SYSTEMATIC REVIEW

The outcome of gynecologic cancer patients with Covid-19 infection: A systematic review and meta-analysis [version 1; peer review: awaiting peer review]

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Abstract

Background: Cancer is a comorbidity that leads to progressive worsening of coronavirus disease 2019 (Covid-19) with increased mortality. This is a systematic review and meta-analysis to yield evidence of adverse outcomes of Covid-19 in gynecologic cancer.

Methods: Searches through PubMed, Google Scholar, ScienceDirect, and medRxiv to find articles on the outcome of gynecologic cancer with Covid-19 (24 July 2021–19 February 2022). The Newcastle-Ottawa Scale tool was used to evaluate the quality of included studies. Pooled odds ratio (OR), 95% confidence interval (CI) and random-effects model were presented.

Results: We accepted 51 studies (a total of 1991 gynecologic cancer patients with Covid-19). Covid-19 infection cases were lower in gynecologic cancer vs hematologic cancer (OR 0.71, CI 0.56-0.90, *p* 0.005). Severe Covid-19 infection and death were lower in gynecologic cancer vs lung and hematologic cancer (OR 0.36, CI 0.16-0.80, *p* 0.01), (OR 0.52, CI 0.44-0.62, *p* <0.0001), (OR 0.26, CI 0.10-0.67 *p* 0.005), (OR 0.63, CI 0.47-0.83, *p* 0.001) respectively. Increased Covid death was seen in gynecologic cancer vs population with breast cancer, non-Covid cancer, and non-cancer Covid (OR 1.50, CI 1.20-1.88, *p* 0.0004), (OR 11.83, CI 8.20-17.07, *p* <0.0001), (OR 2.98, CI 2.23-3.98, *p* <0.0001) respectively.

Conclusion: Gynecologic cancer has higher Covid-19 adverse outcomes compared to non-cancer, breast cancer, non-metastatic, and Covid-19 negative population. Gynecologic cancer has fewer

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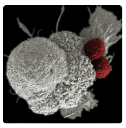
Covid-19 adverse outcomes compared to other cancer types, lung cancer, and hematologic cancer. These findings may aid health policies and services during the ongoing global pandemic.

PROSPERO Registration: CRD42021256557 (22/05/21)

Keywords
COVID-19, Critical care outcome, Female genital neoplasms, Hospitalization, Morbidity, Mortality

This article is included in the Emerging Diseases and Outbreaks gateway.



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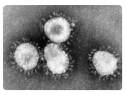

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Introduction

The Covid-19 pandemic has changed the way health care providers around the world manage care provided to their patients. The pandemic has also proven to shift the attitude of standard practice and procedure between providers and patients, for example, to reduce gynecologic cancer patients visiting the hospital as possible because the risk of getting infected with Covid-19 is increased regarding their comorbidities.[1] Despite this circumstance, gynecologic cancer patients are still often required to perform routine hospital visits for treatments or other medical procedures under guidance made by gynecological cancer societies during the Covid-19 pandemic.[2] The cancer incidence and mortality are still increasing around the world. According to Global Cancer Statistic: 2020 for gynecologic cancer, there are 604.127, 417.367, 313.959, 45.240, and 17.908 new cases of cancer of the cervix uteri, corpus uteri, ovary, vulva, and vagina respectively.[3] Most concerns are coming from these patients about how they may proceed to seek or continue their cancer treatment and surveillance during the Covid-19 pandemic.[4] Studies are showing various results on increased mortality and severity among cancer patients infected with Covid-19. Systematic review and meta-analysis studying the outcome of cancer patients with Covid-19 show 2.1–4% proportion of cancer patients among those infected with Covid-19, additionally compared to non-cancer with Covid-19 greater amount of mortality and severity are observed in cancer population with Covid-19.[5–7] However studies and data on the outcome of gynecologic cancer patients with Covid-19 are still lacking. Several SARS-CoV-2 variants of concern listed by WHO (World Health Organization) pose challenges in mitigating the pandemic as these variants often increase transmission rate and severity.[8] The world has been experiencing a wave of active case surges by these variants and on 26 November 2021 the WHO designated the variant Omicron (B.1.1.529) as an addition to the list.[9] Thus we attempt to review the literature and quantify the effect of the SARS-Cov-2/Covid-19 infection among gynecologic cancer patients to assess whether the risk of infection, hospitalization, severity, and mortality are increased than non-gynecologic cancer population.

Methods

We conducted this systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses/PRISMA statement.[10,82] This study and its protocol were registered to PROSPERO (CRD42021256557).

Eligibility criteria

We took into consideration of studies with observational cohort studies, case-control, cross-sectional, case report, and case series designs that evaluate the outcome of gynecologic cancer patients infected with Covid-19 from the year 2019. Each study ought to report Covid-19 associated infection, hospital admission, mortality, severity, or admission to the intensive care unit (ICU); a summary of eligible studies and its extracted outcome of interest were managed in the Microsoft Excel spreadsheet provided in the *Underlying data*.[82] We exclude studies other than the English language, reviews or guidelines, and inconceivable results of the sought outcome.

Comparator(s)/control

Non-cancer Covid-19 patients, non-Covid-19 cancer patients, other cancer types/non-gynecological cancer with Covid-19.

Database and literature search

Study articles were systematically searched through PubMed/Medline, ScienceDirect, Google Scholar, and medRxiv. Relevant articles had been screened from 24 July 2021 to 19 February 2022. Reference searches from retrieved articles citation lists were identified if any were needed. Boolean operators technique used for Pubmed/Medline search with ("COVID-19" or "2019-nCoV" or "SARS-CoV" or SARSCOV2 or 2019-nCov or "2019 coronavirus" or covid19) AND (gynecology or gynaecology) AND (tumor or malignancy or cancer) AND (outcomes or outcome) AND (gyn* tum* or gyn *malign* or gyn* cancer) AND (cancer surgery or oncolog* surger*) AND (brachytherapy or radiotherapy). We used "Gynecologic cancer AND Covid-19" with Google Scholar, Science Direct, and medRxiv. Two authors separately handled the literature search. Findings were accumulated and stored in Mendeley and Zotero for management and automated duplicate identification. Thorough stepwise screening from title and abstract was then conducted to determine possible article inclusion. Potentially eligible studies were then evaluated for in-depth full-text review. Each author would consult senior authors to resolve any differences found during the literature's selection process.

Data extraction and quality assessment

The data was extracted independently by two authors and stored them in the Microsoft Excel spreadsheet. Data was then discussed for an agreement. Name of authors, year of publication, country, type of studies, study period, number of patients, comparators, and target conditions was collected. The NOS/Newcastle-Ottawa Scale was used by authors to assess the quality of the cohort and case-control study, and The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for an analytical cross-sectional study.[11] The assessment was performed by two authors and the results were discussed with the first author.

Meta-analysis outcome

The main outcome of interest was Covid-19 mortality and severity. Covid-19 severity is defined as either ICU admission, acute respiratory distress syndrome (ARDS), or need for mechanical ventilation. Covid-19 infection and hospitalization were decided as secondary outcomes.

Data analysis & synthesis

We performed data analysis mainly using Review Manager 5.4.1 (RevMan 5.4.1) by Cochrane collaboration.[12] If needed, additional synthesis was then performed with STATA-16. We synthesized the dichotomous outcome from each study with an odds ratio (OR). The random-effects model (DerSimonian and Laird) was used to present pooled OR with 95% CI (confidence interval) and the result of overall effect (*p*). We addressed the presence of heterogeneity with I^2 as 0% to 40%: might not be important; 30% to 60%: may represent moderate heterogeneity; 50% to 90%: may represent substantial heterogeneity; 75% to 100%: considerable heterogeneity according to the Cochrane Handbook for Systematic Reviews of Interventions. We performed subgroup analysis by age, gender, other comorbidities status, cancer type, cancer stage, presence of metastatic disease, and active cancer treatment. Sensitivity analysis was performed by dividing multi-center/single-center studies and removing/including the latest study period if concerns were raised of patients population duplication thus we could present robust pooled evidence.[13]

Results

All supplementary files can be found in the *Extended data*.[82]

A total of 51 studies involving the Covid-19 positive population were identified; among them were 1991 gynecologic cancer patients, 221465 non-cancer patients, and 28138 other cancer type patients. In total, 3,717,078 cancer patients were found to be Covid-19 free. Study selection and summary of included studies were presented in Figure 1 and Table 1. The risk of bias in each study was shown in **Figures S1** and **S2**. Due to high heterogeneity found in adverse Covid-19 outcomes (Covid-19 death I^2 82%), (Covid-19 hospitalization I^2 92%), (Covid-19 infection case I^2 72%), we decided to perform subgroup analysis.

