid leukaemias:* ND *Acute lymphoblastic leukaemias:* ND *Hodgkin lymphoma:* ND *Non-Hodgkin lymphomas:* ND *Chronic lymphoproliferative neoplasms:* ND *Indolent lymphomas:* ND *Aggressive lymphomas:* ND *Plasma cell neoplasms:* ND **Clinical Marker:** NR	**Severe COVID-19:** *HR: Hazard ratio* *MR: Mortality ratio* *Mortality, n/N (%), or Median (IQR):* HM vs. general Italian population • MR: 2.04 (95% CI 1.77 – 2.34) **Severity of Condition:** NR *Mortality, n/N (%), or Median (IQR):* Myeloproliferative neoplasms: • reference • 27/83 (32.5%) Myelodysplastic syndromes: • HR: 1.58 (0.69 – 3.62), p = NR • 20/41 (48.8%)

Study	Population and Setting	Exposure	Definitions	Results
hospitalization for COVID-19 **IVA Score:** 26 (Low)	25 and May 18, 2020. Presence of a WHO-defined hematological malignancy and symptomatic and laboratory-confirmed SARS-CoV-2 infection, tested by RT-PCR on nasopharyngeal swabs. **Exclusion Criteria:** NR	• Non-Hodgkin lymphomas: 222/536 (41%) • Chronic lymphoproliferative neoplasms: 69/536 (13%) • Indolent lymphomas: 54/536 (10%) • Aggressive lymphomas: 99/536 (18.4%) • Plasma cell neoplasms: 106/536 (20%) **Control/Comparison Group, n/N (%):** General Italian population: n/N = NR	**Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* ND *Ventilation:* ND *Hospitalization:* ND *Non-elective readmissions*: ND **Comments:** Although the prespecified plan was to report on the epidemiological outcomes at 6 months of follow-up, they reported these outcomes early because the majority of patients had completed their hospital stay. Mortality estimates for COVID-19 in the general Italian population were obtained from the Bollettino Sorveglianza Integrato of the Isituto Superiore di Sanità, released on June 23, 2020.	Acute myeloid leukaemias: • HR: 3.49 (1.56 – 7.81), p = NR • 22/51 (34.1%) Acute lymphoblastic leukaemias: • HR: 1.65 (0.46 – 5.94), p = NR • 3/16 (18.8%) Hodgkin lymphoma: • HR: 1.30 (0.36 – 4.66), p = NR • 3/17 (17.6%) Chronic lymphoproliferative neoplasms: • HR: 1.64 (0.77 – 3.51), p = NR • 22/69 (31.9%) Indolent lymphomas: • HR: 2.19 ((1.07 – 4.48), p = NR • 21/54 (39%) Aggressive lymphomas: • HR: 2.56 (1.34 – 4.89), p = NR • 41/99 (44%) Plasma cell neoplasms: • HR: 2.48 (1.31 – 4.69) p = NR • 39/106 (36.8%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR *Mortality, n/N (%), or Median (IQR):* Age (per year increase) • HR: 1.03 (95%CI: 1.01 – 1.05), p = NR *ICU admission, n/N (%), or Median (IQR):* Age (per year increase)

Study	Population and Setting	Exposure	Definitions	Results
				• HR: 0.97 (95% CI: 0.96 – 0.98), p = NR *Mortality, n/N (%), or Median (IQR):* Sex • Male: reference • Female HR: 0.86 (95% CI: 0.60 - 1.24), p = NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Ramachandran[12] **Year:** 2020 **Data Extractor:** MM **Reviewer:** AH **Study Design:** Cohort **Study Objective:** To analyze the clinical characteristics of cancer patients with COVID-19 and compare the differences with the non-cancer group to identify risk factors that will help stratify patients and potentially open doors for early and effective interventions for better outcomes in cancer patients.	**Population:** N = 188 COVID-19+ **Setting:** Hospital **Data Source:** Medical records **Location:** USA **Study Dates:** March 18 — April 30, 2020 **Inclusion Criteria:** Adult patients more than 18 years old, admitted to the hospital with COVID-19 infection as evidenced by laboratory confirmation by RT-PCR and patients with a history of cancer, and non-cancer patients admitted with COVID-19. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Cancer: 53/188 (28.2%) Hematological cancer: 11/53 (20.0%) • Myeloma: 6/53 (11.3%) • Chronic myeloid leukemia (CML): 1/53 (1.9%) • Chronic myelomonocytic leukemia (CMML): 1/53 (1.9%) • Hodgkin lymphoma: 1/53 (1.9%) • Prostate & hematological: 1/53 (1.9%) **Control/Comparison Group, n/N (%):** No Cancer: 135/188 (71.8%)	**Medical Condition(s):** ND *Hematological cancer:* ND **Severity Measure(s):** ND *Myeloma:* ND *CML:* ND *CMML:* ND *Hodgkin lymphoma:* ND **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%), or Median (IQR):* *Overall cohort cancer:* • Hematologic cancer: 6/11 (55.0%) • No cancer: 49/135 (36.3%) **Severity of Condition:** *Mortality, n/N (%), or Median (IQR):* • Myeloma: 3/6 (50.0%) • CML: 1/1 (100.0%) • CMML: 1/1 (100.0%) • Hodgkin lymphoma: 1/1 (100.0%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR

Study	Population and Setting	Exposure	Definitions	Results
IVA Score: 25 (Moderate)				
Author: Roel[13] **Year:** 2021 **Data Extractor:** MM **Reviewer:** AH **Study Design:** Cohort **Study Objective:** To describe the associations between cancer and the risks of COVID-19 diagnosis, hospitalization with COVID-19 and COVID-19-related death, overall and by different population subgroups, using real-world data. **IVA Score:** 26 (Low)	**Population:** N = 98,951 COVID-19+ **Setting:** Population **Data Source:** Information System for Research in Primary Care **Location:** Spain **Study Dates:** March 1 – May 6, 2020 **Inclusion Criteria:** Adults (aged 18 years or older) registered in the SIDIAP database with at least 1 year of prior history observation available. **Exclusion Criteria:** Patients who had a record of a secondary cancer before a record of a primary cancer, patients with a clinical diagnosis or positive test result for COVID-19 prior to index date and patients hospitalized or living in a nursing home at index date.	**Medical Condition, n/N (%):** Cancer: 5,393/98,951 (5.5%) Hematological cancer: 513/98,951 (0.5%) • Leukemia: 127/513 (24.8%) • Non-Hodgkin lymphoma: 175/513 (34.1%) • Hodgkin lymphoma: 48/513 (9.4%) • Multiple myeloma: 60/513 (11.7%) • Other hematological: 103/513 (20.1%) **Control/Comparison Group, n/N (%):** General population, No Cancer: 93,558/98,951 (94.5%)	**Medical Condition(s):** *Cancer*: any diagnosis of a primary invasive solid or hematological cancer, excluding non-melanoma skin cancer, prior to the index date. The International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) was used to identify cancer diagnoses: C00 to C96, except C44 (non-melanoma skin cancer) and C77-C79 (secondary cancers). **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* overall 28-day mortality *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* hospitalized for COVID-19 *Non-elective readmissions*: NR **Comments:** Patients started the follow-up at the general population and then could transition to three other states: diagnosed with COVID-19 (in an outpatient setting), hospitalized with COVID-19, and death.	**Severe COVID-19:** *aHR: adjusted hazard ratio, model variables include: age, sex, the MEDEA deprivation index, smoking status and comorbidities (autoimmune conditions, chronic kidney disease, chronic obstructive pulmonary disease, dementia, heart disease, hyperlipidemia, hypertension, type-2 diabetes and obesity* *Mortality:* *Diagnosed with COVID-19 to death, n/N (CI at 45 days)* Hematological cancer vs no cancer • aHR: 1.08 (95% CI: 0.84 - 1.39), p = NR • HM: 64/513 (12.5%) • No HM: 2,631/93,558 (3.37%) *Hospitalized with COVID-19 to death, n/N (CI at 45 days)* Hematologic cancer vs no cancer • aHR: 1.73 (1.31 – 2.28), p = NR • HM: 53/513 (10.3%) • No cancer: 1,522/11,428 (15.71%) *Hospitalization, n/N (%), or Median (IQR):* *Diagnosed with COVID-19 to Hospitalization, n/N (CI at 45 days)* Hematological cancer vs no cancer • aHR: 1.37 (95% CI: 1.10 - 1.71), p = NR • HM: 80/513 (15.6%) • No cancer: 6,116/93,558 (6.79%) **Severity of Condition:** *Mortality:* *Diagnosed with COVID-19 to death* • Leukemia: 9/127 (7.1%) • Non-Hodgkin lymphoma: 37/175 (21.1%) • Hodgkin lymphoma: 7/48 (14.6%) • Multiple myeloma: 0/60 (0.0%) • Other hematological: 11/103 (11.0%) *Hospitalized with COVID-19 to death*

Study	Population and Setting	Exposure	Definitions	Results
			Six different transitions were possible: from the general population to either diagnosed with COVID-19, hospitalized with COVID-19 (ie, direct hospitalization) or death; from diagnosed to either hospitalized with COVID-19 or death and from hospitalized with COVID-19 to death.	• Leukemia: 6/127 (4.7%) • Non-Hodgkin lymphoma: 27/175 (15.4%) • Hodgkin lymphoma: 9/48 (19.0%) • Multiple myeloma: 2/60 (3.33%) • Other hematological: 9/103 (8.7%) *Hospitalization, n/N (%), or Median (IQR): Diagnosed with COVID-19 to Hospitalization* • Leukemia: 14/127 (11.0%) • Non-Hodgkin lymphoma: 32/175 (18.3%) • Hodgkin lymphoma: 7/48 (14.6%) • Multiple myeloma: 8/60 (13.3%) • Other hematological: 19/103 (18.4%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality* Years since cancer diagnosis Overall • aHR: 108 (0.84 – 1.39) ≥5 years • aHR: 1.02 (0.72 – 1.43) 1-5 years • aHR: 0.89 (0.57 – 1.38) <1 year • aHR: 3.11 (1.67 – 5.81) *Hospitalization* Years since cancer diagnosis Overall • aHR: 1.37 (1.10 - 1.71)

