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Hospital readmissions and post-discharge all-cause mortality in COVID-19 recovered patients; A systematic review and meta-analysis



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ABSTRACT

Objective: The present study aimed to perform a systematic review and meta-analysis on the prevalence of oneyear hospital readmissions and post-discharge all-cause mortality in recovered COVID-19 patients. Moreover, the country-level prevalence of the outcomes was investigated.

Methods: An extensive search was performed in Medline (PubMed), Embase, Scopus, and Web of Science databases until the end of August 3rd, 2021. A manual search was also performed in Google and Google Scholar search engines. Cohort and cross-sectional studies were included. Two independent reviewers screened the papers, collected data, and assessed the risk of bias and level of evidence. Any disagreement was resolved through discussion. Results: 91 articles were included. 48 studies examined hospital readmissions; nine studies assessed postdischarge all-cause mortality, and 34 studies examined both outcomes. Analyses showed that the prevalence of hospital readmissions during the first 30 days, 90 days, and one-year post-discharge were 8.97% (95% CI: 7.44, 10.50), 9.79% (95% CI: 8.37, 11.24), and 10.34% (95% CI: 8.92, 11.77), respectively. The prevalence of postdischarge all-cause mortality during the 30 days, 90 days and one-year post-discharge was 7.87% (95% CI: 2.78, 12.96), 7.63% (95% CI: 4.73, 10.53) and 7.51% (95% CI, 5.30, 9.72), respectively. 30-day hospital readmissions and post-discharge mortality were 8.97% and 7.87%, respectively. The highest prevalence of hospital readmissions was observed in Germany (15.5%), Greece (15.5%), UK (13.5%), Netherlands (11.7%), China (10.8%), USA (10.0%) and Sweden (9.9%). In addition, the highest prevalence of post-discharge all-cause mortality belonged to Italy (12.7%), the UK (11.8%), and Iran (9.2%). Sensitivity analysis showed that the prevalence of one-year hospital readmissions and post-discharge all-cause mortality in high-quality studies were 10.38% and 4.00%, respectively.

Conclusion: 10.34% of recovered COVID-19 patients required hospital readmissions after discharge. Most cases of hospital readmissions and mortality appear to occur within 30 days after discharge. The one-year post-discharge all-cause mortality rate of COVID-19 patients is 7.87%, and the majority of patients' readmission and mortality happens within the first 30 days post-discharge. Therefore, a 30-day follow-up program and patient tracking system for discharged COVID-19 patients seems necessary.

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1. Introduction

The coronavirus disease 2019 (COVID-19) has become a global pandemic and the statistics are increasing daily. Numerous mutations in the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) have caused an increase in the number of COVID-19 re-infections and related hospital readmissions. There is evidence indicating that these mutations may have reduced the efficacy of current vaccines [1,2]. This re-infection and the decline in immune responses against the SARS-CoV-2 have triggered a re-emergence of the disease in some communities [3,4], bearing in mind that current treatments are not adequately effective in improving the outcome of COVID-19 [5-7]. *Re*-infection and hospital readmissions are important indicators of controlling the COVID-19 pandemic and healthcare performance quality [8]. Hospital readmissions as a public health concern increase resource utilization and impose an additional burden on the healthcare system [9-11]. At the beginning of the pandemic, studies indicated that recurrence/re-infection of COVID-19 was rare [12,13], but more recent evidence has shown that a significant percentage of patients with COVID-19 develop recurrence of symptoms and require readmission [11,14,15]. The prevalence of hospital readmissions in patients with COVID-19 varies between 1% [16] to 48% [14].

Increasing numbers of recovered COVID-19 patients and their follow-up has shown that that the post-discharge mortality of COVID-19 patients occurs one year after discharge from the index hospitalization. Prevalence of post-discharge mortality of COVID-19 patients was

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reported between 0% [17] to 37% [18]. However, most studies are single-site researches, and there exists no comprehensive data on post-discharge mortality of recovered COVID-19 patients. There are also significant differences in follow-up time and setting of COVID-19 patients among current studies, making conclusions in this field challenging.

The current systematic review and meta-analysis has investigated the prevalence of hospital readmissions and post-discharge all-cause mortality in follow-up periods of 30 days, 90 days, and one year, to provide comprehensive figures. As a secondary aim, the prevalence of country-level hospital readmissions and post-discharge all-cause mortality has been reported.

2. Method

2.1. Study design

The present study is a systematic review and meta-analysis of observational studies. The protocol of the present study was designed based on Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guideline [19]. The protocol of the current review was not registered and publicly accessed. In all steps, two independent reviewers screened the papers, collected data, and assessed the risk of bias and level of evidence. Any disagreement was resolved through discussion. The agreement rate was 92.3% to 100% for each level of screening and data extraction.

2.2. Eligibility criteria

In the present study, cohort and cross-sectional studies on the prevalence of hospital readmissions and post-discharge all-cause mortality after recovery from COVID-19 were included. Case-control studies were excluded since the nature of sampling in case-control studies overestimates the prevalence of hospital readmissions and postdischarge all-cause mortality. Case reports, duplicate reports, reviews, and pediatric studies were also excluded. Presenting combined data of in-hospital and post-discharge outcomes without any stratification and reporting data on patients discharged from the emergency department without hospitalization in index admission (first admission) were other exclusion criteria. In addition, studies were excluded if they did not assess hospital readmissions or post-discharge all-cause mortality and did not report the total sample size of their COVID-19 patients.

2.3. Search strategy

An extensive search was performed on PubMed, Embase, Scopus, and Web of Science until the end of August 3rd,2021, without time or language limitations. In addition, a manual search was performed on Google and Google Scholar search engines. Since a significant number of COVID-19 papers were accessible as preprints, the manual search was performed cautiously to include relevant preprint articles. The search term is reported in Supplementary material 1.

2.4. Screening and data collection

Records from systematic and manual searches were gathered into EndNote X8.0 software (Clarivate Analytics, Philadelphia, PA, USA), and duplicates were removed. In a two-step process, related articles were selected based on the inclusion and exclusion criteria. In the first step, the titles and abstracts were reviewed and possibly related articles were identified. In the next step, the full texts of the articles were evaluated and related papers were identified and included in the present study. Collected data include study characteristics (name of the first author, year of publication, country), study design (retrospective or prospective), patients' settings, COVID-19 diagnostic criteria, discharge criteria, sample size, age, and gender distribution, underlying diseases, and follow up duration. Underlying disease or infection was defined as the presence of cirrhosis and liver injury, myocardial infarction, cardio-vascular disease, autoimmune diseases, cancer, fungal infections, HIV infection, rheumatic and musculoskeletal disease, and acute kidney injury.

2.5. Outcome

The outcomes of interest were hospital readmissions and postdischarge all-cause mortality. Hospital readmissions were defined as the readmission of recovered COVID-19 patients who had previously been hospitalized for COVID-19. Post-discharge all-cause mortality was also considered as all post-discharge deaths in recovered COVID-19 patients.

2.6. Risk of bias assessment

The risk of bias was assessed using National, Heart, Lung, and Blood Institute (NHLBI) tools for cohort and cross-sectional studies [20]. NHLBI risk of bias tools contains 14 signaling questions for the assessment of the quality of included studies (Supplementary Table 1). According to the observational nature of the included studies, participation rate less than 50% (item 3), assessment of exposure prior to outcome assessment (item 6), insufficient timeframe for outcome assessment (item 7), not clear and valid measurement of exposure (item 9) and outcomes (item 11) and more than 20% loss to follow-up (item 13) were defined as fatal errors.