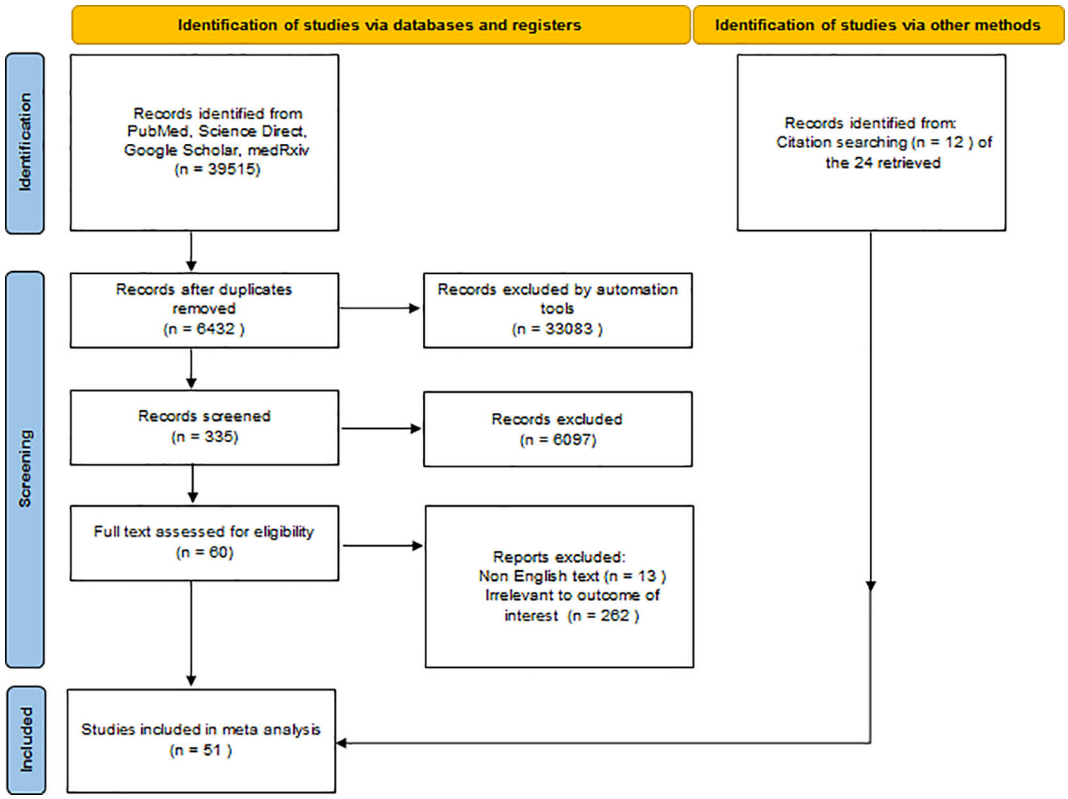

Figure 1. Study flow diagram.

Table 1. Characteristics of included studies.

Author	Location	Type of study	Time of study	Publication year	Non cancer Covid patients	Gynecology Oncology Covid patients	Other Oncology Covid patients	Cancer non Covid patients	Gender*	Cancer stage*	Comorbidities*	Cancer treatment*	Age*	Outcome
Angelis V et al.[14]	United Kingdom	Multi center, prospective cohort	March–April 2020	2020	NA	6	107 (Lung 15, Breast 18, Hematological 18)	13376 (Gynecological 967)	Male 63, Female 50	NA	Hypertension 39, Diabetes 18, Ischemic heart disease 13, COPD 6	SACT 85, Radiotherapy 11	Median 66, IQR: 54–69, range 21–91	Covid infection & Covid death
Ayhan A et al.[15]	Turkey	Multi center, retrospective cohort	March–April 2020	2020	NA	46	NA	642 (Gynecological)	Female 688	NA	Hypertension 29, Diabetes 16, Chronic pulmonary disease 11, Coronary heart disease 6, CKD 1.	Major/Complex Cancer Surgery 688	<65: 34, >65: 12	Covid death
Ayhan M et al.[16]	Turkey	Single center, retrospective cohort	March–June 2020	2021	NA	4 (Ovarian 1, Endometrium 3)	80 (Lung 27, Breast 18)	1065 (Ovarian 59, Endometrium 21)	Female 33, Male 51	I: 2, II: 7, III: 18, IV:57, Metastasis 57, Non-meta 27	Hypertension 12, Diabetes 16, Coronary artery disease 3, COPD 3, CKD 1	SACT 84	Median 61, IQR: 21–84	Covid infection & Covid hospitalization
Ayhan M et al.[17]	Turkey	Single center, retrospective cohort	March–May 2020	2021	2289	7 (Cervix 3, Endometrial 2, Ovarian 2)	85 (Lung 26, Breast 17)	NA	Female 41, Male 51	Metastasis 53, Non-meta 39	Hypertension 31, Dibetes 16, COPD 14, Coronary artery disease 13, CKD 4, Chronic liver disease 2, Cerebrovascular disease 2	SACT 62	<67: 45, >67: 47	Covid death
Basse C et al.[18]	France	Single center, prospective cohort	March 2020	2020	NA	12	129 (Lung 18, Breast 57, Hematological 19)	NA	Female 102, Male 39	Localized 38, Metastasis 84	Chronic lung disease 7, Diabetes 24, Hypertension 48, Other heart disease 21, Systemic disease 6	Surgery 11, Radiotheraphy 13, SACT 120, None 17	>70: 141	Covid death
Bernard A et al.[19]	France	Multi center, retrospective cohort	March–April 2020	2021	83329	185	5537 (Lung 873, Breast 561, Hematological 1389)	NA	Female 39919, Male 45079	Metastasis 1775, Non-meta 2558	Hypertension 28163, Heart failure 6641, Chronic respiratory disease 1334, CKD 6948, Diabetes 16216, COPD 4516, Obesity 8289, Chirosis 673	NA	With cancer: mean 72, Without cancer: mean 65	Covid death
Bersanelli M et al.[20]	Italy	Multi center, prospective cohort	January–April 2020	2020	NA	1 (Endometrial)	13 (Lung 9, Breast 1)	52	Female 3, Male 10	IV: 9	Splenectomy 1, Hypertension 8, HIV 1, Diabetes 1	ICI 13, ICI + Chemotherapy 1	<65: 5, >65: 9	Covid death
Bogani G et al.[21]	Italy	Single center, retrospective cohort	February–March 2020	2020	NA	19 (Ovarian 14, Endometrial 3, Cervical 1, Ovarian+ Endometrial 1)	NA	336 (Gynecological)	Female 19	NA	Cardiovascular disease 5, CKD 1, Hypothyroidism 2, Plummer disease 1	Surgery 5, SACT 8, Planned treatment 6	<65: 9, >65: 10	Covid death
Cavanna L et al.[22]	Italy	Single center, retrospective cohort	April–June 2020	2021	NA	0	10 (Lung 2)	250 (Gynecologic cancer 29)	Female 2, Male 8	NA	NA	SACT 7, Hormonal 1	Mean 69.2, Range 54–80	Covid infection
Chai C et al.[83]	China	Multi center, prospective cohort	January–March 2020	Pre-prints	498	16 (Cervical 9, Ovarian 4, Endometrial 3)	150 (Lung 25, Breast 19, Hematological 17)	498	Female 336, Male 328	NA	Hypertension 226, Diabetes 128, Hyperlipidemia 109, Heart disease 78, Cerebrovascular disease 22, COPD 36, CKD 14, Chronic liver disease 12	NA	Median 65, IQR 59–70	

Table 1. *Continued*

Author	Location	Type of study	Time of study	Publication year	Non cancer Covid patients	Gynecology Oncology Covid patients	Other Oncology Covid patients	Cancer non Covid patients	Gender*	Cancer stage*	Comorbidities*	Cancer treatment*	Age*	Outcome
Dai M et al.[23]	China	Multi center, prospective cohort	January–February 2020	2020	105	8 (Cervical 6, Ovarian 1, Endometrial 1)	97 (Lung 22, Breast 11, Hematological 8)	NA	Female 46, Male 59	I/II: 42, III/IV: 37, Metastasis 17	Hypertension 160, Cardiovascular disease 51, Diabetes 36, Cerebrovascular disease 26, CKD 28, Chronic liver disease 42	Surgery 8, SACT 27, Radiotherapy 13	<65: 54, >65: 51	Covid death and Severe Covid
de Melo AC et al.[24]	Brazil	Single center, retrospective cohort	April–May 2020	2020	NA	22 (Cervical 12, Ovarian 3, Endometrial 5, Vulvar 2)	159 (Lung 7, Breast 40, Hematological 34)	NA	Female 110, Male 71	I/II: 27, III/IV: 124, Metastasis 87	Hypertension 77, diabetes 31, CKD 10, COPD/Asthma 7	Surgery 12, Radiotheraphy 10, SACT 88, Palliative 32, Hormonal 20	<60: 89, 60–74: 67, >75: 25	Covid death and Severe Covid
Dettore G et al.[25]	OnCovid-Europe	Multi center, prospective cohort	February–June 2020	2021	NA	57	1014 (Lung 154, Breast 177, Hematological 87)	NA	Female 231, Male 296	Localized 173, Metastatic 223	Hypertension 251, Diabetes 115, Cardiovascular disease 128, Chronic pulmonary disease 80, CKD 62, Cerebrovascular disease 37, Liver impairment 11, Immunosuppression 16	Ongoing treatment at diagnosis 516, Surgery 510, SACT 319, Radiotherapy 319, Palliative 277	Mean: 67.9	Covid death
Duarte M et al.[26]	Brazil	Multi center, retrospective cohort	January–September 2020	2020	38468	75 (Cervix 47, Uterine 6, Ovaries 22)	606 (Lung 51, Breast 90, Hematological 155)	NA	Female 374, Male 307	I/II: 106, III/IV: 444	Heart disease 143, Diabetes 104, Neurologic disease 13, Chronic lung disease 29, Nephropathy 39	SACT 431	<65: 441, >65: 240	Covid death
Fang M et al.[84]	China	Single center, retrospective cohort	February–April 2020	pre-prints	NA	4	52 (Lung 9, Breast 4, Hematological 10)	NA	Female 24, Male 32	NA	Hypertension 23, Diabetes 7, Cardiovascular disease 5, Chronic pulmonary disease 1, Chirrosis 2, CNS disease 2	NA	Median: 64, IQR 54–71	Covid death
Fernandes G et al.[27]	Brazil	Cross sectional	April–August 2020	2021	NA	26	385 (Lung 18, Breast 93, Hematological 47)	NA	Female 234, Male 177	NA	NA	NA	<60: 215, >60: 196	Covid death
Glasbey J et al.[28]	International	Multi center, prospective cohort	April–June 2020	2020	NA	25	263 (Lung 25, Breast 24, Other 214)	8683 (Gyncecological 1057)	Female 119, Male 169	Early 181, Advance 107	Pre-existing respiratory condition 45, Obese 56	Minor Surgery 36, Major Surgery 252	<50: 30, 50–59: 39, 60–69: 87, 70–79: 96, >80: 36	Covid infection
Grivas P et al.[29]	CCC19-International	Multi center, prospective cohort	March–November 2020	2021	NA	322	4796 (Lung 409, Breast 967, Hematological 1097)	NA	Female 2527, Male 2436	NA	Cardiovascular 1582, Pulmonary 1091, Renal disease 831, Diabetes 1385	Chemotherapy 802, Immunotherapy 248, Targeted therapy 693, Endocirne therapy 483, Locoregional therapy 422	<65: 2282, 65–74: 1309, >75: 1375	Covid hospitalization & Covid death
Hathout L et al.[30]	United States of America	Multi center, retrospective cohort	February–June 2020	2020	NA	3 (Cervical)	0	44 (Endometrial 24, Cervical 12)	Female 3	NA	Respiratory disease 1, Vascular disease 23, Respiratory+Vascular 4, HIV 3	Brachytherapy 3	NA	Covid infection