Study	Population and Setting	Exposure	Definitions	Results
				≥5 years • aHR: 0.96 (0.68 - 1.36) 1-5 years • aHR: 1.85 (1.31 - 2.60) <1 year • aHR: 2.24 (1.34 - 3.76) **Long-term Sequelae:** Non-elective readmissions: NR
Author: Sanchez-Pina[14] **Year:** 2020 **Data Extractor:** AH **Reviewer:** MM **Study Design:** Cohort **Study Objective:** To describe infection in a consecutive series of patients with hematological malignancies who were diagnosed with COVID-19 in the greater Madrid area. **IVA Score:** 24 (Moderate)	**Population:** N = 92 COVID-19+ **Setting:** Community **Data Source:** Medical records **Location:** Spain **Study Dates:** March 7, 2020 – April 7, 2020 **Inclusion Criteria:** For the control group, selected patients were similar to the hematological cases with respect to age and severity index values at admission, but they did not have any history of cancer. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Hematological malignancies (HM): 39/92 (42.4%) • Multiple Myeloma: 12/39 (30.8%) • Lymphoma: 12/39 (30.8%) • Chronic Lymphocytic Leukemia: 6/39 (15.4%) • Acute leukaemia and MDS: 5/39 (12.8%) • cMPN: 2/39 (5.1%) • Histiocytosis: 2/39 (5.1%) **Control/Comparison Group, n/N (%):** No cancer (matched control): 53/92 (57.6%)	**Medical Condition(s):** *Hematological malignancies (HM):* a heterogeneous group of diseases with a high risk of bacterial, fungal, and viral infections **Severity Measure(s):** *Multiple Myeloma:* ND *Lymphoma:* ND *Chronic Lymphocytic Leukemia:* ND *Acute leukaemia and MDS:* ND *cMPN:* ND *Histiocytosis:* ND **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Death due to COVID-19 *ICU admission:* ICU admission due to COVID-19 complications *Intubation:* NR *Ventilation:* NR *Hospitalization:* Hospitalized due to COVID-19 *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%), or Median (IQR):* • OR: 3.68 (95% CI: 1.31 - 10.3), p = 0.013 • aOR: 6.65 (95% CI: 1.86 - 23.68), p = 0.003 • HM: 14/39 (35.9%) • Non-HM: 7/53 (13.2%) • p = 0.01 *ICU admission, n/N (%), or Median (IQR):* • HM: 1/39 (2.6%) • Non-HM: 7/53 (13.2%) • p = 0.73 *Hospitalization, n/N (%), or Median (IQR):* • HM: 34/39 (87.2%) • Non-HM: 46/53 (86.8%) • p = 0.96 **Severity of Condition:** *Mortality, n/N (%), or Median (IQR):* • Multiple Myeloma: 2/12 (16.7%) • Lymphoma: 2/12 (16.7%) • Chronic Lymphocytic Leukemia: 5/6 (83.3%) • Acute leukaemia and MD: 3/5 (60.0%) • cMPN: 0/2 • Histiocytosis: 2/2 (100.0%) *Mortality, n/N (%), or Median (IQR):* *Treatment*

Study	Population and Setting	Exposure	Definitions	Results
				• Autogenic cell transplant: 0/3 (0.0%) • Allogenic cell transplant: 0/1 (0.0%) **Duration of Condition:** NR **Comorbid Conditions:** *Mortality, n/N (%), or Median (IQR):* Hypertension • HM: 10/14 (71.4%) • Non-HM: 4/7 (57.1%) • P = 0.51 **Risk Markers:** *Mortality, n/N (%), or Median (IQR):* Age (mean, range) • HM: 74 (39 – 88) • Non-HM: 75.6 (62 – 89) • P = 0.81 **Long-term Sequelae:** Non-elective readmissions: NR
Author: Shoumariyeh[15] **Year:** 2020 **Data Extractor:** AH **Reviewer:** MM **Study Design**: Cohort **Study Objective:** To determine the influence of cancer on morbidity and mortality of hospitalized Covid-19 cancer patients	**Population:** N = 78 COVID-19+ **Setting:** Hospital **Data Source:** Medical records **Location:** Germany **Study Dates:** February 27 – April 10, 2020 **Inclusion Criteria:** Hospitalized patients at the UHF with an active hematological, solid cancer or cancer in remission, and concomitant SARS-CoV-	**Medical Condition, n/N (%):** Cancer: 39/78 (50.0%) Hematological malignancy: 10/39 (25.6%) • Lymphoma/Myeloma: 7/10 (70.0%) • Leukemia: 3/10 (30.0%) **Control/Comparison Group, n/N (%):** Age-matched Noncancer: 39/78 (50.0%)	**Medical Condition(s):** *Hematological malignancy:* lymphoma, myeloma, or leukemia **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* death due to COVID-19 *ICU admission:* ICU admission as a COVID-19 outcome *Intubation:* NR *Ventilation:* mechanical or non-invasive as a COVID-19 outcome *Hospitalization:* hospitalized due to COVID-19 *Non-elective readmissions*: NR	**Severe COVID-19:** *Mortality, n/N (%), or Median (IQR):* • Hematological malignancy: 2/10 (20.0%) • Noncancer: 14/39 (35.9%) *ICU admission, n/N (%), or Median (IQR):* • Hematological malignancy: 7/10 (70.0%) • Noncancer: 14/39 (35.9%) *Mechanical ventilation, n/N (%), or Median (IQR):* • Hematological malignancy: 3/10 (30.0%) • Noncancer: 11/39 (28.2%) *Non-invasive ventilation, n/N (%), or Median (IQR):* • Hematological malignancy: 4/10 (40.0%) • Noncancer: 4/39 (10.3%) **Severity of Condition:** NR