Since most of the studies collected their data from registries, the unblind outcome assessment (item 12) did not have a considerable effect on the quality of the studies. Therefore, unblinded outcome assessment was not considered a fatal error. Sample size calculation was not reported in any of the included studies. Therefore, if the sample size of a study was lower than 100 patients, item 5 was considered as high risk. In addition, item 14 of the NHLBI risk of bias tool was not applicable for this review.

The overall risk of bias was rated as "high" if any concern (high risk; NR or CD) was presented in items 3, 6, 7, 9, 11, and 13 (fatal error). The overall risk of bias was rated as "some concern" if there were no fatal errors and there were a concern (high risk, NR, or CD) in at least two items [21].

2.7. Level of evidence

The level of evidence was determined based on the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework. The GRADE framework classifies the level of evidence for each outcome based on the risk of bias, imprecision, inconsistency, indirectness, and publication bias [22].

2.8. Statistical analyses

Data were recorded as total sample size and number of events (frequency) and were analyzed in STATA 17.0 statistical program (Stata Corp, College Station, TX, USA). Since considerable heterogeneity was expected among the included studies, it was decided to use a random effect model for the meta-analyses. Follow-up time varied between studies, and therefore, analyses were stratified based on followup time. The studies were divided into three groups: 30-day follow-up (follow-up between 10 and 30 days after discharge), 90-day follow-up (follow-up between 10 and 90 days), and one-year follow-up (follow-up between 10 days to 365 days).

Heterogeneity between the studies was assessed using l^2 statistics and the chi-square test. l^2 above 50% was defined as the presence of obvious heterogeneity. In cases of heterogeneity, the possible sources of heterogeneity were investigated using subgroup analysis. Since one-
year follow-up after recovery included all 30-day and 90-day follow-
up data, subgroup analysis was performed on one-year outcome after
discharge. The country type was defined in two categories as developed
and developing countries according to the World Bank definition; De-
veloped countries were defined as countries with high-income econo-3.

middle-income economies [23]. Meta-regression was performed to investigate the relationship between the mean age of patients and the outcomes. For this purpose, the mean age of patients in each study was entered in the analyses as independent variables, and the hospital readmissions and post-discharge all-cause mortality were considered as dependent variables. Sensitivity analyses were performed according to the quality of the included studies and based on the country-level prevalence of hospital readmissions and post-discharge all-cause mortality. For this purpose, only studies on all COVID-19 patients were included and other settings were excluded. Finally, publication bias was investigated using Egger's test and funnel plots.

mies while developing countries were defined as those with low- and

3. Results

3.1. Article screening process

The systematic search yielded 2531 studies, which included 1610 non-duplicated studies. In the manual search of gray literature and preprints, 18 potentially related papers were included. After reviewing the titles and abstracts of the articles, 157 peer-reviewed papers or preprinted manuscripts were reviewed and a total of 91 articles were entered into the present meta-analysis [8,14-18,24-108]. The reasons for excluding articles are shown in Fig. 1.

3.2. Summary of eligible studies

There were 28 prospective, 61 retrospective, and 2 ambidirectional cohorts. There were 32 studies on the USA population, 18 studies on the Chinese population, 13 studies on the Spanish population, and seven studies on the UK population. Also, three studies were conducted in Iran. These studies included 283,468 patients (51.19% male). The mean age of patients enrolled in the studies ranged from 36.7 to 88.5 years.

The setting of the patients in 76 studies were all COVID-19 patients regardless of the characteristics of included patients. Three studies were performed on the elderly population and two studies were performed on patients with cardiovascular disease. The population of other studies included patients with cirrhosis and liver injury, autoimmune diseases, cancer, fungal infections, human immunodeficiency virus (HIV), rheumatic and musculoskeletal disorders, acute kidney injury, non-severe COVID-19 patients, corticosteroids treated patients, and empiric antibiotics treated patients.

The COVID-19 diagnostic test was Reverse transcription-polymerase chain reaction (RT-PCR) in 63 studies, while 16 studies did not report the diagnostic test. The method of identifying COIVD-19 was mixed in 12 studies. In the mixed-method approach, the diagnostic method was RT-PCR or other diagnostic methods including imaging procedures, serological tests, or clinical symptoms. The discharge criteria were not reported in 69 studies. In 18 studies, discharge criteria included two consecutive negative RT-PCR and clinical improvement. Four studies had discharged patients only based on clinical improvement.

Follow-up time ranged from 10 to 365 days. 48 studies examined hospital readmissions, nine studies examined post-discharge all-cause mortality, and 34 studies examined both outcomes. Table 1 summarizes the characteristics of the studies.

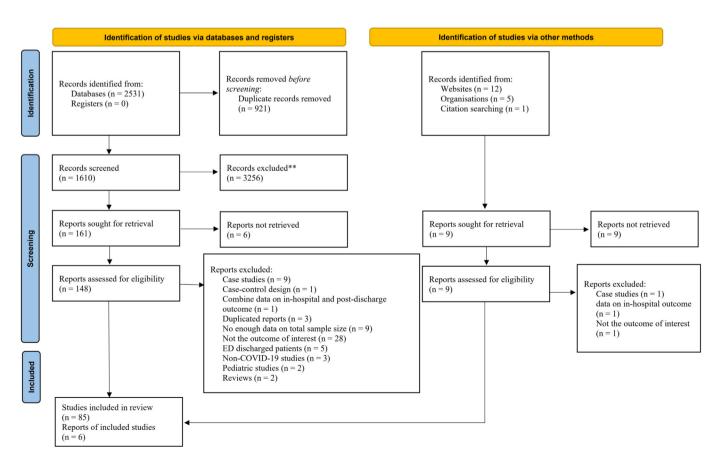


Fig. 1. PRISMA flow diagram for present studies.

Summary characteristics of included studies.

