Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Characteristics, risk factors, and outcomes associated with readmission in COVID-19 patients: A systematic review and meta-analysis

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ABSTRACT

Background: We aimed to determine the characteristics, risk factors, and outcomes associated with readmission in COVID-19 patients.

Methods: PubMed, Embase, Web of Science, and Scopus databases were searched to retrieve articles on readmitted COVID-19 patients, available up to September 25, 2021. All studies comparing characteristics of readmitted and non-readmitted COVID-19 patients were included. We also included articles reporting the reasons for readmission in COVID-19 patients. Data were pooled and meta-analyzed using random or fixed-effect models, as appropriate. Subgroup analyses were conducted based on the place and duration of readmission.

Results: Our meta-analysis included 4823 readmitted and 63,413 non-readmitted COVID-19 patients. The re-hospitalization rate was calculated at 9.3% with 95% Confidence Interval (CI) [5.5%–15.4%], mostly associated with respiratory or cardiac complications (48% and 14%, respectively). Comorbidities including cerebrovascular disease (Odds Ratio (OR) = 1.812; 95% CI [1.547–2.121]), cardiovascular (2.173 [1.545–3.057]), hypertension (1.608 [1.319–1.960]), ischemic heart disease (1.998 [1.495–2.670]), heart failure (2.556 [1.980–3.300]), diabetes (1.588 [1.443–1.747]), cancer (1.817 [1.526–2.162]), kidney disease (2.083 [1.498–2.897]), chronic pulmonary disease (1.601 [1.438–1.783]), as well as older age (1.525 [1.175–1.978]), male sex (1.155 [1.041–1.282]), and white race (1.263 [1.044–1.528]) were significantly associated with higher readmission rates ($P < 0.05$ for all instances). The mortality rate was significantly lower in readmitted patients (OR = 0.530 [0.329–0.855], $P = 0.009$).

Conclusions: Male sex, white race, comorbidities, and older age were associated with a higher risk of readmission among previously admitted COVID-19 patients. These factors can help clinicians and policy-makers predict, and conceivably reduce the risk of readmission in COVID-19 patients.

1. Introduction

The new coronavirus pneumonia began to spread in Wuhan, China, in late December 2019. Later, the World Health Organization (WHO) named it coronavirus disease 2019 (COVID-19) and recognized it a public health emergency [1]. WHO has confirmed 226 million COVID-19 cases and 4.6 million deaths worldwide, as of September 21, 2021 [2].

Numerous characteristics and clinical risk factors, including age, gender, race, and comorbidities have been reportedly associated with mortality, morbidity, and admission in COVID-19 patients [3,4]. Readmission, defined as the unplanned return of patients to the hospital wards, is a crucial quality indicator in the health care system [5]. A recent systematic review has divided the post-discharge situation of COVID-19 patients into three categories of mortality, reinfection, and readmission to different hospital wards. The review estimated the readmission rate in COVID-19 patients at around 7.5% [6].

Certain demographic or clinical features can be associated with greater risk of readmission in COVID-19 patients [7-9]. Only a few sparse studies are present on this subject, which have reported contradictory findings, indicating gender [10,11], age [12,13], and comorbidities [14,15], to be influencing the risk of readmission in COVID-19 patients. The limited number of readmitted patients, even in large cohort studies, has made the findings rather inconclusive [8,16].

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Therefore, this systematic review and meta-analysis was aimed to elucidate the clinical characteristics, risk factors, and outcomes in readmitted and non-readmitted COVID-19 patients in order to provide new insights that can help clinicians and health policy-makers control the pandemic by altering health policies.

2. Methods

2.1. Search strategy

This is a two-phase systematic review that was performed according to the recommendations of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA) [17]. PubMed, Embase, Scopus, and Web of Science were searched for articles evaluating readmission of COVID-19 patients up to September 25, 2021. We also searched Google Scholar and the reference lists of the included articles to find other papers that might meet our inclusion criteria. Two main keywords, "COVID-19" and "Readmission", were used in different combinations to search databases. A complete list of search strategies for all databases is provided in Supplementary Table S1. Articles written in English were included with no limitations in terms of publication date [18]. The present study was approved by the institutional review board of Mashhad University of Medical Sciences (Approval Code: 4001149).