Study	Population and Setting	Exposure	Definitions	Results
compared to age-matched hospitalized noncancer patients with COVID-19. **IVA Score:** 25 (Moderate)	2 infection confirmed by reverse-transcriptase polymerase chain reaction (RT-PCR) assay. For the control cohort, 39 age-matched hospitalized patients with confirmed Covid-19 from the same time span without a cancer diagnosis were recruited. **Exclusion Criteria:** NR		**Comments:** None	**Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality, n/N (%), or Median (IQR):* Age ≥65 years • HR: 6.22, p = 0.0156 **Long-term Sequelae:** Non-elective readmissions: NR
Author: Sorouri[16] **Year:** 2020 **Data Extractor:** AH **Reviewer:** AJ **Study Design:** Case-control **Study Objective:** To determine the prognosis of patients with current or previous cancer with neither PCR-confirmed COVID-19 infection or a probable diagnosis according to chest CT scan. **IVA Score:** 25 (Low)	**Population:** N = 159 COVID-19+ **Setting:** Hospital **Data Source:** Medical records **Location:** Iran **Study Dates:** February 25– April 21, 2020 **Inclusion Criteria:** patients with COVID-19 with history of cancer, matched with noncancerous patients with COVID-19 as controls. COVID-19 was confirmed by SARS-CoV-2 RNA using the real-time reverse transcription-polymerase chain reaction (RT-PCR) assay of nasal and/or	**Medical Condition, n/N (%):** Cancer: 53/159 (33.3%) Hematologic cancer: 24/53 (45.3%) • Acute lymphoblastic leukemia (ALL): 3/53 (5.7%) • Acute myeloid leukemia (AML): 9/53 (17.0%) • Chronic lymphocytic leukemia (CLL): 4/53 (7.5%) • Chronic myelogenous leukemia (CML): 1/53 (1.9%) • Lymphoma: 5/53 (9.4%) • Multiple myeloma (MM): 2/53 (3.8%) **Control/Comparison Group, n/N (%):** No Cancer: 106/159 (66.7%)	**Medical Condition(s):** *Hematologic cancers:* ALL, AML, CLL, CML, lymphoma, MM **Severity Measure(s):** *Acute lymphoblastic leukemia (ALL)*: ND *Acute myeloid leukemia (AML)*: ND *Chronic lymphocytic leukemia (CLL)*: ND *Chronic myelogenous leukemia (CML)*: ND *Lymphoma*: ND *Multiple myeloma (MM)*: ND **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* death due to COVID-19 *ICU admission:* admission due to COVID-19 *Intubation:* intubation due to COVID-19 complications *Ventilation:* ND *Hospitalization:* ND	**Severe COVID-19:** Propensity score matched by age, sex, and underlying diseases including ischemic heart disease (IHD), diabetes mellitus (DM), and hypertension (HTN) *Mortality, n/N (%), or Median (IQR):* • Hematologic cancers: 17/24 (70.8%) • No cancer: 17/106 (16.0%) *ICU admission, n/N (%), or Median (IQR):* • Hematologic cancers: 18/24 (75.0%) • No cancer: 28/106 (26.4%) *Intubation, n/N (%), or Median (IQR):* • Hematologic cancers: 17/24 (70.8%) • No cancer: 25/106 (23.6%) **Severity of Condition:** *Mortality, n/N (%), or Median (IQR): vs. No cancer: 17/106 (16.%)* • ALL: 2/3 (66.7%) • AML: 5/9 (55.6%) • CLL: 4/4 (100.0%) • CML: 1/1 (100.0%) • Lymphoma: 4/5 (80.0%) • MM: 1/2 (50.0%)

Study	Population and Setting	Exposure	Definitions	Results
	pharyngeal specimens alongside of chest CT scans. **Exclusion Criteria:** Transplant recipients (kidney, heart, and bone marrow).		*Non-elective readmissions*: ND **Comments:** The control group were matched by age, sex, underlying disease including ischemic heart disease (IHD), diabetes mellitus (DM), and hypertension (HTN) and hospitalization time.	*ICU admission, n/N (%), or Median (IQR):* vs *No cancer: 28/106 (26.4%)* • ALL: 2/3 (66.7%) • AML: 5/9 (55.6%) • CLL: 4/4(100.0%) • CML: 1/1 (100.0%) • Lymphoma: 4/5 (80.0%) • MM: 2/2 (100.0%) *Intubation, n/N (%), or Median (IQR): vs. no cancer*: 25/106 (23.6%) • ALL: 2/3 (66.7%) • AML: 5/9 (55.6%) • CLL: 4/4 (100.0%) • CML: 1/1 (100.0%) • Lymphoma: 4/5 (80.0%) • MM: 1/2 (50.0%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Suarez-Garcia[17] **Year:** 2021 **Data Extractor:** AJ **Reviewer:** AH **Study Design:** Cohort **Study Objective:**	**Population:** N =13,206 COVID-19+ **Setting:** Hospital **Data Source:** SEMI-COVID registry **Location:** Spain **Study Dates:** March 27th – June 19th, 2020	**Medical Condition, n/N (%):** Immunosuppression (IS): 2111/13206 (16%) Hematologic cancer: 358/13,206 (2.7%) • Leukemia: 164/358 (45.8%) • Lymphoma: 190/358 (53.1%) • Concomitant leukemia and lymphoma: 4/ 358 (1.1%)	**Medical Condition(s):** *Immunosuppression (IS):* Patients that had solid organ (SO) transplantation, active SO malignant neoplasia (with or without metastases), active hematological neoplasia (lymphoma or leukemia), or if they were treated with any immune suppressive treatment on a chronic basis prior to admission, including classical immunosuppressive agents	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression; included model variables: age, sex, level of dependency, smoking status, arterial hypertension, chronic heart failure, chronic obstructive bronchopulmonary disease, asthma, dementia, moderate-severe chronic liver disease, moderate-severe chronic renal failure, diabetes mellitus* *OR: Univariable (Univariate) Logistic Regression* *OR: Odds Ratio* *Mortality, n/N (%), or Median (IQR):*