Study	Study design	Setting of patients	COVID-19 diagnosis	Discharge criteria	Sample size	Male	Mean age (years)	FU (days)	Outcome
An, 2020; China [22]	PCS	All COVID-19 patients	RT-PCR	Two consecutive negative RT-PCR + clinical	242	116	41.3	14	Readmission
Atalla, 2021; USA [15]	RCS	All COVID-19 patients	RT-PCR	improvement Clinical improvement	279	191	61.3	30	Readmission
Ayoubkhani, 2021; UK [24]	RCS	All COVID-19 patients	NR	NR	47,780	26,279	65	253	Readmission, post-discharge mortality
Bajaj, 2021; USA [14]	PCS	All COVID-19 patients, cirrhosis and liver injury	NR	NR	122	46	60.6	90	Readmission, post-discharge mortality
Banerjee, 2021; USA [25]	PCS	All COVID-19 patients	RT-PCR	Stable patients with improving clinical trajectory	621	404	52.5	30	Readmission, post-discharge mortality
Barreto, 2021; Brazil [23]	RCS	All COVID-19 patients	RT-PCR or CT or IgM/IgG	NR	602	247	51.8	140	Readmission
Bowles, 2021; USA [26]	RCS	All COVID-19 patients	RT-PCR	NR	1409	718	67	180	Readmission, post-discharge mortality
Cao, 2020; China [27]	RCS	All COVID-19 patients	RT-PCR	NR	108	NR	NR	30	Readmission
Carrillo Garcia, 2021; Spain [28]	PCS	Elderly	RT-PCR or clinical or imaging or	NR	165	114	88.5	90	Readmission, post-discharge
Chai, 2021; China [29]	PCS	All COVID-19	laboratory RT-PCR	NR	588	328	64.7	365	mortality Post-discharge mortality
Chaudhry, 2021; UK [30]	RCS	patients; cancer Corticosteroids treated patients	NR	NR	196	63	58.7	10	Readmission
Chen J, 2020; China [31]	RCS	All COVID-19 patients	RT-PCR	Two consecutive negative RT-PCR + clinical improvement	1087	452	60.2	52	Readmission
Chen SL, 2020; China [32]	RCS	All COVID-19 patients	RT-PCR	Two consecutive negative RT-PCR + clinical	1282	628	44	28	Readmission
Choi, 2021; USA [33]	RCS	All COVID-19 patients	RT-PCR	improvement NR	1008	NR	NR	30	Readmission
Chopra, 2020; USA [34]	RCS	All COVID-19 patients	NR	NR	1250	648	61.3	60	Post-discharge mortality
Connolly, 2021; Ireland [35]	PCS	All COVID-19 patients	NR	NR	502	179	40	12	Readmission
Divanoglou, 2021; Sweden [36]	AmbidiRCSectional	•	Laboratory assessment	NR	433	246	61.3	135	Post-discharge mortality
[37]	RCS	All COVID-19 patients	NR	NR	1775	1688	69.8	60	Readmission, post-discharge mortality
Frontera, 2021; USA [38]	PCS	All COVID-19 patients	RT-PCR	NR	380	248	67.5	180	Readmission, post-discharge mortality
Gabriel, 2021; Spain [39]	PCS	All COVID-19 patients	NR	NR	102	48	46.2	15	Readmission
García Abellán, 2021; Spain [40]	PCS	All COVID-19 patients	RT-PCR	NR	146	88	65	180	Readmission, post-discharge
Gąsior, 2021; Poland	RCS	MI and cardiovascular	NR	NR	2988	1352	69	180	mortality Post-discharge mortality
[41] Giannis, 2021; Greece [42]	PCS	All COVID-19 patients	NR	NR	4906	2633	61.7	92	Readmission, post-discharge
Gordon, 2020; USA [43]	PCS	All COVID-19 patients	RT-PCR or clinical or imaging	NR	1227	674	54	21	mortality Readmission
Guarin, 2021; USA [44]	RCS	All COVID-19	suspected RT-PCR	NR	275	142	64.69	180	Readmission
Gudipati, 2020; USA [45]	RCS	patients All COVID-19	NR	NR	266	125	61	30	Readmission
Gunster, 2021; Germany [46]	RCS	patients All COVID-19 patients	RT-PCR	NR	6518	4641	68.6	180	Readmission, post-discharge
Gutiérrez, 2021; Spain [47]	RCS	All COVID-19 patients, autoimmune	RT-PCR	NR	13,940	7749	67.3	30	mortality Readmission, post-discharge mortality
Gwin, 2021; USA [48]	RCS	Diseases All COVID-19 patients	RT-PCR	NR	151	88	59.6	30	Readmission

Table 1 (continued)

Study	Study design	Setting of patients	COVID-19 diagnosis	Discharge criteria	Sample size	Male	Mean age (years)	FU (days)	Outcome
Hasan, 2021; Bangladesh [17]	PCS	All COVID-19 patients	RT-PCR	NR	238	159	61.5	30	Readmission, post-discharge mortality
Herc, 2020; USA [49]	RCS	Fungal Infections	NR	NR	31	17	66	30	Readmission
Hernández-Biette, 2020;	PCS	Non-Severe COVID	RT-PCR	NR	74	35	54.6	14	Readmission,
Spain [50]									post-discharg
									mortality
Holloway, 2021; UK [51]	PCS	All COVID-19	RT-PCR	NR	141	NR	NR	30	Readmission
Huang C, 2021; China	ACS	patients All COVID-19	RT-PCR	Two consecutive negative	1733	897	56.3	199	Readmission,
[52]	AC5	patients	RI-I CR	RT-PCR + clinical improvement	1755	057	50.5	155	post-discharg mortality
Huang CW, 2021; USA	RCS	All COVID-19	RT-PCR	NR	2180	1238	54.7	30	Readmission,
[53]		patients							post-discharg mortality
Islam, 2021; UK [54]	RCS	All COVID-19 patients	RT-PCR	NR	403	211	66	60	Readmission, post-discharg mortality
Jain, 2020; USA [55]	PCS	All COVID-19 patients	NR	NR	18	10	65.3	90	Readmission
Jalilian Khave, 2021;	PCS	All COVID-19	RT-PCR	NR	577	449	50.1	14	Readmission
Iran [56]		patients							
Jeon, 2020; South Korea [57]	RCS	All COVID-19 patients	RT-PCR	Two consecutive negative RT-PCR + clinical	7590	3095	47	180	Readmission
Kingery, 2021; USA [58]	RCS	All COVID-19 patients	RT-PCR	improvement NR	1344	746	60.3	30	Readmission, post-discharg
Kirkegaard, 2021; Spain [59]	RCS	All COVID-19 patients	RT-PCR	NR	629	318	60.28	60	mortality Readmission, post-discharg
Lavery, 2020; USA [60]	RCS	All COVID-19 patients	RT-PCR	NR	106,543	54,080	60	60	mortality Readmission
Lee, 2020; USA [61]	RCS	HIV patients	RT-PCR	NR	72	44	61.3	30	Readmission
Leijte, 2020;	RCS	All COVID-19	RT-PCR	NR	596	469	70	90	Readmission,
Netherlands [62]		patients							post-discharg
Leon, 2021; Spain [63]	PCS	Rheumatic and musculoskeletal	RT-PCR	NR	105	38	66.8	210	mortality Readmission, post-discharg
Li, 2020; China [64]	RCS	All COVID-19 patients	RT-PCR	Two consecutive negative RT-PCR + clinical	85	55	48	60	mortality Readmission
Luo, 2020; China [65]	RCS	All COVID-19 patients	RT-PCR	improvement Two consecutive negative RT-PCR + clinical improvement	745	424	42.4	14	Readmission
Maestre-Muñiz, 2021; Spain [66]	RCS	All COVID-19 patients	RT-PCR	NR	266	201	71.5	365	Readmission, post-discharg
Medler, 2020; USA [67]	RCS	All COVID-19	RT-PCR	NR	337	NR	63.6	14	mortality Readmission
Medranda, 2021; USA [68]	RCS	patients MI and cardiovascular	RT-PCR	NR	92	55	63.7	30, 90,	Readmission, post-discharg
Meije, 2021; Spain [69]	PCS	All COVID-19 patients	RT-PCR	NR	323	171	68.8	180 45, 210	mortality Readmission, post-discharg
Menges, 2021;	PCS	All COVID-19	RT-PCR	NR	81	43	59	180	mortality Readmission
Switzerland [70]	DCC	patients	DT DCD	ND	274	101	67	20	Deeder!!-
Mooney, 2021; UK [71] Navvas, 2021; UK [72]	RCS RCS	Elderly All COVID-19	RT-PCR RT-PCR	NR NR	274 402	161 NR	67 NR	30 30	Readmission Post-discharg
Nematshahi, 2021; Iran	PCS	patients All COVID-19	RT-PCR or imaging	NR	416	228	58.8	180	mortality Readmission
[73] Pan, 2021; China [16]	RCS	patients All COVID-19 patients	RT-PCR	RT-PCR + clinical	1350	NR	NR	15	Readmission
Parra, 2020; Spain [74]	RCS	All COVID-19	RT-PCR and	improvement NR	1368	872	64.4	21	Readmission
Pettit, 2021; USA [75]	RCS	patients Patients on empiric	imaging RT-PCR	NR	246	116	60	30	Readmission
Pourhoseingholi, 2021; Iran [76]	RCS	CABP antibiotics All COVID-19 patients	CT scan	NR	1053	773	53	365	Readmission, post-discharg

(continued on next page)

Table 1 (continued)