Table 1. *Continued*

Author	Location	Type of study	Time of study	Publication year	Non cancer Covid patients	Gynecology Oncology Covid patients	Other Oncology Covid patients	Cancer non Covid patients	Gender*	Cancer stage*	Comorbidities*	Cancer treatment*	Age*	Outcome
Jee J et al.[31]	United States of America	Single center, retrospective cohort	March–April 2020	2020	NA	15 (Cervical 2, Endometrial 6, Ovarian 5, Vaginal 1, Vulvar 1)	294 (Lung 29, Breast 56, Hematological 71)	NA	Female 150, Male 159	Metastasis 168	Pulmonary disease 35, Cardiovascular disease 221, Metabolic disease 156, Neurologic disease 29, HIV 3, Liver disease 4	Chemotherapy 102	<60: 158, >60: 151	Covid death and Severe Covid
Johannesen T et al.[32]	Norway	Multi center, retrospective cohort	January–May 2020	2021	NA	33	514 (Lung 13, Breast 85, Hematological 54)	305299 (Gynecologic cancer 23827)	NA	Localized 36, Distant disease 6	NA	SACT 71, Surgery 90, Radiotherapy 7	NA	Covid infection
Kulle C et al.[33]	Turkey	Single center, retrospective cohort	March–June 2020	2021	NA	0	1	403 (Ovarian 14, Endometrial 9, Cervical 5, Uterine Sarcoma 1, Vulva 1)	NA	NA	NA	Surgery 1	NA	Covid infection
Kuru B et al.[34]	Turkey	Single center, retrospective cohort	March–October 2020	2021	2	1 (Ovarian)	0	61	Female 3	NA	Hypertension 2	Surgery 1	>65: 1, <65: 2	Covid infection
Kwon D et al.[85]	United States of America	Multi center, retrospective cohort	February–December 2020	pre-prints	NA	119	1662 (Lung 33, Breast 241, Hematological 321)	48137 (Gynecologic cancer 2877)	Female 950, Male 831	NA	Heart disease 321, Pulmonary disease 294, CKD 273, Diabetes 474, Obese 481	SACT 601, Hormonal therapy 86	18–65: 1044, 65–75: 420, >75: 317	Covid infection
Lara O et al.[35]	United States of America	Multi center, prospective cohort	March–June 2020	2021	NA	193 (Uterine 87, Epithelial Ovarian 62, Cervical 24, Vulva 8, Non-Epithelial Ovarian 3, Vaginal 3)	NA	NA	Female 193	I/II: 74, III/IV: 100	Hypertension 115, Diabetes 70, Asthma 21, COPD 5, Coronary artery disease 13, Autoimune disease 18, CKD 21	Surgery 12, Radiotherapy 8, SACT 98	Median 65, IQR 54–73	Covid hospitalization, Severe Covid & Covid death
Lee L et al.[36]	United Kingdom	Multi center, prospective cohort	March–April 2020	2020	NA	45	755 (Lung 90, Breast 102, Hematological 169)	NA	Female 349, Male 449	Localized 149, Metastatic 347, Advanced stage 78	Cardiovascular disease 109, COPD 61, Diabetes 131, Hypertension 247	SACT 461, Surgery 29, Radiotherapy 76	Median 69, IQR 59–76	Covid death
Lei S et al.[37]	China	Multi center, retrospective cohort	January–February 2020	2020	25	1 (Ovarian)	8	NA	Female 20, Male 14	NA	Hypertension 13, Diabetes 8, Cardiovascular disease 7, Cerebrovascular disease 2, COPD 1, CKD 1	Surgery 9	Median 55, IQR 43–63	Covid death
Li H et al.[38]	United Kingdom	Multi center, retrospective cohort	March–October 2020	2021	275	17 (Uterine 7, Ovarian 10)	272 (Lung 18, Breast 42, Hematological 53)	4161 (Uterine 107, Ovarian 115)	Female 120, Male 168	Localized 235, Metastasis 53	NA	NA	50–59: 28, 60–69: 62, 70–79: 159, 80–84: 39	Covid infection & Covid death
Liang J et al.[39]	China	Single center, retrospective cohort	January–April 2020	2020	NA	10 (Uterine 4, Cervical 5, Ovarian 1)	99 (Lung 14, Breast 11, Hematological 12)	NA	Female 52, Male 57	I/II/III: 86, IV: 23	Hypertension 38, Diabetes 18, Cardiovascular disease 10, Cerebrovascular disease 4, Chronic pulmonary disease 19, CKD 3, Chronic liver disease 10	Surgery 69, Adjuvant 79, Chemo-radiation 71, Targeted-immunotherapy 12	>65: 55, <65: 54	Covid death

Table 1. *Continued*

Author	Location	Type of study	Time of study	Publication year	Non cancer Covid patients	Gynecology Oncology Covid patients	Other Oncology Covid patients	Cancer non Covid patients	Gender*	Cancer stage*	Comorbidities*	Cancer treatment*	Age*	Outcome
Liu C et al.[40]	China	Multi center, prospective cohort	December 2019–March 2020	2020	NA	17	199 (Lung 49, Breast 34)	NA	Female 103, Male 113	I-II: 83, III-IV: 85	Diabetes 33, Hypertension 74, Cardiovascular 27, Cerebrovascular 18, COPD 21, Chronic liver disease 13, CKD 9	78	Median 63, IQR 57–70, 2	Covid death
Mehta V et al.[41]	United States of America	Single center, retrospective cohort	March–April 2020	2020	1090	12	206 (Lung 11, Breast 29, Hematological 108)	NA	Female 91, Male 127	Metastasis 42, Active cancer 92	DM 80, Hypertension 147, Chronic lung disease 62, CKD 53, Coronary artery disease 43, CHF 33	Chemotherapy 42, Immunotherapy 5, Radiotherapy 49	0–17: 3, 18–44: 13, 45–64: 64, 65–74: 59, >75: 79	Covid death
Modi C et al.[42]	United States of America	Multi center, prospective cohort	April–July 2020	2021	NA	1	4 (Lung 1, Breast 1)	331 (Gynecologic 26)	Female 3, Male 2	I-II: 3, III-IV: 2	Comorbidity score*: 2: 2, 5: 2, 8: 1	Radiotherapy 5	<65: 3, >65: 2	Covid infection
Monroy-Iglesias MJ et al.[43]	Italy	Multi center, prospective cohort	March–September 2020	2021	NA	2	14	3014 (Gynecological 382)	Female 2	NA	NA	Surgery 16	NA	Covid infection, Severe Covid & Covid death
Mousavi S et al.[44]	Iran	Single center, retrospective cohort	February–April 2020	2021	NA	3 (Ovarian)	30 (Lung 4, Breast 6)	NA	Female 15, Male 18	I/II/III: 17, IV:16	Cardiovascular & cerebrovascular disease 9, Diabetes 8, Chronic pulmonary disease 5, Chronic liver disease 1	Cytotoxic chemotherapy 18	Mean 63.9	Covid death
Nakamura S et al.[45]	Japan	Single center, restrospective cohort	January–May 2020	2020	NA	1 (Cervical)	31 (Lung 2, Breast 2, Hematological 7)	NA	Female10, Male 22	Active cancer 17	Diabetes 7, Hypertension 13, Coronary heart disease 4, COPD 4, Asthma 2	Surgery 13, SACT 17	>70: 20, <70: 12	Covid death
Ning M et al.[46]	United States of America	Single center, prospective cohort	March–April 2020	2020	NA	2 (Endometrial 1, Vaginal 1)	5 (Breast 1)	114 (Gynecological 12)	Female 2	Metastasis 2, III-IV: 2, Recurrent disease 2	NA	Radiotherapy 7	<65: 4, >65: 3	Covid death, Covid infection & Covid death
OnCovid Study Group[47]	OnCovid-Europe	Multi center, prospective cohort	February 2020–February 2021	2021	NA	115	2413 (Lung 11, Breast 29, Hematological 108)	NA	Female 1240, Male 1390	Localized 1237, Advanced 1244	0–1: 1414, >2: 1220	1305	<65: 1083, >65: 1538	Covid death
Ramaswamy A et al.[48]	India	Single center, prospective cohort	April–June 2020	2020	NA	13	217 (Lung 12, Breast 30, Hematological 90)	NA	Female 106, Male 124	Advanced 52, I-III: 93	Diabetes 30, Hypertension 25, Cardiac illness 2	SACT 230	Median 42, IQR1–75	Covid death
Roel E et al.[49]	Spain	Multi center, retrospective cohort	March–May 2020	2021	93558	436 (Corpus Uterus 291, Cervix 81, Ovary 64)	4957 (Lung 159, Breast 1236, Hematological 513)	255274 (Corpus Uterus 12665, Cervix 3232, Ovary 3564)	Female 57507, Male 41444	NA	Autoimmune 6322, CKD 4167, COPD 2476, Heart disease 11076, Diabetes 6239, Obese 27840, Dementia 2011, Hyperlipidemia 11015	NA	18–39: 30648, 40–59: 44909, 60–69: 10602, 70–79: 6419, >80: 6373	Covid infection, Covid hospitalization & Covid death