Study	Population and Setting	Exposure	Definitions	Results
To evaluate the clinical characteristics and outcome of immunosuppressed (IS) patients hospitalized with COVID-19 compared to non-IS patients. **IVA Score:** 26 (Low)	**Inclusion Criteria:** COVID-19 positive patients registered, with complete information on June 19th, 2020. COVID-19 was confirmed in all patients either by a positive real-time polymerase chain reaction (RT-PCR) testing of a nasopharyngeal or sputum sample, or by a positive result on serological testing and compatible clinical presentation. **Exclusion Criteria:** Patients with invalid or missing data.	**Control/Comparison Group, n/N (%):** Non-IS: 11095/13206 (84.0%)	(cytotoxic agents such as calcineurin inhibitors, purine analogues, folate antagonists, alkylating agents, inosine monophosphate inhibitors, mTOR inhibitors and janus-kinase inhibitors), biological treatments, or systemic corticosteroids *Non-IS:* patients fulfilled none of the conditions listed for immunosuppression *Hematologic cancer:* leukemia or lymphoma **Severity Measure(s):** *Leukemia:* ND *Lymphoma:* ND **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* in-hospital death *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: ND **Comments:** Four patients were included in the denominator for both the leukemia and lymphoma mortality severity proportions. These four patients had concomitant leukemia and lymphoma.	Hematologic cancer • aOR 2.31 (95%CI: 1.76 – 3.03), p < 0.001 • OR: 2.42 (95%CI: 1.92 – 3.05), p < 0.001 • Non-IS: reference • Hematologic cancer: 139/358 (38.8%) • Non-IS: 2143/11,095 (19.3%) Immunosuppressed vs non-Immunosuppressed • Non-IS: reference • IS aOR: 1.60 (1.42 - 1.79), p < 0.001 • IS OR: 1.90 (1.72 - 2.11) **Severity of Condition:** NR *Mortality, n/N (%), or Median (IQR):* Leukemia • aOR 2.20 (95%CI: 1.49 – 3.25), p < 0.001 • OR: 2.70 (95%CI: 1.89 – 3.84), p < 0.001 • Non-IS: reference • Leukemia: 66/168 (39.3%) • Non-IS: 2143/11095 (19.3%) Lymphoma • aOR 2.94 (95%CI: 2.19 – 3.95), p < 0.001 • OR: 2.75 (95%CI: 2.16 – 3.51), p < 0.001 • Non-IS: reference • Lymphoma: 77/194 (39.7%) • Non-IS: 2143/11095 (19.3%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR

Study	Population and Setting	Exposure	Definitions	Results
Author: Wang[18] **Year:** 2021 **Data Extractor:** AJ **Reviewer:** MM **Study Design:** Case-control **Study Objective:** To study a nation-wide database of patient electronic health records (EHRs) of 73 million patients in the US for COVID-19 and eight major types of hematologic malignancies. **IVA Score:** 25 (Moderate)	**Population:** N = 17,130 COVID-19+ **Setting:** 360 Hospitals **Data Source:** Electronic medical records **Location:** United States **Study Dates:** up to September 1, 2020 **Inclusion Criteria:** All patients with hematologic malignancies, who were previously diagnosed with and are living with or in remission from hematologic malignancies (acute lymphoid leukemia, acute myeloid leukemia, chronic lymphoid leukemia, essential thrombocythemia, multiple myeloma, myelodysplastic syndrome, non-Hodgkin lymphoma, and polycythemia vera), patients with recent hematologic malignancies patients (i.e. new cases) who were diagnosed with the cancer within the	**Medical Condition, n/N (%):** Hematologic malignancy (HM) (all-time diagnosis):420/17,130 (2.5%) • HM with recent diagnosis: 270/420 (64.3%) **Control/Comparison Group, n/N (%):** No hematologic malignancies: 16,860/17,130(98.4%)	**Medical Condition(s):** ND **Severity Measure(s):** NR *Recent cancer diagnosis:* malignancy diagnosed in the past year **Clinical Marker:** ND **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** The death rates for patients with all-time diagnosis of hematologic malignancies were similar to those for recent diagnosis (aOR: NR).	**Severe COVID-19:** *Mortality, n/N (%), or Median (IQR):* *HM with recent cancer diagnosis vs no HM* • HM: 40/270(14.8%) • No HM: 860/16,860 (5.1%) • p < 0.001 *Hospitalization, n/N (%):* *HM with recent cancer diagnosis vs no HM* • HM: 140/270 (51.9%) • No HM: 3960/16,860 (23.5%) • p < 0.001 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Exposure	Definitions	Results
	past year, and non-cancer patients. **Exclusion Criteria:** Hospital cohorts with less than 10 patients.			
Author: Yigenoglu[19] **Year:** 2020 **Data Extractor:** AH **Reviewer:** MM **Study Design:** Cohort **Study Objective:** To report the outcome of COVID-19 in patients with hematological malignancies treated in Turkey. **IVA Score:** 26 (Low)	**Population:** N = 1,480 COVID-19+ **Setting:** Community **Data Source:** Ministry of health database **Location:** Turkey **Study Dates:** March 11–June 22, 2020 **Inclusion Criteria:** patients with COVID-19 with hematological malignancy were included in the study and age, sex, and comorbidity matched patients with COVID-19 without cancer at 1:1 ratio. **Exclusion Criteria:** NR	**Medical Condition, n/N (%):** Hematologic malignancies: 740/1,480 (50.0%) • Non-Hodgkin lymphoma (NHL): 223/740 (30.1%) • Myeloproliferative neoplasm (MPN): 116/740 (15.7%) • Myelodysplastic syndrome (MDS): 146/740 (19.7%) • Multiple myeloma (MM): 77/740 (10.4%) • Chronic lymphocytic leukemia (CLL): 54/740 (7.3%) • Acute myeloid leukemia (AML): 40/740 (5.4%) • Chronic myeloid leukemia (CML): 30/740 (4.1%) • Hodgkin's lymphoma (HL): 27/740 (3.6%) • Acute lymphoblastic leukemia (ALL): 18/740 (2.4%) • Hairy cell leukemia (HCL): 9/740 (1.2%) **Control/Comparison Group, n/N (%):**	**Medical Condition(s):** *Hematological malignancies:* HL, CLL< MM, ALL, MPN, CML, NHL, MDS, AML, HCL **Severity Measure(s):** *HL:* ND CLL: ND MM: ND ALL: ND MPN: ND CML: ND NHL: ND MDS: ND AML: ND HCL: ND **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation: mechanical ventilation* *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** Hypertension was the most common comorbid disease in COVID-19 patients with hematological malignancy (51.2%).	**Severe COVID-19:** *Mortality, n/N (%), or Median (IQR):* • Hematologic malignancy: 102/740 (13.8%) • No cancer: 50/740 (6.8%) • p = 0.001 *ICU admission, n/N (%), or Median (IQR):* • Hematologic malignancy: 140/740 (18.9%) • No cancer: 85/740 (11.5%) • P = 0.001 *Mechanical ventilation, n/N (%), or Median (IQR):* • Hematologic malignancy: 102/740 (13.8%) • No cancer: 53/740 (7.2%) • P= 0.001 *Hospitalization, n/N (%), or Median (IQR):* • Hematologic malignancy: 452/740 (61.1%) • No cancer: 409/740 (55.3%) • p= 0.023 **Severity of Condition:** *Mortality, n/N (%):* • HL: 4/27 (14.8%) • CLL: 9/54 (16.6%) • MM: 15/77 (19.5%) • ALL: 3/18 (16.6%) • MPN: 10/116 (8.6%) • CML: 3/30 (10.0%) • NHL: 24/223 (10.8%) • MDS: 22/146 (15.0%) • AML: 8/40 (20.0%)

Study	Population and Setting	Exposure	Definitions	Results
		No cancer: 740/1,480 (50.0%)		• HCL: 4/9 (44.0%) • No cancer: 50/740 (6.8%) **Duration of Condition:** NR **Comorbid Conditions:** *Mortality, n/N (%), or Median (IQR):* ≥2 comorbidities • Hematological malignancy: 59/102 (57.8%) • No cancer: 26/50 (52.0%) • p = 0.8 1 comorbidity • Hematological malignancy: 28/102 (27.5%) • No cancer: 16/50 (32.0%) No comorbidity • Hematological malignancy: 15/102 (14.7%) • No cancer: 8/50 (16.0%) **Risk Markers:** *Mortality, n/N (%), or Median (IQR):* Sex Male • Hematological malignancy: 65/102 (63.7%) • No cancer: 38/50 (76.0%) • p = 0.13 Female • Hematological malignancy: 37/102 (36.3%) • No cancer: 12/50 (24.0%) Age, median (y) • Hematological malignancy: 69 (24 – 92) • No cancer: 71.5 (48 – 87) • p = 0.44 **Long-term Sequelae:** Non-elective readmissions: NR

B.3.c. Internal Validity Assessments of Extracted Studies

Table 17 Internal Validity Assessments (IVA) of Extracted Studies Reporting the Association Between HM and Severe COVID-19 Outcomes

	Author & Year	Al-Mozaini[1] 2021	Altuntas[2] 2021	Arcani[3] 2021	Bange[4] 2021
OUTCOME MEASURE		Mortality	Mortality, ICU admission, mechanical ventilation, hospitalization	Mortality, ICU admission, mechanical ventilation	Mortality, ICU admission, intubation
Domain	**Signaling question**				
Study Elements	Design appropriate to research question	1	1	1	1
	Well-described population	1	1	1	1
	Well-described setting	1	1	1	1
	Well-described intervention/ exposure	1	1	1	1
	Well-described control/ comparator	1	1	1	1
	Well-described outcome	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0
	Allocation adequately concealed	0	0	0	0
	Population sampling appropriate to study design	1	1	1	0
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1