Study	Study design	Setting of patients	COVID-19 diagnosis	Discharge criteria	Sample size	Male	Mean age (years)	FU (days)	Outcome
Qiao,2020; China [77]	RCS	All COVID-19 patients	RT-PCR	Two consecutive negative RT-PCR + clinical improvement	15	8	36.7	30	Readmission
Quilliot, 2021; France [78]	PCS	All COVID-19 patients	RT-PCR or CT	NR	296	156	59.8	30	Readmission, post-discharge mortality
Ramos Martínez, 2021; Spain [79]	RCS	All COVID-19 patients	RT-PCR	NR	7137	4022	65.4	30	Readmission, post-discharge mortality
Reyes Gill, 2021; USA [80]	RCS	All COVID-19 patients	RT-PCR	NR	150	81	58.1	30	Readmission, post-discharge mortality
Richardson, 2020; USA	PCS	All COVID-19	RT-PCR	NR	2081	1162	63.3	10	Readmission
[81] Rodriguez, 2021; USA [82]	PCS	patients All COVID-19 patients	RT-PCR	NR	3111	1250	60.9	30	Readmission
[02] Roig-Marín, 2021; Spain [83]	RCS	Elderly	RT-PCR	NR	221	152	81.6	365	Post-discharge mortality
Romero-Duarte, 2021; Spain [84]	RCS	All COVID-19 patients	RT-PCR	NR	797	428	63	180	Readmission, post-discharge
Saab, 2021; USA [85]	RCS	All COVID-19	RT-PCR	NR	99	64	59.8	86	mortality Readmission
Shallal, 2020; USA [86]	RCS	patients All COVID-19	RT-PCR	NR	585	302	59.8	30	Readmission
Siddiqui, 2021; USA [87]	RCS	patients All COVID-19 patients; cirrhosis	RT-PCR	NR	11,534	972	63.8	30	Readmission
Somani, 2020; USA [88]	RCS	and liver injury All COVID-19	RT-PCR	NR	2864	1663	65.7	14	Readmission
Spence, 2021; UK [89]	RCS	patients All COVID-19 patients	NR	NR	106	54	78.8	30, 60, 90	Readmission, post-discharge
Spinicci, 2021; Italy [90]	RCS	All COVID-19 patients	NR	NR	107	59	67.3	56	mortality Readmission, post-discharg mortality
Stockman, 2021; Germany [91]	RCS	AKI	NR	NR	37	NR	64.5	150	Post-discharg mortality
Suárez-Robles, 2020; France [92]	PCS	All COVID-19 patients	RT-PCR	NR	134	62	58.53	90	Readmission, post-discharg mortality
Tian, 2020; China [93]	PCS	All COVID-19 patients	RT-PCR	Two consecutive negative RT-PCR + clinical improvement	147	NR	NR	47	Readmission
Todt, 2021; Brazil [94]	RCS	All COVID-19 patients	RT-PCR	NR	251	150	53.6	90	Readmission, post-discharge
Uyaroglu, 2021; Turkey [8]	RCS	All COVID-19 patients	RT-PCR or symptoms	Clinical improvement	154	77	44.5	30	mortality Readmission
van den Borst,2021; Netherlands [95]	PCS	All COVID-19 patients	RT-PCR or symptoms	NR	98	74	59	90	Post-discharg mortality
Venturelli, 2021; Italy [96]	RCS	All COVID-19 patients	RT-PCR or IgM/IgG or symptoms	Two consecutive negative RT-PCR + clinical	767	512	63	90	Post-discharge mortality
Verna, 2021; USA [97]	RCS	All COVID-19	Laboratory	improvement NR	29,659	14,965	63.5	30	Readmission
Wang, 2020; China [98]	PCS	patients All COVID-19 patients	assessment RT-PCR	Two consecutive negative RT-PCR + clinical	94	59	49	30	Readmission
Weber, 2021; USA [18]	PCS	All COVID-19 patients	NR	improvement NR	408	243	62.3	180	Readmission, post-discharg
Wu, 2021; China [99]	RCS	All COVID-19 patients	RT-PCR	Two consecutive negative RT-PCR + clinical	132	165	40.7	180	mortality Readmission, post-discharg
Yan, 2020; China [100]	RCS	All COVID-19 patients	RT-PCR	improvement Two consecutive negative RT-PCR + clinical	272	154	44.3	14	mortality Readmission
Yang, 2020; China [101]	RCS	All COVID-19 patients	RT-PCR	improvement Two consecutive negative RT-PCR + clinical	479	224	42.8	90	Readmission
Ye S, 2021; USA [102]	RCS	All COVID-19 patients	RT-PCR	improvement symptoms improvement	409	245	57.3	14	Readmission

Table 1 (continued)

Study	Study design	Setting of patients	COVID-19 diagnosis	Discharge criteria	Sample size	Male	Mean age (years)	FU (days)	Outcome
Ye X, 2021; China [103]	RCS	All COVID-19 patients	RT-PCR	Two consecutive negative RT-PCR + clinical improvement	141	73	45	30	Readmission
Yeo, 2021; USA [104]	RCS	All COVID-19 patients	RT-PCR	NR	1062	632	56.5	30	Readmission
Yuan, 2020; China [105]	RCS	All COVID-19 patients	RT-PCR	Two consecutive negative RT-PCR + clinical improvement	172	NR	NR	14	Readmission
Zheng, 2020; China [106]	RCS	All COVID-19 patients	RT-PCR	Two consecutive negative RT-PCR + clinical improvement	289	128	48.3	14	Readmission

COVID-19: Coronavirus disease 2019; CT: Computed tomography scan; FU: Follow up duration; NR: Not reported; PCS: Prospective cohort study; RCS: Retrospective cohort study; RT-PCR: Reverse transcriptase-polymerase chain reaction.

3.3. Hospital readmission rate of recovered COVID-19 patients after hospital discharge

82 studies examined hospital readmissions after patient recovery. These studies contained data from 266,677 patients. Analyses showed that the prevalence of one-year hospital readmissions was 10.34% (95% CI: 8.92, 11.77; 99.46%; $I^2 = 99.46\%$) (Fig. 2). Hospital readmissions during the first 30 and 90 days after discharge were 8.97% (95% CI: 7.44, 10.50; $I^2 = 99.04\%$) and 9.79% (95% CI: 8.37, 11.24; $I^2 = 99.33\%$), respectively (Supplementary Figs. 1 and 2). As can be seen, most hospital readmissions occur within the first 30 days.

Subgroup analysis on one-year follow-up showed that differences in country type and patient setting may be potential sources of heterogeneity since stratification of analyses according to these factors led to a decrease in heterogeneity. The hospital readmission rate was 10.68% in developed countries and 6.88% in developing countries. Also, the rate of hospital readmissions in elderly patients with COVID-19 (15.28%) and COVID-19 patients with underlying disease (19.63%) was higher than in other groups (Table 2).

3.4. Post-discharge all-cause mortality of COVID-19 patients

43 studies examined post-discharge all-cause mortality of COVID-19 patients. These studies contained data from 103,107 patients. Analyses showed that the prevalence of all-cause mortality during the one year after discharge was 7.51% (95% CI: 5.30, 9.72; 99.60%; $I^2 = 99.60\%$) (Fig. 3). All-cause mortality during the first 30 and 90 days were 7.87% (95% CI: 2.78, 12.96; $I^2 = 99.79\%$) and 7.63% (95% CI: 4.73, 10.53; $I^2 = 99.46\%$), respectively (Supplementary figs. 3 and 4). Most post-discharge deaths occur within the first 30 days.