2.2. Selection criteria

Initially, all studies that reported information on readmitted COVID-19 patients were included. Then, in phase 1 of the study, all articles comparing demographic data of readmitted and non-readmitted COVID-19 patients were included. Studies that combined the information of dead patients with live patients were excluded [19-22]. Moreover, we excluded letters if they reported fewer than 10 readmitted patients [23].

In phase 2 of the study, we included studies that reported the readmission causes. We excluded review articles, case-reports, letters, conference abstracts, case-control studies, and gray literature such as unpublished data, reports based on websites, and government regulatory documents [20].

2.3. Eligibility assessment

Four reviewers (A.A., A.F., M.A., and M.R.) were involved in the process of study selection based on the title, abstract, and full text of the articles. In cases where there was no agreement, the decision-making was resolved a fifth reviewer (A.Z.) checked eligibility to determine final inclusion.

2.4. Data extraction

Study characteristics including the first author's surname, publication date, title, study design, site of study (hospital(s), city, province or state, and country), COVID-19 confirmation method, and discharge criteria were extracted from the included articles. Characteristics of COVID-19 patients including date and length of index admission, duration of readmission, place of readmission, demographics, comorbidities, intensive care unit (ICU) admission, and use of different ventilation were also extracted. Data were stored in a Microsoft Excel spreadsheet (Redmond, WA).

2.5. Quality assessment

Two reviewers (A.G. and E.F.) independently screened included articles for quality assessment. The included studies were appraised using the Joanna Briggs Institute (JBI) assessment tools, which provide an appraisal tool for most types of the studies, including observational studies [24]. Any disagreement was resolved by discussion between investigators or a third reviewer.

2.6. Quantitative analysis

The magnitudes of the estimated effects were expressed as odds ratios (OR), with respective 95% confidence intervals (CIs) in brackets. We converted median values to mean using an estimation formula described by Wan et al. [25]. $P < 0.05$ was considered statistically significant in all calculations. Heterogeneity was quantitatively calculated by the I^2 index. If the heterogeneity was high (Cochran's $Q < 0.05$), we used the random-effects model; otherwise, we used the fixed-effects model. Potential publication bias was investigated using funnel plots, Egger's test, and Begg's test [26,27]. Sensitivity analysis was done by changing the statistical models or removing letter papers. We ran subgroup analyses regarding 30-day readmissions and hospital readmissions. All statistical analyses were done by CMA V.3.

3. Results

A total of 2130 studies were identified through searching the databases, of which 901 were duplicates (Fig. 1). Eventually, 36 studies were included in the present systematic review and 28 were incorporated in the meta-analysis [7,8,9,10,11,13-16,19,20,23,28–35,36–42,44–53]. Overall, 28 articles were included in phase 1 to determine risk factors and outcome of readmitted COVID-19 patients, and 19 articles were included in phase 2 to determine the cause of readmissions.

Twelve studies were suspected of having the same patients as the Verna et al. study [9]. Out of these 12 studies, five that reported data on fewer than 50 patients were removed from the meta-analysis. We excluded two studies from the meta-analysis due to low quality, heterogeneity, or unclear data [28,53].

3.1. Characteristics of studies

Of the 28 articles included in the meta-analysis, 25 were original articles and three were letters. The majority of the studies (14, 50%) were done in the United States. Overall, 18 studies had assessed readmission in 30 or fewer days (range: 3–30 days), while nine assessed it over longer periods (range: 60–180 days), and one included both periods. Characteristics of the included studies are summarized in Table 1. Quality assessment showed that the included studies were of acceptable quality (Supplementary Table S2). Among the 28 included studies, only two studies did not use a polymerase chain reaction (PCR) test for confirmation of COVID-19 diagnosis [40,54].

3.2. Risk factors and outcomes

Overall, 4823 readmitted and 63,413 none-readmitted patients were included in the meta-analysis. The overall re-hospitalization rate among live discharged patients was about 9.3% [95% CI: 5.5%–15.4%]. As shown in Table 2 and Supplementary Fig. S1, males were more likely to be readmitted and there was no strong association between ethnicity and readmission. The meta-analysis and sensitivity analysis showed different associations between age and readmission (Table 2).

We conducted a specific subgroup analysis for the age variable after removing two studies that contained only COVID-19 re-positive patients. Subgroup meta-analysis and sensitivity analysis showed that age was another risk factor for readmission (OR = 1.525 [95% CI: 1.175–1.978], $P = 0.001$). Supplementary Tables S3 and S4 present the crude data of all included studies on demographic/inpatient factors and comorbidities, respectively.