	Author & Year	Al-Mozaini[1] 2021	Altuntas[2] 2021	Arcani[3] 2021	Bange[4] 2021
	Attrition <10-15% of population	1	1	1	1
	Attrition appropriately analyzed	1	1	1	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	1	1	1
	Measure of outcome is valid	1	1	1	1
	Fidelity to intervention is measured	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0
	Prospective study	1	1	1	1
	Adequately powered to detect result	0	0	1	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0
	Study participant blinded	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0
	Data collection methods described in sufficient detail	1	0	1	1
	Data collection methods appropriate	1	0	1	1
	Sufficient follow up to detect outcome	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	0	0	1	1
	Appropriate statistical analyses are conducted correctly	0	0	1	1
	Confidence interval is narrow	0	0	0	0
Confounding	Potential confounders identified	1	1	1	1

	Author & Year	Al-Mozaini[1] 2021	Altuntas[2] 2021	Arcani[3] 2021	Bange[4] 2021
	Adjustment for confounders in study design phase	0	0	0	1
	Adjustment for confounders in data analysis phase	0	0	0	1
Reporting Bias	All pre-specified outcomes are adequately reported	1	0	1	1
Other Bias	No other sources of bias	1	0	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1
IVA SCORE	Threat to internal validity	21	17	24	24
	Low, Moderate, High	Moderate	High	Moderate	Moderate

	Author & Year	Bernard[5] 2021	Chai[6] 2021	Dai[7] 2020	Fu[8] 2021
OUTCOME MEASURE		Mortality, ICU admission	Mortality, 1-year all-cause mortality	Mortality, ICU admission, invasive mechanical ventilation	Mortality, ICU admission
Domain	**Signaling question**				
Study Elements	Design appropriate to research question	1	1	1	1
	Well-described population	1	1	1	1
	Well-described setting	1	1	1	1
	Well-described intervention/ exposure	1	1	1	1

	Author & Year	Bernard[5] 2021	Chai[6] 2021	Dai[7] 2020	Fu[8] 2021
	Well-described control/ comparator	1	1	1	1
	Well-described outcome	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0
	Allocation adequately concealed	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	0	1	1
	Attrition <10-15% of population	1	0	1	1
	Attrition appropriately analyzed	1	1	1	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	1	1	1
	Measure of outcome is valid	1	1	1	1
	Fidelity to intervention is measured	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0
	Prospective study	1	1	1	1
	Adequately powered to detect result	1	1	1	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0
	Study participant blinded	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0

	Author & Year	Bernard[5] 2021	Chai[6] 2021	Dai[7] 2020	Fu[8] 2021
	Data collection methods described in sufficient detail	1	1	1	1
	Data collection methods appropriate	1	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1	1
	Confidence interval is narrow	1	0	0	0
Confounding	Potential confounders identified	1	1	1	1
	Adjustment for confounders in study design phase	1	1	1	1
	Adjustment for confounders in data analysis phase	1	1	1	1
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1
IVA SCORE	Threat to internal validity	27	24	26	25
	Low, Moderate, High	Low	Moderate	Low	Moderate

	Author & Year	Kalicinska[9] 2021	Mehta[10] 2020	Passamonti[11] 2020	Ramachandran[12] 2020
OUTCOME MEASURE		Mortality	Mortality	Mortality	Mortality
Domain	**Signaling question**				
Study Elements	Design appropriate to research question	1	1	1	1
	Well-described population	1	1	1	1
	Well-described setting	1	1	1	1
	Well-described intervention/ exposure	1	1	1	1
	Well-described control/ comparator	1	1	1	1
	Well-described outcome	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0
	Allocation adequately concealed	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1
	Attrition <10-15% of population	1	1	1	1
	Attrition appropriately analyzed	1	1	1	1

	Author & Year	Kalicinska[9] 2021	Mehta[10] 2020	Passamonti[11] 2020	Ramachandran[12] 2020
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	1	1	1
	Measure of outcome is valid	1	1	1	1
	Fidelity to intervention is measured	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0
	Prospective study	1	1	1	1
	Adequately powered to detect result	1	0	1	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0
	Study participant blinded	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0
	Data collection methods described in sufficient detail	0	1	1	1
	Data collection methods appropriate	0	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1	1
	Confidence interval is narrow	0	0	0	0
Confounding	Potential confounders identified	1	1	1	1
	Adjustment for confounders in study design phase	1	1	1	1

	Author & Year	Kalicinska[9] 2021	Mehta[10] 2020	Passamonti[11] 2020	Ramachandran[12] 2020
	Adjustment for confounders in data analysis phase	1	1	1	1
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1
Other Bias	No other sources of bias	1	0	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1
IVA SCORE	Threat to internal validity	24	24	26	25
	Low, Moderate, High	Moderate	Moderate	Low	Moderate