Subgroup analysis showed that diversity in the characteristics of the patients may be a possible source of heterogeneity since stratification of the analyses based on the characteristics of patients led to a decrease in heterogeneity. The post-discharge all-cause mortality rate in COVID-19 patients with underlying disease (12.03%) was almost 100% higher than that of all COVID-19 patients regardless of underlying disease (6.59%) (Table 3).

3.5. Meta-regression

Meta-regression was performed to investigate the relationship between the mean age of patients and the outcomes. The findings showed that the mean age of COVID-19 patients at the time of admission was not related to the prevalence of hospital readmissions (meta-regression coefficient = 0.038; p = 0.656). However, the prevalence of postdischarge all-cause mortality increased with age (meta-regression coefficient = 0.360; p = 0.009) (Supplementary Fig. 5).

3.6. Sensitivity analysis

3.6.1. Quality of included studies

The risk of bias was high in 50 studies, some concern in four studies, and low in 37 papers (Supplementary Table 1). The prevalence of oneyear hospital readmission in low-risk studies (high-quality studies) was 10.38% (Table 2), while the prevalence of 30-day hospital readmission in low-risk studies was 9.98%.

The prevalence of post-discharge all-cause mortality was 4.00% in low-risk studies (Table 3). Moreover, 30-day post-discharge all-cause mortality in low-risk studies was 3.24%.

3.6.2. Country-level differences of hospital readmissions and post-discharge mortality of COVID-19 patients

Sensitivity analysis showed that the highest prevalence of one-year hospital readmissions was observed in Germany (15.5%), Greece (15.5%), the UK (13.5%), Netherlands (11.7%), China (10.8%), USA (10.0%), and Sweden (9.9%). While the lowest hospital readmissions rate was seen in Brazil (5.4%), South Korea (4.3%), and France (4.1%).

The highest prevalence of one-year post-discharge all-cause mortality belonged to Italy (12.7%), the UK (11.8%), and Iran (9.2%). The lowest post-discharge all-cause mortality rates were observed in the Netherlands (3.8%), France (2.7%), Brazil (3.4%), Brazil (2.4%), Sweden (2.1%), China (1.2%), and Bangladesh (0.0%) (Fig. 4 and Table 4).

3.7. Publication bias and level of evidence

There was no evidence of publication bias regarding the hospital readmissions (p = 0.473) and post-discharge all-cause mortality (p = 0.435) assessments (Supplementary Fig. 6).

The overall level of evidence was very low in reporting the hospital readmissions and post-discharge all-cause mortality. According to the GRADE framework, the level of evidence for observational studies starts at low quality. A serious risk of bias and significant inconsistency was observed in the assessment of hospital readmission. Therefore, the quality of evidence was down-rated and reached very low. Also in the post-discharge all-cause mortality study, a high risk of bias and serious inconsistency was observed. Therefore, the certainty of the evidence was rated as very low (Supplementary Table 2).

4. Discussion

The present meta-analysis summarized the available pieces of evidence regarding hospital readmissions and post-discharge all-cause mortality in recovered COVID-19 patients. One-year follow-up showed that the prevalence of hospital readmissions and post-discharge allcause mortality of recovered COVID-19 patients was 10.34% and 7.87%,

Study	Sample size	Events	Follow up		Effect size Weight with 95% CI (%)
Pan, 2021	1350	14	15	0	1.04 [0.45, 1.62] 1.31
Huang C, 2021	1733	25	199	0	1.44 [0.85, 2.04] 1.31
Gutiérrez, 2021	13578	205	30	o	1.51 [1.30, 1.72] 1.31
Gutiérrez, 2021	362	7	30	Θ	1.93 [0.35, 3.51] 1.29
Somani, 2020	2864	56	14	0	1.96 [1.43, 2.48] 1.31
Richardson, 2020	2081	45	10	0	2.16 [1.51, 2.81] 1.31
Pourhoseingholi, 2021	1053	29	365	Θ	2.75 [1.71, 3.79] 1.31
Verna, 2021	29659	1070	30	0	3.61 [3.39, 3.82] 1.31
Quilliot, 2021	296	11 10	30 365	0	3.72 [1.38, 6.06] 1.27
Maestre-Muñiz, 2021	266	298	365	0	3.76 [1.27, 6.25] 1.26
Ramos- Martínez, 2021	7137 1062	45	30	0	4.18 [3.70, 4.65] 1.31 4.24 [2.98, 5.50] 1.30
Yeo, 2021 Jeon, 2020	7590	328	180	0	4.24 [2.98, 5.50] 1.30 4.32 [3.86, 4.79] 1.31
Romero-Duarte, 2021	7390	320	180	0	4.39 [2.90, 5.88] 1.30
Huang CW, 2021	2180	97	30	0	4.45 [3.56, 5.34] 1.31
Parra, 2020	1368	61	21	0	4.46 [3.33, 5.59] 1.30
Meije, 2021	323	15	210	0	4.64 [2.18, 7.10] 1.27
Shallal, 2020	585	28	30	0	4.79 [2.97, 6.61] 1.29
Barreto, 2021	602	30	140	0	4.98 [3.16, 6.81] 1.29
Saab, 2021	99	5	86	Ð	5.05 [0.18, 9.92] 1.14
Suárez-Robles, 2020	134	7	90	0	5.22 [1.05, 9.39] 1.18
Choi, 2021	1008	53	30	Θ	5.26 [3.83, 6.69] 1.30
Kirkegaard, 2021	629	34	60	Θ	5.41 [3.56, 7.26] 1.29
Herc, 2020	31	2	30	-0-	6.45 [-3.86, 16.77] 0.78
Qiao,2020	15	1	30		6.67 [-9.22, 22.56] 0.50
Todt, 2021	251	17	90	Θ	6.77 [3.46, 10.09] 1.23
Atalla, 2021	279	19	30	0	6.81 [3.67, 9.95] 1.24
Jalilian Khave, 2021	577	40	14	o	6.93 [4.77, 9.09] 1.28
Spinicci, 2021	100	7	56	0	7.00 [1.48, 12.52] 1.10
Holloway, 2021	141	10	30	0	7.09 [2.49, 11.69] 1.16
Uyaroglu, 2021	154	11	30	0	7.14 [2.74, 11.54] 1.17
Cao, 2020	108	8	30	0	7.41 [2.00, 12.82] 1.11
Wang, 2020	94	7	30	-0-	7.45 [1.60, 13.30] 1.08
Chen J, 2020	1087	81	52	0	7.45 [5.84, 9.06] 1.29
Ye S, 2021	409	31	14	0	7.58 [4.89, 10.27] 1.26
Yan, 2020	272	21	14	Θ	7.72 [4.36, 11.08] 1.23
Connolly, 2021	502	42	12	Θ	8.37 [5.84, 10.89] 1.26
Ye X, 2021	141	12	30	•	8.51 [3.55, 13.47] 1.13
Banerjee, 2021	621	53	30	0 0	8.53 [6.26, 10.81] 1.27
Rodriguez, 2021	3111	270	30	0	8.68 [7.67, 9.68] 1.31
Islam, 2021	403	35	60	0	8.68 [5.81, 11.56] 1.25
Guarin, 2021	275	24	30	Θ	8.73 [5.21, 12.24] 1.22
Lavery, 2020	106543	9504	60	o	8.92 [8.75, 9.09] 1.32
Hasan, 2021	238	22	30	Θ	9.24 [5.36, 13.13] 1.20
Zheng, 2020	289	27	14	ø	9.34 [5.82, 12.87] 1.22
Bowles, 2021	1409	137	180	Θ	9.72 [8.14, 11.31] 1.29
Kingery, 2021	1344	132	30	Θ	9.82 [8.19, 11.45] 1.29
Menges, 2021	81	8	180	-0-	9.88 [2.79, 16.96] 0.99
Chaudhry, 2021	196	20	10	¢	10.20 [5.72, 14.69] 1.16
Leon, 2021	105	11	210	- \$ -	10.48 [4.16, 16.79] 1.05
Gordon, 2020	1227	129	21	φ	10.51 [8.76, 12.27] 1.29
Wu, 2021	132	14	180	- • -	10.61 [4.99, 16.22] 1.09
Siddiqui, 2021	1302	141	30	0 0 0 0	10.83 [9.10, 12.56] 1.29
Mooney, 2021	274	31	30	ę	11.31 [7.39, 15.24] 1.20
Spence, 2021	106	12	90	-	11.32 [4.84, 17.80] 1.03
Pettit, 2021	246	28	30	ę	11.38 [7.22, 15.55] 1.18
Leijte, 2020	596	70	90		11.74 [9.08, 14.41] 1.26
Gwin, 2021	151	18	30	-0-	11.92 [6.44, 17.40] 1.10
Nematshahi, 2021	416	51	180	θ	12.26 [8.99, 15.53] 1.23
Medler, 2020	337	42	14	0	12.46 [8.79, 16.13] 1.21
Tian, 2020	147	20	47	0	13.61 [7.75, 19.46] 1.08
Lee, 2020	72	10	30	0	13.89 [5.29, 22.49] 0.89
Bajaj, 2021	93	13	90	0	13.98 [6.45, 21.51] 0.96
Frontera, 2021	380	54	180	Θ	14.21 [10.57, 17.85] 1.21
Yuan, 2020	172	25	14	0	14.53 [9.00, 20.07] 1.10
Reyes Gill, 2021	150	22	30	0	14.67 [8.70, 20.63] 1.07
Chen SL, 2020	1282	189	28	0	14.74 [12.76, 16.72] 1.28
Giannis, 2021	4906	759	92	O	15.47 [14.45, 16.49] 1.31
Gunster, 2021	6518	1011	180	Θ	15.51 [14.62, 16.40] 1.31
Gabriel, 2021	102	16	15	0	15.69 [8.20, 23.18] 0.97
An, 2020	242	38	14	0	15.70 [10.93, 20.48] 1.15
Li, 2020	85	15	60	0	17.65 [9.05, 26.25] 0.89
Yang, 2020 Donnolly, 2021	479	93	90	0	19.42 [15.78, 23.06] 1.21
Donnelly, 2021	1775	354	60	0	19.94 [18.06, 21.83] 1.29
Carrillo- Garcia, 2021	165	33 30	90	-0-	20.00 [13.63, 26.37] 1.04
García- Abellán, 2021 Wahar 2021	146		180		20.55 [13.70, 27.40] 1.01
Weber, 2021 Cudinati, 2020	408	84	180	0	20.59 [16.55, 24.62] 1.19
Gudipati, 2020 Luo, 2020	266	55 157	30 14	0 0	20.68 [15.64, 25.71] 1.13
Luo, 2020 Jain 2020	745 18	157	14 90	-	21.07 [18.08, 24.07] 1.24
Jain, 2020 Hernández-Biette, 2020	18 74	4	90 14		22.22 [1.61, 42.84] 0.35 22.97 [12.86, 33.09] 0.79
Guarin, 2021	275	66	14	0	24.00 [18.79, 29.21] 1.12
				0	
Siddiqui, 2021	232 47780	56 14060	30 253	0	24.14 [18.44, 29.83] 1.09 29.43 [29.02, 29.84] 1.31
Avoubkhani 2021					
Ayoubkhani, 2021 Medranda, 2021					
Ayoubkhani, 2021 Medranda, 2021 Bajaj, 2021	92 29	37 14	180 90	-0-	