As Table 2 implies, patients with kidney disease, heart failure, and chronic obstructive pulmonary disease (COPD) had higher odds of hospital readmission (OR = 2.478 [95% CI: 2.195–2.798], 2.742 [2.107–2.567], 2.086 [1.657–2.626], respectively; $P < 0.001$). Table 2

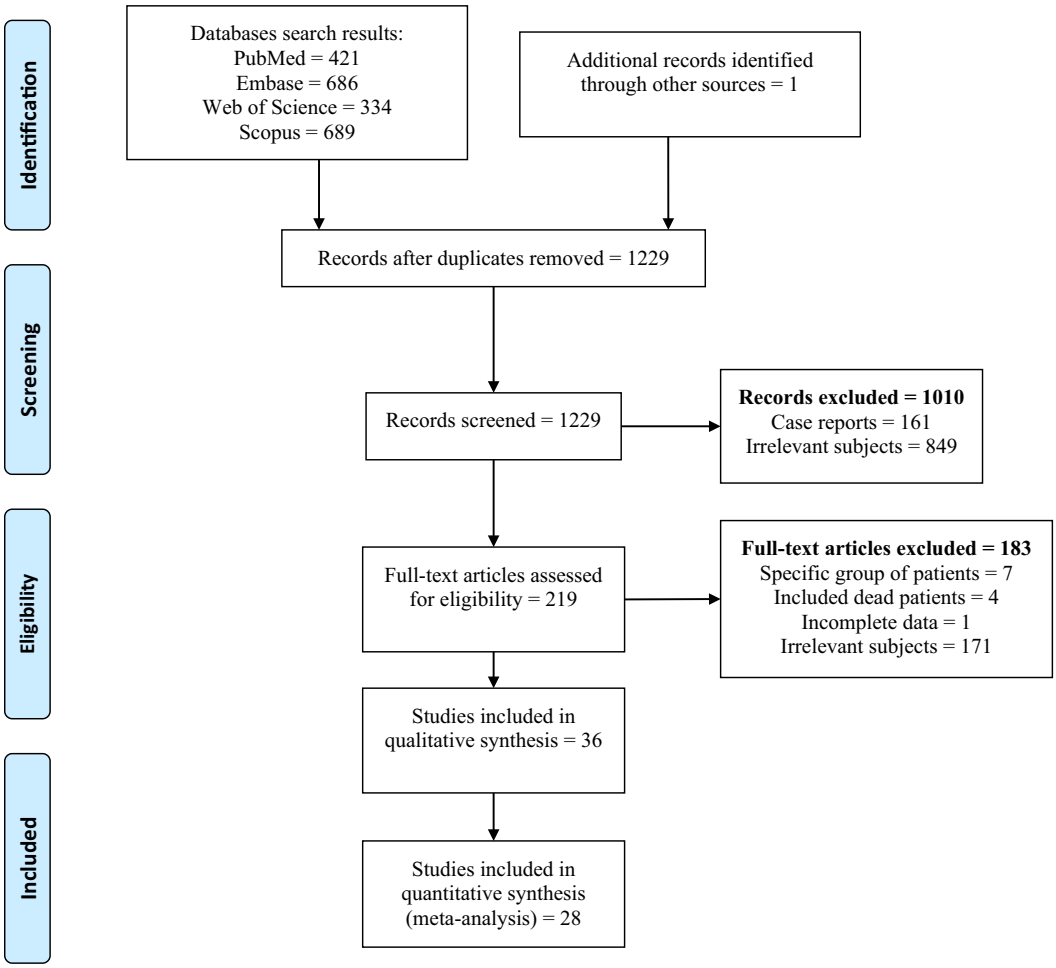

Fig. 1. PRISMA flow diagram of the study.

also shows effects of inpatient factors on readmission. Moreover, the mortality rate was lower in the second admission compared to the index admission (OR = 0.530 [95% CI: 0.329–0.855], I^2 = 78%, P = 0.009).

3.3. Publication bias and sensitivity analysis

The funnel plots for all studied variables are presented in Fig. S1. The Egger's and Begg's tests showed no significant publication bias regarding any of the variables, except for Asian ethnicity [hospital/emergency department (ED)] that showed moderate publication bias in the Eggers test (Table 2). Furthermore, sensitivity analysis showed that the results pertaining to Hispanic and white ethnicities, age, no-comorbidity, liver disease, ICU admission, and length of hospital stay may not be reliable (Table 2).