	Author & Year	Roel[13] 2021	Sanchez-Pina[14] 2020	Shoumariyeh[15] 2020	Sorouri[16] 2020
OUTCOME MEASURE		Mortality, hospitalization	Mortality, ICU admission, hospitalization	Mortality, ICU admission, ventilation, hospitalization	Mortality, ICU admission, intubation
Domain	**Signaling question**				
Study Elements	Design appropriate to research question	1	1	1	1
	Well-described population	1	1	1	1
	Well-described setting	1	1	1	1
	Well-described intervention/ exposure	1	1	1	1
	Well-described control/ comparator	1	1	1	1

	Author & Year	Roel[13] 2021	Sanchez-Pina[14] 2020	Shoumariyeh[15] 2020	Sorouri[16] 2020
	Well-described outcome	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0
	Allocation adequately concealed	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1
	Attrition <10-15% of population	1	1	1	1
	Attrition appropriately analyzed	1	1	1	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	1	1	1
	Measure of outcome is valid	1	1	1	1
	Fidelity to intervention is measured	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0
	Prospective study	1	1	1	1
	Adequately powered to detect result	0	1	0	1
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0
	Study participant blinded	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0

	Author & Year	Roel[13] 2021	Sanchez-Pina[14] 2020	Shoumariyeh[15] 2020	Sorouri[16] 2020
	Data collection methods described in sufficient detail	1	0	1	1
	Data collection methods appropriate	1	0	1	1
	Sufficient follow up to detect outcome	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1	1
	Confidence interval is narrow	1	0	0	0
Confounding	Potential confounders identified	1	1	1	1
	Adjustment for confounders in study design phase	1	1	1	1
	Adjustment for confounders in data analysis phase	1	1	1	1
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1
IVA SCORE	Threat to internal validity	26	24	25	26
	Low, Moderate, High	Low	Moderate	Moderate	Low

	Author & Year	Suarez-Garcia[17] 2021	Yigenoglu[19] 2020	Wang[18] 2021
OUTCOME MEASURE		Mortality, hospitalization	Mortality, ICU admission, ventilation, hospitalization	Mortality, hospitalization
Domain	**Signaling question**			
Study Elements	Design appropriate to research question	1	1	1
	Well-described population	1	1	1
	Well-described setting	1	1	0
	Well-described intervention/ exposure	1	1	1
	Well-described control/ comparator	1	1	0
	Well-described outcome	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0
	Allocation adequately concealed	0	0	1
	Population sampling appropriate to study design	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1
	Attrition <10-15% of population	1	1	1
	Attrition appropriately analyzed	1	1	1

	Author & Year	Suarez-Garcia[17] 2021	Yigenoglu[19] 2020	Wang[18] 2021
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	1	1
	Measure of outcome is valid	1	1	1
	Fidelity to intervention is measured	0	0	0
	Fidelity to intervention is valid	0	0	0
	Prospective study	1	1	1
	Adequately powered to detect result	1	1	1
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0
	Study participant blinded	0	0	0
	Investigator/ data analyst blinded	0	0	0
	Data collection methods described in sufficient detail	1	1	1
	Data collection methods appropriate	1	1	1
	Sufficient follow up to detect outcome	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1
	Confidence interval is narrow	0	0	0
Confounding	Potential confounders identified	1	1	1
	Adjustment for confounders in study design phase	1	1	1

	Author & Year	Suarez-Garcia[17] 2021	Yigenoglu[19] 2020	Wang[18] 2021
	Adjustment for confounders in data analysis phase	1	1	1
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1
Other Bias	No other sources of bias	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1
IVA SCORE	Threat to internal validity	26	26	25
	Low, Moderate, High	Low	Low	Moderate

C. Abbreviations

Table 18 Abbreviations.

Acronym	**Full**
95% CI	95% confidence interval
ALL	acute lymphocytic or lymphoblastic leukemia
AML	acute myeloid leukemia
ANOVA	analysis of variance
ARDS	acute respiratory distress syndrome
BADL	basic activities of daily living
BMI	body mass index
CAR	chimeric antigen receptor

CAR-T	chimeric antigen receptor- t-cell
CDC	Centers for Disease Control and Prevention
CLL	chronic lymphocytic or lymphoblastic leukemia
CML	chronic myeloid leukemia
COI	conflict of interest
COPD	chronic obstructive pulmonary disease
COVID-19	coronavirus disease 2019, a disease caused by the SARS-CoV-2 virus
ED	emergency department
EEG	electroencephalogram
EHR	electronic health records
EMR	electronic medical records
HCT	hematopoietic cell transplant
HSCT	hematopoietic stem cell transplant
HL	Hodgkin's lymphoma
HM	hematologic malignancy
HR	hazard ratio
ICF	intermediate care facility
ICU	intensive care unit
IVA	internal validity assessment
MDS	myelodysplastic syndrome
MM	multiple myeloma

MPN	myeloproliferative neoplasms
MRI	magnetic resonance imaging
MS	multiple sclerosis
NHL	non-Hodgkin's lymphoma
NA	not applicable
ND	not defined
NR	not reported
NY	New York
NYC	New York City
OR	odds ratio
PCR	polymerase chain reaction
PECO	population, exposure, comparator, outcomes
RR	risk ratio
RT	real time
RTX	rituximab
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SI	secondary immunosuppression
SOFA	sequential organ failure assessment
TF	task force
UK	United Kingdom
US	United States

USA	United State of America
WHO	World Health Organization

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