Heterogeneity: $\tau^2 = 40.24$, $I^2 = 99.46\%$, $H^2 = 185.76$ Test of $\theta_i = \theta_j$: Q(85) = 18700.46, p = 0.00

Test of $\theta = 0$: z = 14.22, p = 0.00

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American Journal of Emergency Medicine 51 (2022) 267–279

respectively. Sensitivity analysis showed that the prevalence of hospital readmissions and post-discharge all-cause mortality in high-quality studies were 10.38% and 4.00%, respectively.

30-day hospital readmissions and post-discharge mortality were 8.97% and 7.87%, respectively. In addition, 30-day hospital readmissions and post-discharge mortality in high-quality studies were 9.98% and 3.24%, respectively. Therefore, most cases of hospital readmissions and mortality appear to occur within the first 30 days after discharge.

One of the interesting points in the present study was the higher hospital readmissions rate in developed countries compared to that of developing countries. The reason for this finding may be attributed to the higher medical benefits (better insurance coverage) provided in developed countries. Health insurance coverage in developing societies is much less widespread than in developed countries. In addition, access to medical services is limited in developing countries. Evidence shows that patients with poor insurance coverage account for a lower rate of readmissions. For example, Jeon et al. showed that the likelihood of readmission for COVID-19 patients with higher medical benefits is up to 5 times more than other patients [59]. Moreover, the data registries and follow-up of patients in developing countries in many instances do not exist, and in some other situations, patients' data loss is another obstacle. Therefore, the hospital readmissions rate may also be underestimated in developing countries.

A similar finding was observed for all-cause mortality. Postdischarge mortality was 7.78% in COVID-19 patients in developed countries and 3.84% in developing countries (Table 3). In addition to inaccurate tracking and recording of deaths in developing countries, the diversity of age distribution among communities should also be considered. The mean age of the population of developing countries is often lower than that of the population of developed countries, so this difference may be another reason for higher post-discharge all-cause mortality in developed countries compared to that of developing countries.

The relationship between age and increased post-discharge allcause mortality of COVID-19 patients has been studied in some studies, the findings of which are sometimes contradictory. Some of these studies show a significant relationship between age and post-discharge all-cause mortality [39,48,60], while others do not report such a relationship [28,63]. The elderly population is heterogenous and suffers from various underlying diseases such as dementia, Parkinson's, and delirium, all of which affect the outcome of COVID-19 [109-111]. Therefore, differences between the populations included in these studies may be the cause of the contradictory findings. The present meta-analysis showed that age is a possible influencing factor on post-discharge allcause mortality of COVID-19 patients. However, prospective studies need to be designed to examine the effect of age on mortality, alongside other confounders such as underlying disease.

The present study showed that the prevalence of hospital readmissions and post-discharge mortality is higher in COVID-19 patients with underlying diseases. This finding is somewhat in line with previous studies, showing that underlying diseases are possible risk factors of in-hospital outcomes of COVID-19 patients [112-116]. However, the number of studies examining risk factors for hospital readmissions and post-discharge mortality is small, and sometimes their quality is low due to various reasons. Drewett et al. (sample size = 169) showed that the presence of underlying disease is not associated with hospital readmissions [117]. While Joen et al., in their study of 7590 patients, showed that the risk of hospital readmissions increases to up to five times with increasing Charlson comorbidity index [18]. Also, Ramos-Martínez et al. showed that the presence of underlying respiratory diseases is a risk factor for hospital readmission, but there was no relationship between cardiovascular and kidney diseases and hospital readmissions [81]. Therefore, there seems to be a potential relationship

Fig. 2. Forest plot for prevalence of hospital readmission during one-year after recovery of COVID-19 patients. CI: Confidence interval.

Subgroup analysis for determination of source of heterogeneity in assessment of 1-years hospital readmission.