3.4. Causes of readmission

After discharge, most of the readmission causes were COVID-19-related respiratory complications, cardiac complications, thromboembolism, bacterial infection, trauma, kidney-related complications, and hemorrhages. Supplementary Table S5 presents the most important readmission causes. The respiratory complications of COVID-19 caused 3.5 times more readmissions compared with the cardiac complications; out of a total of 3342 readmitted patients in studies that reported both respiratory and cardiac-related readmissions, 1571 patients were readmitted due to respiratory complications and only 455 were because of cardiac complications.

4. Discussion

Recognizing the risk factors associated with readmission in COVID-19 patients is essential for healthcare professionals and health policymakers to review and change existing rules and standards of practice and provide more effective health management strategies. In this study, we assessed the characteristics, risk factors, and outcomes of readmitted COVID-19 patients. We also assessed the main causes of readmission.

We estimated the pooled rate of readmission among patients previously admitted with COVID-19 to be around 9.3% [95%CI: 5.5%–15.4%]. The discrepancies in the readmission rates reported by different studies can be attributed to the differences in readmission period, readmission setting, discharge criteria, treatment approach, and characteristics of the admitted patients.

We found that male COID-19 patients and those who had comorbidities were more likely to be readmitted to hospital wards. The comorbidities that were associated with higher likelihood of readmission were cerebrovascular disease, hypertension, ischemic heart disease, cardiovascular disease, heart failure, diabetes, cancer, kidney disease, and chronic pulmonary diseases. In terms of ethnicity, white patients were more likely to be readmitted, compared to Hispanics. Moreover, patients who needed invasive mechanical ventilation during their index admission had a lower rate of readmission.

Previous studies have also reported some characteristics to be more common among certain race groups. For example, obesity, hypertension, asthma, and human immunodeficiency virus (HIV) infection are more prevalent among the black race, while diabetes is more common among Asians [36].

Table 1
Characteristics of the included studies.