Table 1. *Continued*

Author	Location	Type of study	Time of study	Publication year	Non cancer Covid patients	Gynecology Oncology Covid patients	Other Oncology Covid patients	Cancer non Covid patients	Gender*	Cancer stage*	Comorbidities*	Cancer treatment*	Age*	Outcome
Russell B et al.[50]	United Kingdom	Single center, retrospective cohort	March–June 2020	2021	NA	10	180 (Lung 22, Breast 27, Hematological 33)	1962	Female 78, Male 112	I-II: 55, III-IV: 110	NA	SACT 92, Combination therapy 11	<50: 30, 50–59: 36, 60–69: 55, 70–79: 40, >80: 29	Covid infection
Shi Z et al.[86]	United Kingdom	Multi center, prospective cohort	June 2020	pre-prints	1306	9 (Cervix 2, Corpus Uteri 2, Ovary 5)	409 (Lung 10, Breast 47, Hematological 49)	2139 (Vulva 6, Cervix 7, Corpus Uteri 26, Ovary 20)	Female 746, Male 816	NA	COPD 239, Asthma 240, Heart disease 672, Stroke 67, Hypertension 689, Obese 124, Diabetes 232	NA	Cancer: Mean 61.36, IQR 56.5–67.5, Non cancer: Mean 56.11, IQR 47.5–64.5	Covid infection & Covid death
Song C et al.[51]	China	Multi center, retrospective cohort	December 2019–March 2020	2020	NA	17 (Ovarian 3, Endometrial 4, Cervical 10)	206 (Lung 39, Breast 31, Hematological 15)	NA	Female 107, Male 116	NA	BMI >25: 30	126	Median 63, IQR 56–71	Covid death
Song K et al.[52]	China	Multi center, retrospective cohort	January–July 2020	2020	NA	10	238 (Lung 61, Breast 37)	NA	Female 120, Male 128	I-III: 148, IV: 66	Diabetes 38, Hypertension 83, Cardiovascular 28, Cerebrovascular 18, COPD 21	Surgery 25, Radiotherapy 10, Combined 15, SACT 51	Median 63, IQR 57–70	Covid death and Severe Covid
Tian J et al.[53]	China	Multi center, retrospective cohort	January–March 2020	2020	519	15 (Cervical 11, Endometrial 3, Ovarian 1)	217 (Lung 23, Breast 31, Hematological 12)	NA	Female 379, Male 372	I-III: 192, IV: 34	Hypertension 292, Diabtes 198, Coronary heart disease 74, CKD 23, Cerebrovascular disease 23, Hepatitis 10, COPD 4	Surgery 197, Chemo/ Radiotherapy 214, Targeted/ Immunotherapy 32	Median 64, IQR 57–69	Covid death and Severe Covid
Villegas A et al.[54]	Spain	Single center, retrospective cohort	March–April 2020	2020	NA	1 (Ovarian)	6	138	Female 2, Male 1	Advance 1, Initial staging 1, Recurrence 1	NA	NA	>65: 3	Covid infection & Covid death
Wang Q et al.[55]	United States of America	Multi center, Case control	August 2020	2020	NA	30 (Endometrial)	1440 (Lung 140, Breast 370, Hematological 220)	3070260 (Endometrial 41710)	Female 9700, Male 6830	NA	NA	NA	<18: 20, 18–65: 11610, >65: 3900	Covid infection
Yang F et al.[56]	China	Single center, retrospective cohort	January–April 2020	2020	NA	6 (Cervical 4, Endometrial 1, Ovarian 1)	46 (Lung 10, Breast 9)	NA	Female 24, Male 28	NA	Hypertension 17, Diabetes 7, Coronary heart disease 5, Cerebrovascular disease 4, COPD 4, CKD 1, Cirrhosis 1	Chemotherapy 6, Surgery 2, Immunotherapy 1	<60: 20, >60: 32	Covid death
Yang K et al.[57]	China	Multi center, retrospective cohort	January–March 2020	2020	NA	9 (Cervical)	142 (Lung 24, Breast 40, Hematological 22)	NA	Female 109, Male 96	I-II: 109, III-IV: 40	Hypertension 67, Diabetes 22, COPD 5, Coronary heart disease 16, CKD 4	Surgery 140, Radiotherapy 37, SACT 129	<60: 86, >60:119	Covid death
Yang S et al.[58]	China	Single center, retrospective cohort	January 2020	2020	1	2 (Ovarian 1, Cervical 1)	NA	31	Female 3	I: 1, III: 1	Diabetes & Hypertension 2, Hypertension 1	Surgery 2	>45: 3	Covid infection

Table 1. *Continued*

Author	Location	Type of study	Time of study	Publication year	Non cancer Covid patients	Gynecology Oncology Covid patients	Other Oncology Covid patients	Cancer non Covid patients	Gender*	Cancer stage*	Comorbidities*	Cancer treatment*	Age*	Outcome
Zhang L et al.[59]	China	Multi center, retrospective cohort	January–February 2020	2020	NA	3 (Ovary 1, Endometrial 1, Cervix 1)	25 (Lung 7, Breast 3)	NA	Female 11, Male 17	I/II/III: 18, IV: 10	Diabetes 4, Cardio&Cerebrovascular disease 4, Chronic pulmonary disease 1, Chronic liver disease 2	Surgery 21, Chemo/ radiotherapy 25, Target/ Immunotherapy 6	Median 65, IQR 56–70	Covid death and Severe Covid
Zhou K et al.[60]	France	Multi center, retrospective cohort	June–November 2020	2021	NA	5	65 (Lung 8, Breast 36)	808 (Gynecological 81)	Female 56, Male 14	Localized 19, Locally advanced 9, Metastasis 32	Hypertension 18, Diabetes 6, CKD 7, Heart failure 2, Autoimmune disease 2	SACT 70, Radiotherapy 2, Surgery 4	Median 61, IQR 27–81	Covid infection

CCC19: the clinical impact of Covid-19 patients with cancer study, CKD: chronic kidney disease, COPD: chronic obstructive pulmonary disease, IQR: interquartile range, NA: not addressed, SACT: systemic anti-cancer therapy.
*Covid-19 population.
#Charlson comorbidity index.

Gynecologic cancer VS other cancer

Covid-19 infection was equivalent between gynecologic cancer and other cancer patients gathered from eight studies (OR 1.02, CI 0.84–1.22, *p* 0.87, I^2 57%) **Figure S3**.[32,38,49,50,54,55] Gynecologic cancer patients had fewer Covid-19 associated deaths compared to other cancers according to 30 studies (OR 0.82, CI 0.71–0.94, *p* 0.006, I^2 0%) Figure 2.[17–19,23–27,29,31,36,38–41,44,45,47,49,51–54,56,57,59] Covid-19 associated severity was not significant from six studies between gynecologic cancer and other cancer types (OR 0.56, CI 0.30–1.03, *p* 0.06, I^2 0%) **Figure S4**.[23,24,31,52,53,59] Data from two studies also showed no significant difference in Covid-19 hospitalizations between gynecologic cancer patients than other cancers (OR 0.73, CI 0.50–1.06, *p* 0.10, I^2 82%) **Figure S5**.[29,49]

Gynecologic cancer VS non-cancer

Covid-19 infection among gynecologic cancer patients and the non-cancer population was not significant from six studies (OR 1.55, CI 0.81–2.95, *p* 0.18, I^2 90%) **Figure S6**.[34,38,49,55,58] Data from 11 studies revealed death from Covid-19 was higher in gynecologic cancer than non-cancer patients (OR 2.98, CI 2.23–3.98, $p < 0.0001$, I^2 30%) Figure 3.[17,19,23,26,37,38,41,49,53] However, severe Covid-19 cases showed no significant difference between gynecologic cancer than non-cancer patients from two studies (OR 1.85, CI 0.77–4.44, *p* 0.17, I^2 0%) **Figure S7**.[23,53]

Gynecologic cancer VS non-covid

Data represented from five studies revealed that gynecologic cancer patients were experiencing higher Covid-19 associated death in comparison to other cancer patients without Covid-19 infection (OR 11.83, CI 8.20–17.07, $p < 0.0001$, I^2 5%) Figure 4.[15,38,43,49]

Cancer treatment group

We analyzed the effect of active cancer treatment comprising SACT (systemic anti-cancer therapy), radiotherapy, cancer surgery, and hormonal therapy. Data from nine studies showed that, among those who receive active cancer treatment, Covid-19 infection was not significant in gynecologic cancer patients compared to other cancer types (OR 0.75, CI 0.55–1.02, *p* 0.07, I^2 0%) **Figure S8**.[14,16,22,28,30,33,42,46,60] Covid-19 death was not significant among cancer treatment between gynecologic cancer and other cancer types gathered from nine studies (OR 0.86, CI 0.41–1.78, *p* 0.68, I^2 0%) **Figure S9**.[14,20,23,24,31,37,43,46,48] Severe Covid-19 cases among those who were receiving active cancer treatment showed no significant difference between gynecologic cancer than other cancer according to six studies (OR 0.63, CI 0.18–2.25,