Variable	Number of analyses*	Prevalence (95% CI)	I2 (p value)
Country type			
Developed	79	10.68 (9.14, 12.22)	99.53 (<0.0001)
Developing	7	6.88 (4.52, 9.24)	85.48 (<0.0001)
Study design			
Prospective	27	11.52 (9.26, 13.79)	95.42 (<0.0001)
Retrospective	58	9.93 (8.15, 11.71)	99.63 (<0.0001)
Ambidirectional	1	1.44 (0.85, 2.04)	NA
Setting of patients			
All COVID-19 patients	77	9.71 (8.35, 11.06)	99.40 (<0.0001)
Elderly	2	15.28 (6.80, 23.76)	80.68 (0.023)
Presence of underlying disease or infection**	7	19.63 (7.41, 31.83)	96.22 (<0.0001)
COVID-19 diagnostic criteria			
RT-PCR	63	9.52 (8.04, 11.00)	99.26 (<0.0001)
Mixed criteria***	9	7.22 (4.02, 10.43)	98.14 (<0.0001)
NR	14	16.58 (12.24, 20.92)	97.89 (<0.0001)
Risk of bias score			
Low risk	36	10.38 (8.52, 12.24)	98.30 (<0.0001)
Some concern	3	17.16 (4.67, 38.98)	96.99 (<0.0001)
High risk	47	10.01 (7.99, 12.02)	99.64 (<0.0001)

NR: Not reported; CI: Confidence interval.

* Since some studies stratified their data according to different subgroups (such as according to underlying disease) the number of analyses is higher than number of studies.

** Underlying disease or infection included cirrhosis and liver injury, myocardial infarction, cardiovascular disease, autoimmune diseases, cancer, fungal infections, HIV infection, rheumatic and musculoskeletal and acute kidney injury.

** Mixed criteria: RT-PCR or laboratory or clinical or imaging.

Study	Sample size	Events	Follow up	,	Effect size with 95% CI	Weight (%)
Hasan, 2021	238	0	30	0	0.00 [-0.77, 0.77]	2.29
Stockman, 2021	37	0	150	-0-	0.00 [-4.74, 4.74]	2.08
Suárez-Robles, 2020	134	0	90	Θ	0.00 [-1.36, 1.36]	2.28
Chai, 2021	456	2	365	Θ	0.44 [-0.32, 1.20]	2.29
Bowles, 2021	1409	8	180	0	0.57 [0.13, 1.00]	2.30
Huang CW, 2021	2180	19	30	0	0.87 [0.46, 1.29]	2.30
Romero-Duarte, 2021	797	8	180	Θ	1.00 [0.24, 1.77]	2.29
van den Borst,2021	98	1	90	0	1.02 [-1.74, 3.78]	2.22
Bajaj, 2021	93	1	90	0	1.08 [-1.83, 3.98]	2.21
Ramos- Martínez, 2021	7137	85	30	0	1.19 [0.93, 1.45]	2.30
Banerjee, 2021	621	8	30	Θ	1.29 [0.31, 2.27]	2.29
Kirkegaard, 2021	638	9	60	0	1.41 [0.40, 2.42]	2.29
Wu, 2021	132	2	180	0	1.52 [-1.08, 4.11]	2.23
Huang C, 2021	1733	33	199	0	1.90 [1.23, 2.58]	2.29
Leon, 2021	105	2	210	-0-	1.90 [-1.34, 5.14]	2.19
Divanoglou, 2021	433	9	135	0	2.08 [0.60, 3.56]	2.28
Kingery, 2021	1344	32	30	0	2.38 [1.53, 3.24]	2.29
Todt, 2021	251	6	90	0	2.39 [0.27, 4.51]	2.25
Hernández-Biette, 2020	74	3	14	-0-	4.05 [-1.22, 9.33]	2.03
Meije, 2021	323	14	210	0	4.33 [1.95, 6.72]	2.24
Giannis, 2021	4904	237	92	0	4.83 [4.22, 5.44]	2.29
Reyes Gill, 2021	150	8	30	-0-	5.33 [1.38, 9.29]	2.14
García- Abellán, 2021	146	8	180	0	5.48 [1.42, 9.54]	2.13
Quilliot, 2021	296	17	30	0	5.74 [2.92, 8.57]	2.22
Gunster, 2021	6518	405	180	ø	6.21 [5.62, 6.81]	2.29
Leijte, 2020	596	38	90	ø	6.38 [4.33, 8.42]	2.25
Spinicci, 2021	107	7	56	-0-	6.54 [1.37, 11.71]	2.04
Chopra, 2020	1250	84	60	0	6.72 [5.29, 8.15]	2.28
Islam, 2021	403	29	60	0	7.20 [4.55, 9.85]	2.23
Carrillo- Garcia, 2021	165	14	90	-0-	8.48 [3.93, 13.04]	2.09
Donnelly, 2021	1775	162	60	e	9.13 [7.76, 10.49]	2.28
Pourhoseingholi, 2021	1053	97	365	0	9.21 [7.42, 11.01]	2.26
Roig-Marín, 2021	221	21	365	-0-	9.50 [5.41, 13.59]	2.20
Chai, 2021	132	15	365		11.36 [5.59, 17.14]	1.99
Ayoubkhani, 2021	47780	5875	245	0	12.30 [12.00, 12.59]	2.30
Maestre-Muñiz, 2021	266	34	365	-0-	12.30 [12.00, 12.39]	2.30
Maestre-Muniz, 2021 Navvas, 2021	402	54	305	-0-	13.43 [9.98, 16.89]	2.12
Bajaj, 2021	29	4	90		- 13.79 [-0.09, 27.68]	1.20
	106	4	90			1.20
Spence, 2021 Madranda, 2021						
Medranda, 2021 Vanturalli, 2021	92	16	180	-0		1.74
Venturelli, 2021	767	141	90	-0	1	2.22
Frontera, 2021	380	75	180	-0		2.13
Gąsior, 2021 Cutiórman, 2021	2988	636	180 30		1	2.28
Gutiérrez, 2021	13578	2968			,,	2.29
Weber, 2021	408	104	180		• 25.49 [21.15, 29.83]	2.11
Gutiérrez, 2021	362	115	30		- O - 31.77 [26.85, 36.69]	2.06
Overall	2	2		•	7.51 [5.30, 9.72]	
Heterogeneity: $\tau^2 = 55$.			51.56			
Test of $\theta_i = \theta_j$: Q(45) = 2	7854.95, p = 0.	.00				
Test of $\theta = 0$: $z = 6.67$, p	0 = 0.00					

Fig. 3. Post-discharge all-cause mortality of COVID-19 patients during one-year after recovery. CI: Confidence interval.

between post-discharge of COVID-19 patients and underlying disease. But the current evidence is contradictory and comes from studies that have a low level of evidence and more research is needed in this field.

There were no eligibility criteria based on comorbidity in the current meta-analysis, and many hospitalized COVID-19 patients have at least one comorbidity [118,119]. Most of the included studies have been performed on a heterogeneous population of COVID-19 patients, from which some patients had a history of an underlying disease and others had no underlying diseases. On the other hand, many of comorbidities are exacerbated by COVID-19, such as cardiovascular diseases and coagulopathies [112-116,120]. In general, it seems that even in the presence of comorbidity COVID-19 is likely to be the main cause of readmission, because most of these readmissions occur within the first month after discharge.

Sensitivity analysis showed that hospital readmissions and postdischarge all-cause mortality varied across the countries. Part of this difference is related to socio-economic differences between countries. However, the included sample sizes are small in some countries. The included number of patients in the analysis of hospital readmissions and post-discharge all-cause mortality was less than 1000 patients in 8 (out of 16 countries) and 6 (out of 13 countries) countries, respectively. In other words, in almost half of the countries, the sample size included in the analysis was low, and therefore, care should be taken to interpret the findings regarding countries with low sample sizes.