Author	Study design	Hospital(s)/City/Province (State)	Country	Date of primary admission	Readmission period (Days) (Max)	Place of index admission	Place of readmission	Reason for readmission
Jeon W.	Retrospective cohort	Nationwide Study	Republic of Korea	2020	3	Hospital	Hospital	Related to COVID-19
Kilaru A[‡]	Retrospective cohort	5 Hospitals/Pennsylvania and New Jersey	United States	1 March-28 May, 2020	3	ED	Hospital	All-cause readmission
Muñoz F.	Retrospective cohort	Infanta Cristina Hospital (ICH)/Madrid	Spain	17 March-25 April, 2020[†]	6	ED/ Hospital	Hospital	Related to COVID-19
Carroll O.[‡]	Prospective cohort	Vincent's University Hospital/Dublin	Ireland	2020	10	Hospital	Hospital	All-cause readmission
Somani S.	Retrospective cohort	Mount Sinai Health System (MSHS)/New York City Hospitals	United States	27 February-12 April, 2020	14	ED/Hospital	ED/Hospital	Related to COVID-19
Ye S.[*]	Retrospective cohort	Tertiary Care Medical Center-Columbia-New York-Presbyterian Hospital	United States	26 March-8 April, 2020	14	ED/Hospital	ED/Hospital	UC
Menditto V.	Retrospective cohort	Ospedali Riuniti and Marche Nord/ Ancona and Pesaro	Italy	1 March-28 April, 2020	15	ED/Hospital	Hospital	UC
Llorens P.	Retrospective cohort	General University Hospital of Alicantet	Spain	3 March-30 April, 2020	19	ED	ED	Related to COVID-19
Parra L.	Retrospective cohort	University Hospital in Madrid/Madrid	Spain	26 February-20 April, 2020	21	Hospital	Hospital	Related to COVID-19
Chen S.	Retrospective cohort	Multicentre/Guangdong	China	12 January-10 March, 2020[†]	28	Hospital	Hospital	Related to COVID-19
Gwin M.[*]	Retrospective cohort	Washington	United States	28 February-13 May, 2020[†]	30	Hospital	ED/Hospital	All-cause readmission
Yeo I.[*]	Retrospective cohort	Presbyterian Queens Hospital/New York City	United States	13 March-9 April, 2020	30	Hospital	ED/Hospital	All-cause readmission
Uyaroglu O.	Retrospective cohort	E-Pulse System	Turkey	20 March-26 April, 2020	30	ED/Hospital	Hospital	UC
Ramos-Martínez A.	Retrospective cohort	Nationwide Study	Spain	1 March-30 April, 2020[†]	30	Hospital	Hospital	All-cause readmission
Verna E.	Retrospective cohort	Nationwide Study	United States	15 February-9 June, 2020	30	Hospital	Hospital	All-cause readmission
Ye X.	Retrospective cohort	Wenzhou Central Hospital	China	17 January-5 March, 2020	30	Hospital	Hospital	UC
Lobelo F.	Retrospective cohort	Kaiser Permanente Georgia Affiliated (KPGA) Hospitals/Atlanta/Georgia	United States	3 March-21 October, 2020	30	ED/Hospital	Hospital	All-cause readmission
Lenehan P.[§]	Retrospective cohort	Tertiary Medical Centers in Minnesota, Arizona, and Florida	United States	Start of the COVID-19 pandemic-12 December, 2020	30	Hospital	Hospital	All-cause readmission
Huang C.[‡]	Retrospective cohort	15 Kaiser Permanente Southern California (KPSC) Medical Centers	United States	1 April-31 July, 2020 [†]	30	Hospital	Hospital	All-cause readmission
Loerinc L.[*]	Retrospective cohort	Four Emory Healthcare Affiliated Hospitals/Georgia	United States	26 March-21 April, 2020 [†]	30	ED/Hospital	ED/Hospital	Related to COVID-19
Samuels S.	Retrospective cohort	Memorial Healthcare System (MHS) Facilities/ South Florida	United States	2 March-31 May, 2020	30	ED/Hospital	Hospital	UC
Kirkegaard C.	Retrospective cohort	Valld'Hebron University Hospital/Barcelona	Spain	1 March-31 May, 2020	60	Hospital	Hospital	All-cause readmission
Lobelo F.	Retrospective cohort	KPGA Affiliated Hospitals/Atlanta/Georgia	United States	3 March-21 October, 2020	60	ED/Hospital	Hospital	All-cause readmission
Saab F.[*]	Case-series	University Of California, Los Angeles (UCLA) Medical Center	United States	1 March-1 May, 2020	86	Hospital	ED/Hospital	Related to COVID-19
Pawlowskia C.[*]	Retrospective cohort	Mayo Clinic and Hospitals Affiliated to the Mayo Rochester (Minnesota)/Florida/ Arizona	United States	15 February-27 October, 2020	90	Hospital	Hospital	All-cause readmission
Yang C.	Retrospective cohort	All Hospitals of the Shenzhen	China	1 February-5 May, 2020	113	Hospital	Hospital	Related to COVID-19
Green H.	Retrospective cohort	Rabin Medical Center/Petah Tiqva	Israel	March-10 October, 2020	161	Hospital	Hospital	All-cause readmission
Guarin G.[*]	Retrospective cohort	Einstein Medical Centre Philadelphia/Philadelphia/Pennsylvania	United States	1 March-24 April, 2020	180	Hospital	Hospital	UC
Günster D.	Retrospective cohort	Nationwide Study	Germany	1 February-30 April, 2020	180	Hospital	Hospital	All-cause readmission
Drewett G.	Retrospective cohort	Austin Health/Melbourne	Australia	1 March-1 October, 2020	180	Hospital	Hospital	All-cause readmission
Lovinsky-Desir S.	Retrospective cohort	New York Presbyterian Hospital Network/New York City	United States	11 February-7 May, 2020	-	Hospital	Hospital	UC

UC: Unclear; ED: emergency department.
[*] Possible data duplication.
[†] Date of first discharge.
[‡] Type of article was letter.
[§] The paper mentioned case control study.

Table 2
The results of meta-analysis on the risk factors of readmission.