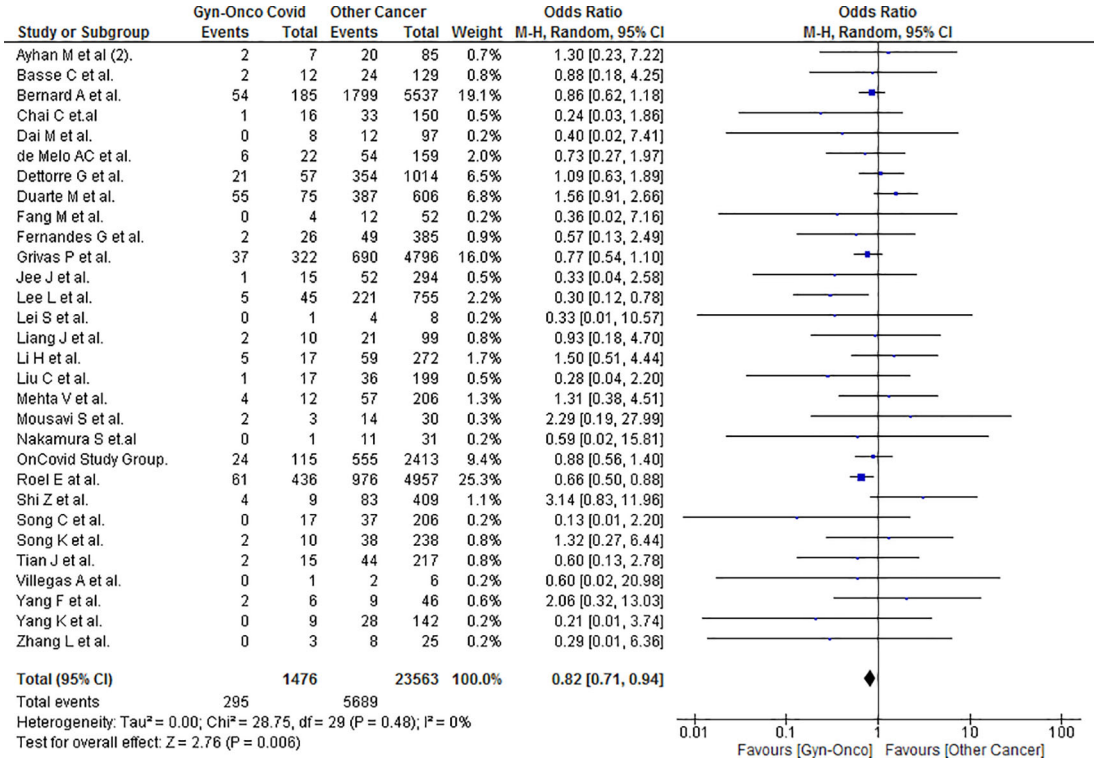

Figure 2. Gynecologic cancer VS other cancer, Covid-19 death. M-H; mantel-haenszel, CI; confidence interval.

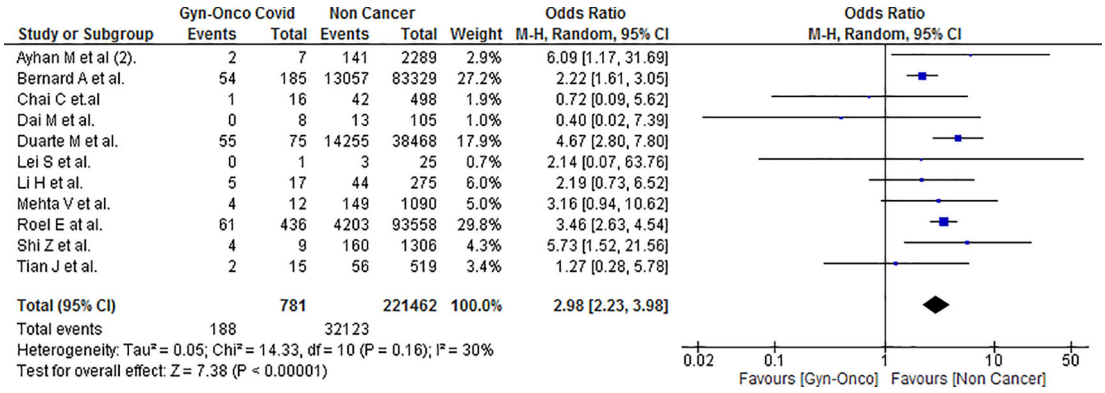

Figure 3. Gynecologic cancer VS non-cancer, Covid-19 death. M-H; mantel-haenszel, CI; confidence interval.

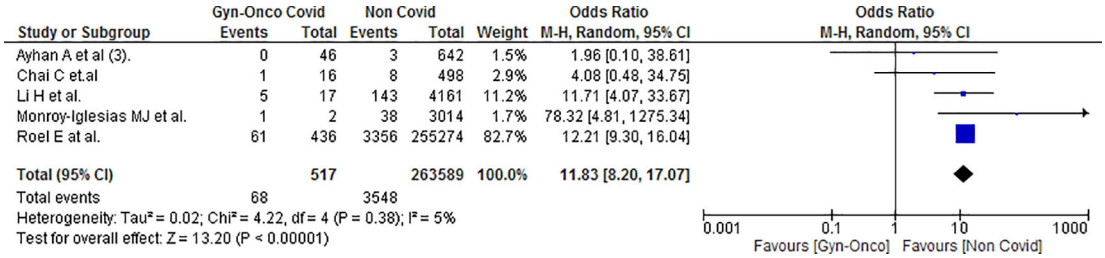

Figure 4. Gynecologic cancer with Covid-19 VS other cancer non-Covid, Covid-19 death. M-H; mantel-haenszel, CI; confidence interval.

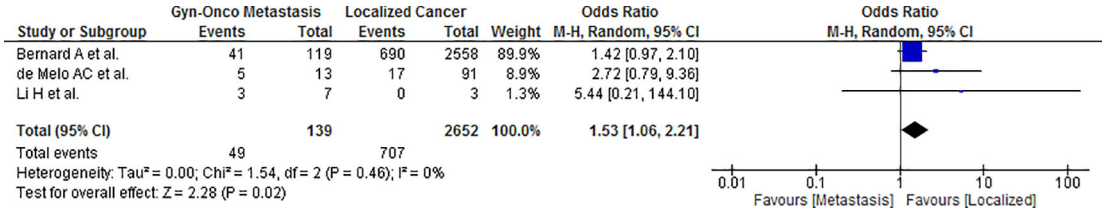

Figure 5. The Covid-19 death, gynecologic cancer with metastasis VS no metastasis. M-H; mantel-haenszel, CI; confidence interval.

p 0.48, I^2 18%) **Figure S10**.[23,24,31,43,46,59] According to five studies, Covid-19 associated death was comparable in gynecologic cancer with active cancer treatment compared to those who were not receiving cancer treatment (OR 1.06, CI 0.57–1.98, p 0.86, I^2 0%) **Figure S11**.[21,23,24,31,35] Lastly, five studies showed severity from Covid-19 was not significant in gynecologic cancer patients who had active cancer treatment compared to those who had none (OR 0.45, CI 0.17–1.20, p 0.11, I^2 26%) **Figure S12**.[23,24,31,35,59]

Cancer stage and metastatic cancer

There were two studies available for cancer stage analysis.[23,24] Overall, adverse Covid-19 events (infection/hospitalization/severity/death) showed no significance between stage I-II gynecologic cancer against stage III-IV other cancer, stage III-IV gynecologic cancer against stage I-II other cancer, and among all cancer patients who had stage III-IV cancer (OR 0.78, CI 0.04–16.18, p 0.88, I^2 67%), (OR 0.48, CI 0.15–1.53, p 0.21, I^2 0%), (OR 0.59, CI 0.22–1.58, p 0.29, I^2 0%) respectively **Figures S13–S15**. No significance on Covid-19 adverse events between stage III-IV and I-II gynecologic cancer was found in three studies (OR 0.72, CI 0.39–1.33, p 0.29, I^2 0%) **Figure S16**.[23,24,35]

There were three studies that provided data on metastatic status.[19,24,38] Gynecologic cancer with metastasis had increased Covid-19 associated death than those with localized cancer (OR 1.53, CI 1.06–2.21, p 0.02, I^2 0%) Figure 5. Contrary,

among those who had metastatic diseases, Covid-19 death was not significant between gynecologic cancer compared to other cancer types (OR 0.77, CI 0.54–1.11, p 0.17, I^2 0%) **Figure S17**.