HIV infection was reported as a risk factor for COVID-19 mortality in previous studies [121] and may cause a severe form of SARS-CoV-2 infection. In our meta-analysis, only one study assessed the post-COVID-19 readmission rate in HIV-infected patients. We performed a sensitivity analysis to assess the effect of this study on the findings. Excluding the HIV population from the analysis did not change the overall readmission rate of COVID-19 patients (10.34% vs 10.31%). Therefore, in the current study HIV infection was not a source of heterogeneity.

Another limitation of the present study was the lack of reporting patients' discharge criteria in the included studies. The standard criterion for discharge of COVID-19 patients is two consecutive negative RT-PCR, in addition to symptoms improvement [122], which was used only in 18 studies. However, in the remaining 73 studies, discharge criteria were not reported or relied only on symptoms improvement. A review

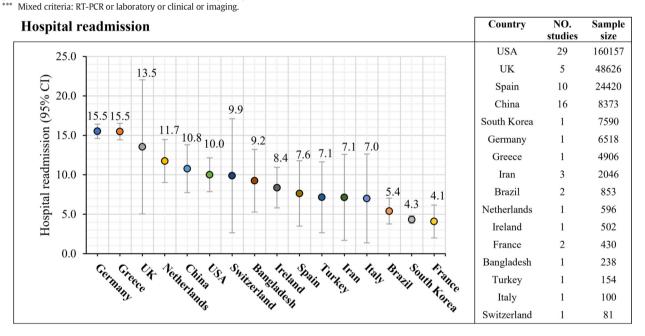
Subgroup analysis for determination of source of heterogeneity in assessment of post-discharge all-cause mortality.

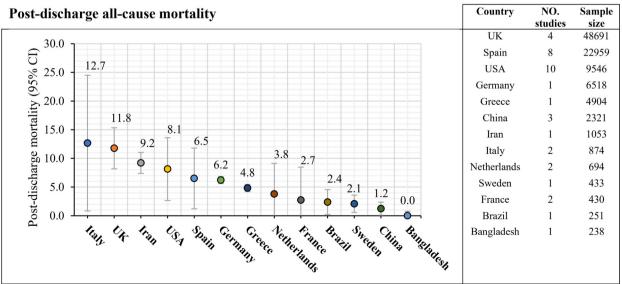
Variable	Number of analyses*	Prevalence (95% CI)	I2 (p value)
Country type			
Developed	43	7.78 (5.46, 10.11)	99.63 (<0.0001)
Developing	3	3.84 (-1.60, 9.27)	97.39 (<0.0001)
Study design			
Prospective	17	6.01 (2.58, 9.44)	98.76 (<0.0001)
Retrospective	27	8.84 (5.85, 11.84)	99.73 (<0.0001)
Ambidirectional	2	1.93 (1.32, 2.55)	0.00 (0.833)
Setting of patients			
All COVID-19 patients	37	6.59 (4.48, 8.74)	99.57 (<0.0001)
Elderly	2	9.05 (6.00, 12.09)	0.00 (0.754)
Presence of underlying disease or infection**	7	12.03 (3.03, 21.03)	97.86 (<0.0001)
COVID-19 diagnostic criteria			
RT-PCR	29	6.44 (3.68, 9.20)	99.64 (<0.0001)
Mixed criteria***	6	7.45 (2.39, 12.50)	96.33 (<0.0001)
NR	11	10.54 (5.62, 15.46)	99.43 (<0.0001)
Risk of bias score			
Low risk	19	4.00 (2.17, 5.83)	99.06 (<0.0001)
Some concern	2	9.17 (-5.98, 24.32)	91.54 (<0.0001)
High risk	25	10.00 (6.55, 13.46)	99.36 (<0.0001)

NR: Not reported; CI: Confidence interval.

* Since some studies stratified their data according to different subgroups (such as according to underlying disease) the number of analyses is higher than number of studies. ** Underlying disease or infection included cirrhosis and liver injury, myocardial infarction, cardiovascular disease, autoimmune diseases, cancer, fungal infections, HIV

patients, rheumatic and musculoskeletal and acute kidney injury.





Country level hospital readmission and post-discharge mortality of COVID-19 patients

	-	-		-
Country	Number of	Number of	Prevalence	95% confidence
	studies	patients		interval
Hospital readm	nission			
Germany	1	6518	15.5	14.6, 16.4
Greece	1	4906	15.5	14.4, 16.5
UK	5	48,626	13.5	5.2, 21.9
Netherlands	1	596	11.7	9.1, 14.4
China	16	8373	10.8	7.8, 13.7
USA	29	160,157	10.0	7.9, 12.1
Switzerland	1	81	9.9	2.8, 17.0
Bangladesh	1	238	9.2	5.4, 13.1
Ireland	1	502	8.4	5.8, 10.9
Spain	10	24,420	7.6	3.6, 11.7
Turkey	1	154	7.1	2.7, 11.5
Iran	3	2046	7.1	1.8, 12.5
Italy	1	100	7.0	1.5, 12.5
Brazil	2	853	5.4	3.8, 7.0
South Korea	1	7590	4.3	3.9, 4.8
France	2	430	4.1	2.0, 6.1
Post-discharge	all-cause mortal	ity		
Italy	2	874	12.7	1.1, 24.3
UK	4	48,691	11.8	8.3, 15.3
Iran	1	1053	9.2	7.4, 11.0
USA	10	9546	8.1	2.8, 13.5
Spain	8	22,959	6.5	1.3, 11.7
Germany	1	6518	6.2	5.6, 6.8
Greece	1	4904	4.8	4.2, 5.4
Netherlands	2	694	3.8	-1.5, 9.0
France	2	430	2.7	-2.9, 8.4
Brazil	1	251	2.4	0.3, 4.5
Sweden	1	433	2.1	0.6, 3.6
China	3	2321	1.2	0.1, 2.4
Bangladesh	1	238	0.0	-0.8, 0.8

study found that of the 10 countries with the highest prevalence of COVID-19, five did not have a discharge criterion, and in the other five countries there was considerable diversity in discharge criteria. This review strongly recommends defining uniform, standard and simple criteria for hospital discharge of COVID-19 patients [123]. During the COVID-19 pandemic and its outbreaks, the lack of hospital beds, medical facilities, and human resources caused patients to be discharged too early, leading to increased hospital readmissions and possible post-discharge deaths. Therefore, it is very important to define and standard discharge criteria in the treatment protocols of COVID-19 patients, to reduce the hospital readmission rates and deaths following the disease. Finally, it should be noted that the included studies were heterogeneous. Nevertheless, the possible sources of heterogeneity were found to be differences in population age, underlying diseases, and country type, the residual source of heterogeneity remained unclear.

5. Conclusion

Although the level of evidence was calculated to be very low, the current meta-analysis showed that 10.34% of recovered COVID-19 required hospital readmissions after discharge. Also, the one-year postdischarge all-cause mortality rate of COVID-19 patients is 7.87%. Most hospital readmissions and post-discharge all-cause mortality appear to occur within 30 days post-discharge. Therefore, in addition to adopting a standard criterion for discharge of COVID-19 patients, a 30-day followup program and patient tracking system for discharged COVID-19 patients seems necessary. Further prospective cohort studies are needed to explore the independent risk factors of hospital readmission and post-discharge mortality of COVID-19 patients.

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Author contribution

ZSR participated in designing, data gathering, analysis, and drafting of the paper.

Availability of data

All data used in the present study will be made available to qualified researchers on reasonable request.

Declaration of Competing Interest

There is no conflict of interest.

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Appendix A. Supplementary data

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