Variables		Odds ratio [95% confidence intervals]	*P*-value	I^2 (%)	Model	Number of studies	Sample Size (Readmitted/Non-readmitted)
Demographics							
Male	≤30-Days	1.168 [1.078–1.266]	0.00	23	F	16	2563/55953
	[Hospital/ED]	1.155 [1.041–1.282]	0.007	36	R	21	4484/62184
	[Hospital]	1.190 [1.060–1.336]	0.003	45	R	20	4407/62156
	>30-Days	1.076 [0.829–1.396]	0.584	55	R	6	1996/6956
Hispanic ethnicity	≤30-Days	0.833 [0.632–1.099]	0.197	50	R[†,*]	10	953/15780
	[Hospital/ED]	0.767 [0.647–0.909]	0.002	44	F[†,*]	11	1012/15953
	[Hospital]	0.966 [0.640–1.457]	0.868	76	R	10	910/15894
Asian ethnicity	≤30-Days	1.119 [0.806–1.554]	0.500	0	F	6	830/13744
	[Hospital/ED][‡]	1.038 [0.759–1.419]	0.815	0	F	9	974/14714
	[Hospital]	1.095 [0.785–1.528]	0.593	0	F	8	877/14660
	>30-Days	0.486 [0.172–1.374]	0.174	0	F	3	144/970
Black ethnicity	≤30-Days	1.129 [0.766–1.664]	0.541	60	R	9	607/14776
	[Hospital/ED]	1.072 [0.746–1.540]	0.377	55	R	11	974/15023
	[Hospital]	0.945 [0.749–1.193]	0.635	43	F	10	977/14969
	>30-Days	0.760 [0.500–1.154]	0.198	0	F	3	237/1356
White ethnicity	≤30-Days	1.248 [1.019–1.529]	0.032	44	F[†,*]	8	607/7937
	[Hospital/ED]	1.263 [1.044–1.528]	0.016	32	F[†,*]	10	676/8186
	[Hospital]	1.410 [1.145–1.735]	0.001	0	F	9	605/8257
	>30-Days	1.355 [0.935–1.962]	0.109	0	F	3	144/970
Age	[Hospital/ED]	1.214 [0.793–1.858]	0.372	93	R[†]	20	1424/18624
	[Hospital]	1.204 [0.761–1.907]	0.428	93	R[†]	18	1296/18496
	≤30-Days	1.347 [0.869–2.088]	0.182	91	R[†]	14	1122/16673
	>30-Days	0.967 [0.327–2.863]	0.952	95	R[†]	6	302/1931
Comorbidities							
No comorbidity	[Hospital/ED]	0.983 [0.516–1.873]	0.958	87	R[†]	7	645/10217
	[Hospital]	0.979 [0.510–1.878]	0.949	87	R[†]	7	635/10227
	≤30 Days	1.108 [0.498–2.469]	0.801	89	R[†]	6	581/9029
Immunosuppressed	[Hospital/ED]	1.437 [0.879–2.351]	0.148	30	F	6	409/8096
	[Hospital]	1.357 [0.798–2.307]	0.260	54	F	5	353/8101
	<30 Days	1.156 [0.627–2.133]	0.642	47	F	4	365/7501
Cerebrovascular	[Hospital/ED]	1.812 [1.547–2.121]	0.00	0	F	5	1935/44267
	≤30 Days	1.781 [1.517–2.091]	0.00	0	F	4	1885/43783
Cardiovascular	[Hospital/ED]	2.173 [1.545–3.057]	0.00	61	R	4	1578/36605
	[Hospital]	2.100 [1.494–2.951]	0.00	69	R	3	1557/36521
Hypertension	[Hospital/ED]	1.608 [1.319–1.960]	0.00	61	R	14	2461/51616
	[Hospital]	1.734 [1.404–2.140]	0.00	65	R	13	2384/51532
	≤30 Days	1.650 [1.328–2.050]	0.00	66	R	12	2361/50812
	>30 Days	1.258 [0.855–1.852]	0.244	0	F	4	159/1061
Ischemic heart disease	[Hospital/ED]	1.998 [1.495–2.670]	0.00	13	F	8	672/12717
	[Hospital]	2.278 [1.685–3.080]	0.00	0	F	8	606/12783
	≤30 Days	1.695 [1.188–2.419]	0.004	8	F	6	490/12090
Heart failure	[Hospital/ED]	2.556 [1.980–3.300]	0.00	16	F	10	867/15205
	[Hospital]	2.742 [2.107–2.567]	0.00	0	F	10	801/15271
	≤30 Days	2.598 [1.920–3.517]	0.00	42	F	6	602/13744
	>30 Days	2.456 [1.527–3.950]	0.00	0	F	4	199/1461
Obesity	[Hospital/ED]	0.963 [0.719–1.289]	0.798	71	R	8	1739/40956
	[Hospital]	0.932 [0.690–1.260]	0.647	74	R	7	1718/40872
	≤30 Days	1.055 [0.750–1.486]	0.757	77	R	6	1641/39173
	>30 Days	0.799 [0.525–1.216]	0.295	27	F	3	147/1956
Diabetes	[Hospital/ED]	1.588 [1.443–1.747]	0.00	33	F	14	2400/51891
	[Hospital]	1.609 [1.461–1.771]	0.00	21	F	13	2323/51863
	≤30 Days	1.588 [1.414–1.718]	0.00	27	F	12	2316/50812
	>30 Days	1.950 [1.316–2.891]	0.001	34	F	4	143/1336
Liver disease	[Hospital/ED]	1.391 [0.681–2.841]	0.365	74	R[†]	7	1786/40913
	[Hospital]	1.362 [0.639–2.905]	0.424	74	R[†]	7	1730/40969
	≤30 Days	1.201 [0.496–2.908]	0.684	82	R[†]	5	1782/39834
Cancer	[Hospital/ED]	1.817 [1.526–2.162]	0.00	36	F	8	1767/40866
	[Hospital]	1.868 [1.568–2.225]	0.00	48	F	8	1711/40922
	≤30 Days	1.788 [1.497–2.135]	0.00	41	F	7	1677/40327
Kidney disease	[Hospital/ED]	2.083 [1.498–2.897]	0.00	51	R	8	1968/42652
	[Hospital]	2.478 [2.195–2.798]	0.00	47	F	8	1912/42708
	≤30 Days	2.519 [1.229–2.848]	0.00	44	F	6	1868/41758
	>30 Days	1.574 [0.967–2.563]	0.068	0	F	4	159/1061
HIV	[Hospital]	1.506 [0.959–2.367]	0.076	0	F	4	1484/36121
Chronic pulmonary disease(COPD/Asthma)	[Hospital/ED]	1.601 [1.438–1.783]	0.00	34	F	14	2432/51684
	[Hospital]	1.605 [1.440–1.789]	0.00	38	F	13	2355/51656
	≤30 Days	1.658 [1.324–2.077]	0.00	50	R	10	2218/49210
	>30 Days	1.496 [1.047–2.139]	0.027	0	F	6	273/2733
COPD	[Hospital/ED]	2.071 [1.652–2.597]	0.00	40	F	7	946/18630
	[Hospital]	2.086 [1.657–2.626]	0.00	43	F	7	875/18701
	≤30 Days	2.137 [1.682–2.716]	0.00	57	F	5	787/17569
Asthma	[Hospital/ED]	1.404 [1.100–1.793]	0.006	0	F	10	998/19689
	[Hospital]	1.428 [1.111–1.834]	0.005	0	F	10	927/19760