Gynecologic cancer VS lung cancer

A total of 13 studies provided data on Covid-19 infectivity, infection was not significant in gynecologic cancer than lung cancer (OR 0.86, CI 0.61–1.20, p 0.37, I^2 73%) **Figure S18**.[14,16,22,28,32,38,42,49,50,55,60] Data from 30 studies revealed that gynecologic cancer had fewer Covid-19 deaths than lung cancer patients (OR 0.52, CI 0.44–.062, $p < 0.0001$, I^2 0%) Figure 6A.[14,17–20,23–27,29,31,36,38,39–41,44,45,47–49,51–53,56,57] Data from six studies showed that gynecologic cancer was having less severity from Covid-19 than lung cancer (OR 0.36, CI 0.16–0.80, p 0.01, I^2 0%) Figure 6B.[23,24,31,52,53,59] Lastly, two studies reported fewer hospitalizations associated with Covid-19 in gynecologic cancer than lung cancer (OR 0.54, CI 0.40–0.73, $p < 0.0001$, I^2 0%) Figure 6C.[16,29]

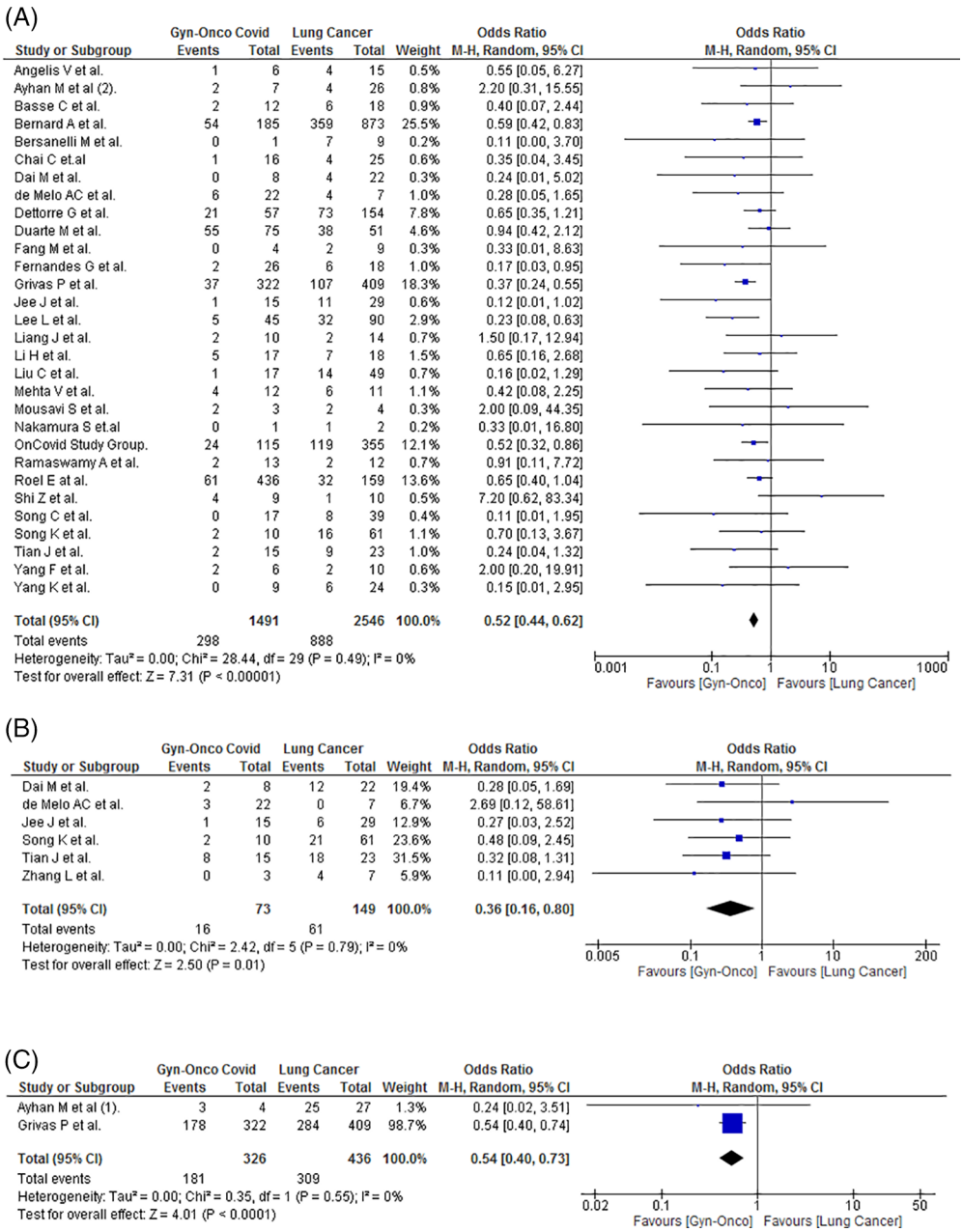

Figure 6. Gynecologic cancer VS lung cancer, (A) Covid-19 death, (B) Severe Covid-19, (C) Covid-19 hospitalization. M-H; mantel-haenszel, CI; confidence interval.

Gynecologic cancer VS breast cancer

Data from 13 studies showed gynecologic cancer and breast cancer were equivalent on the rate of Covid-19 infection (OR 1.05, CI 0.94–1.17, p 0.37, I^2 7%) **Figure S19**.[14,16,28,32,38,42,46,49,50,55,60] Interestingly, from 25 studies, gynecologic cancer patients experience higher Covid-19 death compared to breast cancer patients (OR 1.50, CI 1.20–1.88, p 0.0004, I^2 19%) Figure 7A.[14,17–19,24–27,29,31,36,38–41,44,47–49,52,53,56,57] Covid-19 severity was not significant from seven studies between gynecologic cancer and breast cancer patients (OR 0.83, CI 0.40–1.72, p 0.62, I^2 0%) **Figure S20**.[23,24,31,46,52,53,59] Lastly, data from two studies showed gynecologic cancer patients experience higher hospitalization from Covid-19 compared to breast cancer (OR 1.52, CI 1.18–1.96, p 0.001, I^2 0%) Figure 7B.[16,29]

Gynecologic cancer VS hematologic cancer

Data available from eight studies revealed gynecologic cancer patients had less Covid-19 infections compared to hematologic cancer patients (OR 0.71, CI 0.56–0.90, p 0.005, I^2 68%) Figure 8A.[14,32,38,49,50,55] Data also showed that gynecologic cancer patients were experiencing fewer Covid-19 deaths compared to hematologic cancer from 24 studies (OR 0.63, CI 0.47–0.83, p 0.001, I^2 46%) Figure 8B.[14,18,19,23–27,29,31,36,38,39,41,45,47–49,51,53,57] Lastly, four studies also showed that gynecologic cancer patients were having less severity from Covid-19 compared to hematologic cancer (OR 0.26, CI 0.10–0.67, p 0.005, I^2 0%) Figure 8C.[23,24,31,53]

Gynecologic cancer VS men

Based on 10 studies available for synthesis, there was no significance on Covid-19 infection between gynecologic cancer population and men with cancer (OR 0.58, CI 0.27–1.22, p 0.15, I^2 94%) **Figure S21**.[16,22,28,38,42,50,55,60] Compared to men with cancer, the Covid-19 associated death retrieved from 23 studies showed no significant difference (OR 0.75, CI 0.54–1.05, p 0.09, I^2 23%) **Figure S22**.[14,17,20,23,24,26,27,29,31,36,38–41,45,48,51,52,56,57] According to six studies, severe Covid-19 was higher in men with cancer compared to gynecologic cancer patients (OR 0.47, CI 0.25–0.88, p 0.02, I^2 0%)

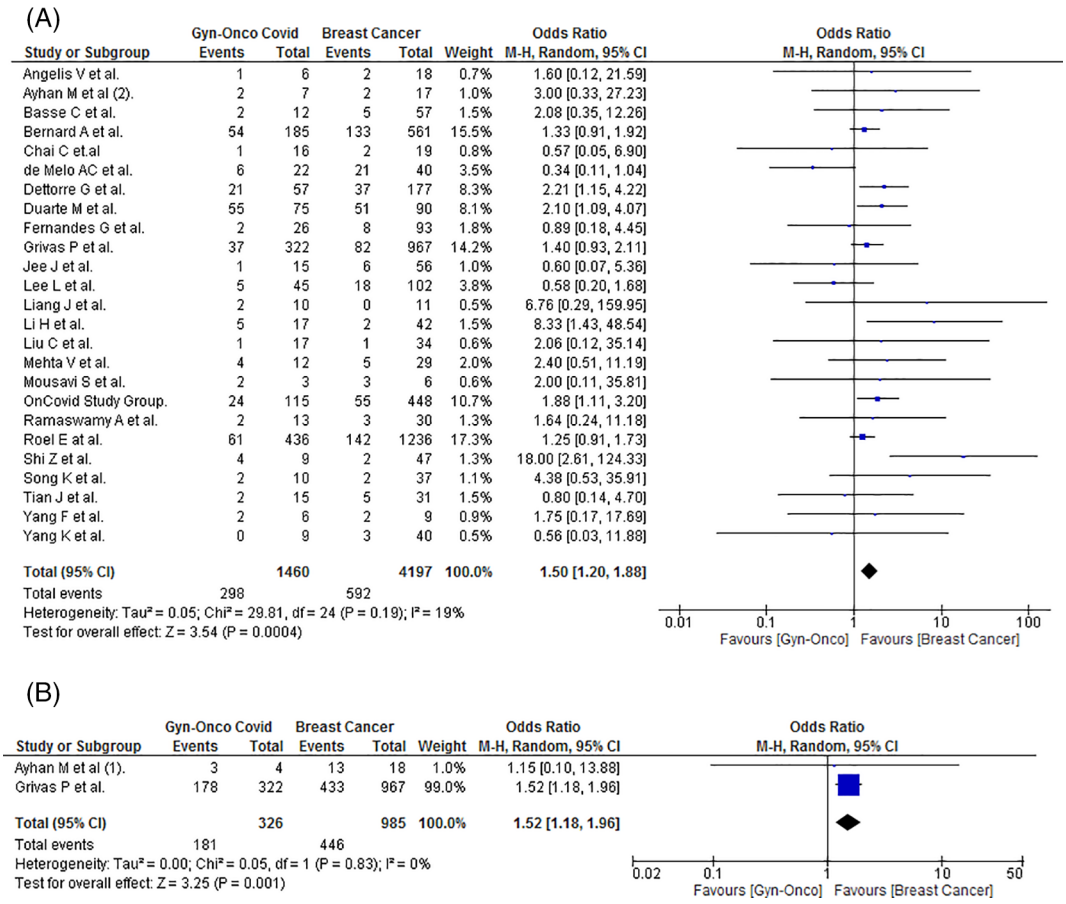

Figure 7. Gynecologic cancer VS breast cancer, (A) Covid-19 death, (B) Covid-19 hospitalization. M-H; mantel-haenszel, CI; confidence interval.