Table 2 (*continued*)

Variables		Odds ratio [95% confidence intervals]	*P*-value	I^2 (%)	Model	Number of studies	Sample Size (Readmitted/Non-readmitted)
	≤30 Days	1.458 [1.096–1.939]	0.010	0	F	5	775/17440
	>30 Days	1.266 [0.788–2.032]	0.329	0	F	5	223/2249
Inpatient factors							
Mechanical ventilation	[Hospital]	0.517 [0.399–0.668]	0.000	0	F	3	1248/30732
ICU admission	[Hospital/ED]	0.907 [0.549–1.498]	0.703	85	R†	7	1998/47631
	[Hospital]	0.945 [0.570–1.564]	0.825	84	R	7	1942/47687
	≤30 Days	0.813 [0.478–1.382]	0.444	86	R†	6	1964/47036
Length of initial hospital stay	[Hospital/ED]	1.055 [0.693–1.605]	0.804	95	R†	10	2300/49740
	[Hospital]	1.082 [0.705–1.662]	0.362	95	R†	10	2244/49796
	≤30 Days	0.804 [0.536–1.207]	0.292	94	R†	8	2173/48759
	>30 Days	1.703 [0.331–8.771]	0.524	94	R†	3	137/1065

ED: Emergency department; F: Fixed-effects model; R: Random-effects model; COPD: Chronic Obstructive Pulmonary Disease; HIV: Human immunodeficiency virus; I^2: Heterogeneity index.

* Sensitivity analysis, removing letter papers, show different results.

† Sensitivity analysis, change fixed or random-effects together, show different results.

‡ Presence of publication bias, based on Egger's test.