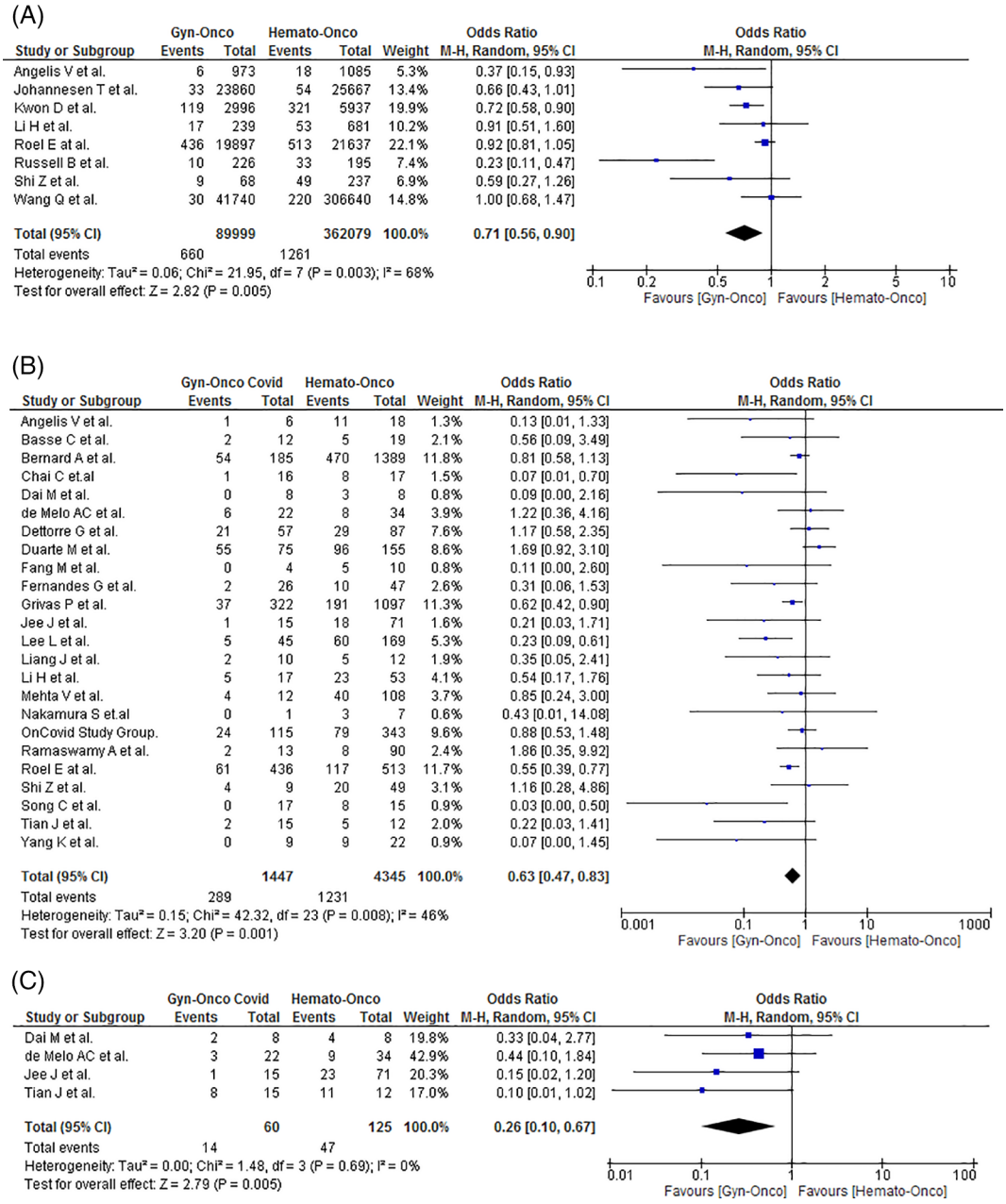

Figure 8. Gynecologic cancer VS hematologic cancer, (A) Covid-19 infection, (B) Covid-19 death, (C) Severe Covid-19. M-H; mantel-haenszel, CI; confidence interval.

Figure 9A.[23,24,31,52,53,59] Hospitalization from Covid-19 was also higher in men with cancer compared to gynecologic cancer patients synthesized from two studies (OR 0.71, CI 0.56–0.89, p 0.004, I^2 0%) Figure 9B.[16,29]

Age stratification

Data from four studies showed that among the gynecologic cancer population, those who were > 65 compared to <65 years of age had comparable overall adverse Covid-19 outcomes (infection/hospitalization/severity/death), (OR 1.13, CI 0.48–2.62, p 0.78, I^2 14%) **Figure S23**.[15,21,23,24] We performed a pairwise comparison of gynecologic cancer with <65 years old against other cancer with >65 years old, and gynecologic cancer with >65 years old against other cancer with <65 years old.[23,24,59] Covid-19 adverse outcome was found to be lower in <65 year old gynecologic cancer than >65 years old other cancer population (OR 0.16, CI 0.06–0.47, p 0.0007, I^2 0%) Figure 10. Contrary, there

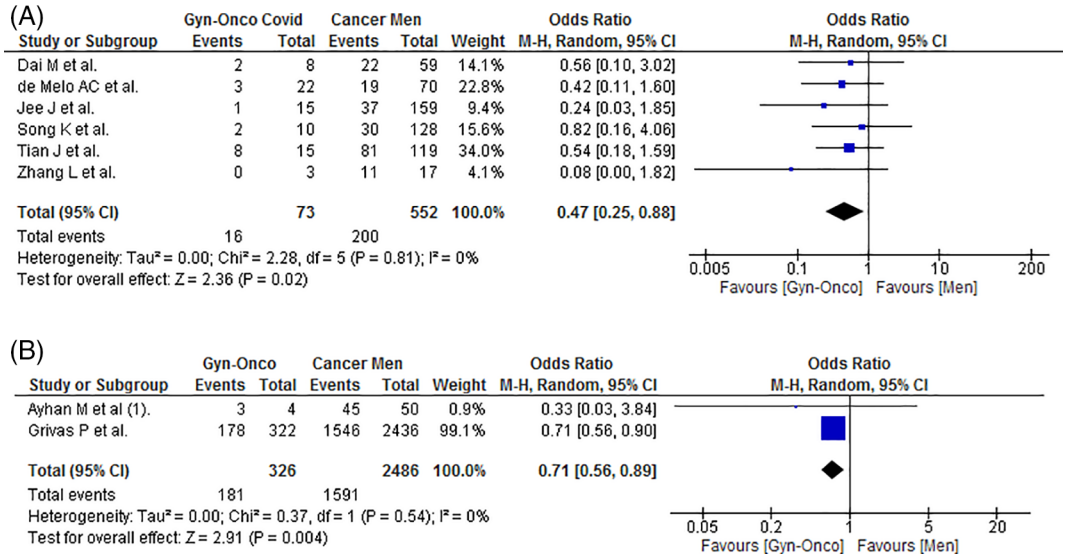

Figure 9. Gynecologic cancer patients VS men with cancer, (A) Severe Covid-19, (B) Covid-19 hospitalization. M-H; mantel-haenszel, CI; confidence interval.

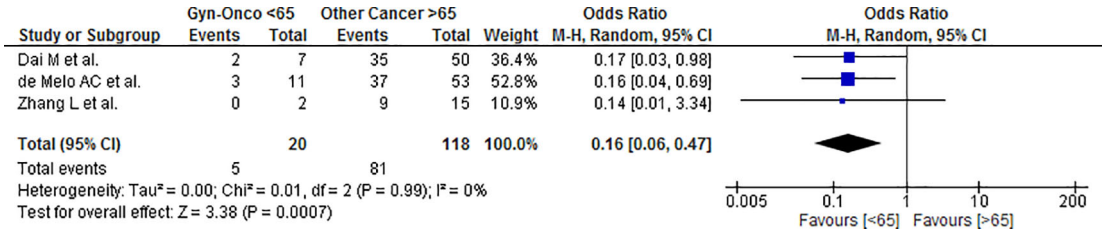

Figure 10. The Covid-19 adverse outcome, <65 years old gynecologic cancer VS >65 years old other cancer population. M-H; mantel-haenszel, CI; confidence interval.

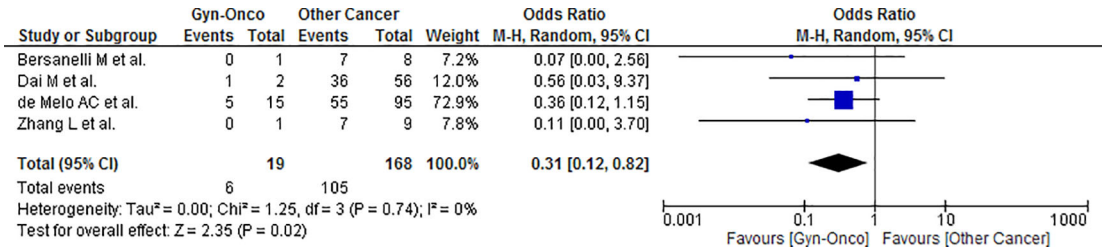

Figure 11. The Covid-19 adverse outcome with comorbidities, gynecologic cancer VS other cancer. M-H; mantel-haenszel, CI; confidence interval.

was an equivalent Covid-19 adverse outcome between gynecologic cancer with >65 years old and other cancer with <65 years old (OR 1.08, CI 0.36–3.26, *p* 0.89, I^2 0%) **Figure S24**.