The difference between males and females in infectious pandemics has been reportedly linked to differences in various aspects including the immune system, genetics, and body physiology [55]. A previous meta-analysis by Subramaniam et al. has also reported the same results regarding gender [56].

We also found that the rate of mortality was lower in the second admission than in the first admission, because high-risk patients mostly expire during the index admission. According to the results of our meta-analysis, race and ethnicity had no robust effects on COVID-19 patients' readmissions. Pulmonary and cardiac complications were the most prevalent causes of readmission among COVID-19 patients.

The effects of comorbidities on increasing the risk of readmission could be explained by intensified inflammatory responses and organ defects; angiotensin-converting enzyme 2 (ACE2) has been reported to have a key role in this regard [57]. On the other hand, Patients who suffer from comorbidities are usually under treatment with certain medications or do not have proper lifestyle and nutrition status. Hence, they may have a recurrence of the disease or may not recover well and need to be readmitted.

Our results did not exhibit a significant relationship between immunosuppression and patients' readmission. However, Monreal et al. showed the protective role of non-severe immunosuppression against a possible hyper-inflammatory host response seen in COVID-19 patients [58], which alludes that it may help reduce the risk of readmission in these patients.

We found that obesity was not significantly associated with readmission. Suresh et al. found that obese COVID-19 patients are mostly younger and female, both of which are potential protective factors against readmission of COVID-19 patients; however, other comorbidities were more prevalent among obese COVID-19 patients, which may increase the likelihood of readmission in these patients [59]. Liver diseases are also reported as risk factors for hospitalization in COVID-19 patients [60], but we could not find a clear link between this comorbidity and the likelihood of readmission in these patients.

Our results are partially consistent with the recent meta-analysis by Subramaniam et al. [56]. Consistent with our findings, they also found the rate of ICU admission to be similar between the readmitted and non-readmitted patients. In contrast with our results, they found that some comorbidities like congestive heart failure and ischemic heart disease had no significant effects on readmission. They also reported that readmitted patients had a shorter hospital stay in their index admission, while we could not find robust evidence in this regard. These inconsistencies can mainly be attributed to the low number of studies and thus, smaller sample size of their study in comparison to the present meta-analysis.

Our subgroup analysis on the relation between age and readmission illustrated that although all-cause readmission was higher among older patients, readmissions due to COVID-19 reinfection may not be significantly associated with age, and this association should be investigated in further studies. A higher rate of all-cause readmission among older patients can be justified by the frequent existence of various comorbidities among them [61]. These results were in line with a previous systematic review that examined the risk factors of hospitalization, mortality, and severe infection among COVID-19 patients [62]. Similarly, Li et al. showed that being male, suffering from comorbidities, and older age were risk factors for severe COVID-19 disease [63].

4.1. Limitations

This study had some limitations. First, the causes of readmission were heterogeneous between studies. For instance, some studies included only patients who were readmitted because of COVID-19-related complications, while some assessed all-cause readmissions, and some others assessed only re-positive patients who were readmitted. Moreover, since two studies were performed on vast populations, it is probable that they included patients assessed in other studies. We tried to address this issue and reduce the chance of duplication by removing studies with fewer than 50 readmitted patients. Finally, the readmission period of included studies was different. Although we tried to address this limitation by performing subgroup analysis, some disparities still exist in subgroups.

5. Conclusion

Male sex, white race, and comorbidities including cerebrovascular disease, hypertension, cardiovascular disease, diabetes, cancer, kidney disease, and chronic pulmonary diseases are probably associated with a higher risk of readmission. The second admission can be widely associated with pulmonary and cardiac complications of COVID-19. Our findings can help clinicians and policymakers plan better strategies to reduce the rate of readmission in patients previously admitted with COVID-19 during the remaining days of the pandemic.

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Author contributions

E.F. and A.A. designed the study. A.A. and M.A. were involved in searching the databases. A.A., A.F., M.A., and M.R. screened the papers

and extracted the relevant data. E.F. and A.G. were involved in the quality assessment of included articles. A.A. and A.Z. analyzed and interpreted the data. A.A., A.F., and M.R. wrote the manuscript, which E.F., A.Z., M.A., and A.G. revised. All authors read and approved the final manuscript.

Data availability statement

The data that support the findings of this study are provided in the supplementary files and are available from the corresponding author on request.

Declaration of Competing Interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajem.2021.12.012.

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