Comorbidities

Cancer is a comorbidity, aside from which we tried to analyze other comorbidities (hypertension, diabetes, cardiovascular disease, pulmonary disease, renal disease, liver disease, immune disease, metabolic-endocrine disease) present within the cancer population. Among those with comorbidities, gynecologic cancer patients had fewer adverse Covid-19 outcomes than other cancer populations according to four studies (OR 0.31, CI 0.12–082, *p* 0.02, I^2 0%) Figure 11.[20,23,24,59] Data from five studies showed there was no significant adverse Covid-19 outcome between gynecologic cancer patients with comorbidities against no comorbidities (OR 2.34, CI 0.59–9.79, *p* 0.24, I^2 79%) **Figure S25**.[15,21,23,24,35] Gynecologic cancer patients without comorbidities against other cancer patients with comorbidities had no significant difference in

adverse Covid-19 outcomes, according to three studies (OR 0.29, CI 0.04–2.22, p 0.23, I^2 56%) **Figure S26**. [23,24,59] Gynecologic cancer patients with comorbidities against other cancer patients without comorbidities also showed no significant difference in adverse Covid-19 outcomes, according to four studies (OR 0.61, CI 0.22–1.72, p 0.35, I^2 0%) **Figure S27**.[20,23,24,59]

Sensitivity analysis

We performed sensitivity analysis by reproducing each outcome synthesis to pre-specified single center to multi-center studies, furthermore excluding overlapped study periods associated with its study centers, thus only one center with the most recent study period was included in **Table S1**. After exclusion of three studies, a difference of significance was found in severe Covid-19 between gynecologic cancer and cancer men population (OR 0.47, CI 0.19–1.17, p 0.10, I^2 0%)[24,31,52] Aside from that, the remainder of the calculated OR from reproducing each outcome synthesis by exclusion were within good accordance.

Publication bias

We found no publication bias within our included studies though at first, we identified an asymmetrical funnel plot; it was caused solely by heterogeneity nonetheless (**Figures S28–31**). After subgroup identification, the funnel plot was corrected and the calculated Egger & Begg's test for overall Covid death, severity, and hospitalization were p 0.15 and p 1.6. For data associated with Covid-19 infection, the values were p 0.17 and p 1.87.

Discussion

We believe this is the first comprehensive meta-analysis with a large population regarding the outcome of Covid-19 on the gynecologic cancer population. With the 1991 Covid-19 positive gynecologic cancer, we hope we provide new insight into how the global pandemic is affecting practice and services affecting gynecologic cancer. Several meta-analyses showed the prevalence of cancer with Covid-19 infection was 2–4%, Covid-19 mortality was also higher in the cancer patients cohort.[5–7,61–65] In this meta-analysis, it was found that gynecologic cancer patients are at an increased risk of Covid-19 death compared to the non-cancer population (OR 2.98, CI 2.23–3.98, $p < 0.0001$, I^2 30%), most studies also support this finding by providing evidence of greater Covid-19 adverse outcome in cancer patients.[5–7,61–65] Contrary to the National COVID Cohort Collaborative (*N3C*) multicenter study from the United States, our result present a significant increase of death in gynecologic cancer with Covid-19 than other cancer types without Covid-19 (OR 11.83, CI 8.20–17.07, $p < 0.0001$, I^2 5%).[66] Our finding shows gynecologic cancer with metastatic disease has an increased Covid-19 death compared to those whose cancer is localized (OR 1.53, CI 1.06–2.21, p 0.02, I^2 0%), most studies also report identical outcomes to ours.[65,67,68] Our analysis also shows gynecologic cancer is associated with higher Covid-19 death and hospitalization compared to breast cancer patients (OR 1.50, CI 1.20–1.88, p 0.0004, I^2 19%), (OR 1.52, CI 1.18–1.96, p 0.001, I^2 0%) respectively. Other meta-analyses, as well as studies done by the clinical impact of Covid-19 patients with cancer (*CCC19*) and the "*N3C*" also supported this finding.[62,66,67] Our analysis presents that gynecologic cancer patients have lower Covid-19 death compared to overall other cancer types (OR 0.82, CI 0.71–0.94, p 0.006, I^2 0%). Further analysis shows that gynecologic cancer patients with Covid-19 have fewer adverse outcome compared to Covid-19 lung and hematologic cancer. Our findings are (OR 0.52, CI 0.44–.062, $p < 0.0001$, I^2 0%), (OR 0.36, CI 0.16–0.80, p 0.01, I^2 0%), (OR 0.54, CI 0.40–0.73, $p < 0.0001$, I^2 0%) for Covid-19 associated death, severity, and hospitalization versus lung cancer respectively. Hematologic cancer (OR 0.71, CI 0.56–0.90, p 0.005, I^2 68%), (OR 0.63, CI 0.47–0.83, p 0.001, I^2 46%), (OR 0.26, CI 0.10–0.67, p 0.005, I^2 0%) for Covid-19 infectivity, death, and severity respectively. The "*TERAVOLT*" study and the one conducted by Luo *et al.* also support our finding of a high level of Covid-19 associated adverse outcomes among lung cancer patients.[69,70] Other meta-analyses show lung cancer with Covid-19 has a 32.9% case fatality rate (378 lung cancer), compared to the non-lung cancer population the Covid-19 death among lung cancer is also higher (92 lung cancer, 554 control, OR 1.83, p 0.05), (78 lung cancer, 482 control, RR 1.46, p 0.7).[5,62,63] Lastly, most studies also support our findings on the increased Covid-19 adverse outcome in the hematologic cancer population, as their results are 34.2% case fatality rate (480 hematologic cancer), (120 hematologic cancer, 758 control, OR 2.39, p 0.02).[62,63,65–68] We believe our meta-analysis results correspond to several studies that present the safety of continuing gynecologic cancer care and service during the global pandemic. Safety protocols have been published for gynecologic cancer patients who are seeking treatment and some even recommend the implementation of ERAS (Enhanced Recovery After Surgery).[2,71,72] Data from the French Society for Pelvic and Gynecological Surgery (SCGP) and the French (FRANCOGYN) Group reveal there are changes in cancer management strategy during the pandemic time and from 181 gynecologic cancer patients, eight tested positive for Covid-19.[73] A multicenter study from three New York City hospitals also show a similar result; among 302 gynecologic cancer patients, 117 experienced a COVID-19-related treatment modification, 19 had a positive Covid-19 result and among them three were asymptomatic, 11 had mild symptoms, three were hospitalized, and two died.[74] Lastly, data from the United Kingdom, Turkey, and Italy show that while maintaining gynecologic cancer treatment during the pandemic time the Covid-19 infection rate is found at a low level, 1/289 is Covid-19 positive and 1 post-operative death suspected of Covid-19 (UK), 2/200 is suspected with

Covid-19 but neither was positive for COVID-19 on polymerase chain reaction testing (Turkey), and 1/930 is Covid-19 positive (Italy).[75–77] Other meta-analysis shows Covid-19 infection with existing comorbidities such as hypertension (OR 1.95, $p < 0.0001$), diabetes (OR 1.97, $p < 0.0001$), respiratory disease (OR 2.74, $p < 0.0001$), cardiovascular disease (OR 3.05, $p < 0.0001$), cerebrovascular disease (OR 4.78, $p < 0.0001$), kidney disease (OR 4.90, $p < 0.0001$), and cancer (OR 1.89, $p < 0.0001$) increase the risk of mortality.[78] Our analyzed population comprises cancer as the main comorbidity, however with comorbidities other than cancer, our study shows that the gynecologic cancer population with additional comorbidities has fewer adverse events than other cancer with comorbidities (OR 0.31, CI 0.12–082, p 0.02, I^2 0%). Other meta-analyses prove that men have increased Covid-19 severity and mortality.[78,79] Our findings correspond by showing that severity and hospitalization from Covid-19 were higher in men with cancer compared to gynecologic cancer patients (OR 0.47, CI 0.25–0.88, p 0.02, I^2 0%), (OR 0.71, CI 0.56–0.89, p 0.004, I^2 0%) respectively. Age thresholds above 50 and 60 years old have an effect on Covid-19 mortality.[78,80] In our study Covid-19 adverse outcome was lower in <65 years old gynecologic cancer than <65 years old other cancer patients (OR 0.16, CI 0.06–0.47, p 0.0007, I^2 0%). Other meta-analysis on Covid-19 with active cancer treatment shows that cancer surgery (OR 1.14, $p <$ 0.01), chemotherapy (OR 1.60, <0.01), and overall cancer treatment type (OR 1.16, $p < 0.01$) have a higher risk of death.[81] However in our study Covid-19 death is equivalent in gynecologic cancer with active cancer treatment compared to those who are not receiving cancer treatment (OR 1.06, CI 0.57–1.98, p 0.86, I^2 0%).

We hope these findings will be useful among gynecologist-oncologists in cancer centers or tertiary cancer referral centers who provide care to gynecologic cancer patients during the ongoing Covid-19 pandemic.

In several data syntheses with the statistically nonsignificant value, we analyze few data regarding severity, hospitalization, age, cancer stage/metastatic status, other comorbidities aside from cancer, and cancer treatment type due to limited data, however those aforementioned are well represented and distributed through other synthesis based on the patient's characteristics available in Table 1.

Data availability

Underlying data

Figshare: Systematic review and Meta-analysis file. https://doi.org/10.6084/m9.figshare.19470131.[82]

This project contains the following underlying data:

- Outcome of Gynaecologic Cancer Patients With The Covid-19 Infection A Systematic Review And Meta Analysis (26.3.2022).rm5
- Meta Qulitative.xlsx
- Meta Data.xlsx
- Table 1.docx

Extended data

This project contains the following extended data:

- Supplementary Materials.docx

Reporting guidelines

Figshare: PRISMA checklist and flow diagram for 'The outcome of gynecologic cancer patients with Covid-19 infection: A systematic review and meta-analysis'. https://doi.org/10.6084/m9.figshare.19470131.[82]

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