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Severity and mortality of COVID-19 among people with disabilities: A systematic review and meta-analysis protocol

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This protocol contains 1530 words.

ABSTRACT

Introduction: As the COVID-19 pandemic and the subsequent global healthcare crisis continues, people with disabilities may face greater health risks than their non-disabled peers in a wide range of aspects. This systematic review and meta-analysis aimed to determine the severity and mortality of people with disabilities due to COVID-19.

Methods and analysis: We will search PubMed, WHO database, Cochrane Library databases, MedRxiv and Google Scholar to identify studies published from inception to December 31, 2021. Cohort, case-control and cross-sectional studies assessing the severity and mortality of people with disabilities due to COVID-19 will be included. The outcomes of interest include the risk of COVID-19 infection, rate of hospitalization, severity, hospital stay, mortality and others variables where data are available. Two reviewers will extract data and perform risk of bias assessment independently. The Newcastle-Ottawa Scale will be used to assess risk of bias. Review Manager V.5.4 and Stata version 16.0 software will be used for statistical analysis. Heterogeneity will be analyzed using I^2 statistics. Odds ratio with 95% CI will be used to calculate treatment effect for outcome variables.

Ethics and dissemination: Ethical approval and informed consent are not required as this was a literature review. The final results will be published in a peer reviewed journal and presented at national and international conferences.

PROSPERO registration number: CRD42022306361

Strengths and limitations of this study

- Data extraction and risk of bias assessment will be performed by two reviewers independently.
- The Newcastle-Ottawa Scale will be used to assess the risk of bias of the included studies.
- The risk of publication bias and sensitivity analysis for outcomes will be assessed.
- The absence of sufficient high-quality studies focusing on disability and COVID-19, heterogeneity in severity of COVID-19 measures and small sample size might be the limitations for this systematic review and meta-analysis.

INTRODUCTION

The number of globally registered coronavirus disease 2019 (COVID-19) cases exceeded 320 million, with more than 5.5 million deaths (as of January 14, 2022).[1] There is a growing concern that people with disability might be more exposed to severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) infection, more likely to present with severe COVID-19 outcomes and having poorer health during and after the outbreak depending on their disability status.[2,3,4] According to the International Classification of Functioning, Disability and Health (ICF), disability is the umbrella term for impairments, activity limitations and participation restrictions, and it happens when difficulties encountered in any or all three areas of functioning.[5] It is not easy to practice COVID-19 prevention measures such as social distance in most disable people with visual impairment and walking problems. It is relevant to notice that people with disabilities are financially dependent on others for their daily lives, so it is difficult to afford COVID-19 prevention measures as well as to practice quarantine and stay home. In addition, people with disabilities were systemically vulnerable for COVID-19 due to inaccessible health information and marginalization.[6,7]

Previous studies have outlined that older age and presence of underlying comorbidities such as cancer, diabetes, cardiovascular disease, hypertension, heart failure, chronic kidney disease, HIV/AIDS and obesity, increased the risk of infection and mortality from COVID-19.[8,9,10,11,12,13] There are also ongoing and newly published review studies investigating the severity and mortality of COVID-19 in patients with sleep disorder and mental disorders.[14,15] Studies have identified that people with disabilities have higher prevalence of co-morbidities, such as hypertension, heart disease, respiratory disease, diabetes, and depression, which are in-turn identified as risk factors for poor outcomes from COVID-19.[2] Even though, there exist limitations in data collection, recent studies have highlighted that COVID-19 related disease severity and death rate in people with disabilities were higher than the general population.[2,3] Thus, disability and COVID-19 infection seems to be closely associated.

With nearly 1 billion (15% of the world's population) people with disabilities across the globe,[16] it remains urgent to characterize the outcomes of COVID-19 among this group. This study aimed to explore the association between disability and the mortality and severity of COVID-19 in general. We will also explore the rate of hospitalization, rate of Intensive Care Unit (ICU)

admission, hospital stay, laboratory findings and other relevant clinical symptoms due to COVID-19. To our knowledge, this will be the first systematic review and meta-analysis to investigate the mortality and severity of people with disabilities due to COVID-19 pandemic in the literature.

METHODS AND ANALYSIS

The review will be developed according to the recommendations from the Meta-analysis of Observational Studies in Epidemiology (MOOSE)[17] and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-P)[18] statements for reporting of systematic review and meta-analysis which is presented in figure 1.

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow chart

Search strategy

Literature search will be conducted in PubMed, WHO database, Cochrane Library databases, MedRxiv and Google Scholar databases and articles published from inception to December 31, 2021 will be included. Observational studies (cohort, case-control and cross-sectional studies) assessing the severity and mortality of people with disabilities due to COVID-19 will be considered. The following predefined search terms determined by the Medical Subject Headings (MeSH) and keywords including multiple combinations will be used: (“COVID-19” OR “coronavirus” OR “SARS-CoV-2” OR "2019-nCoV" OR "SARS nCoV2" OR "novel coronavirus 2019" OR "novel coronavirus disease 2019" OR) AND (“mortality” OR “severity” OR “hospitalization” OR “ICU admission” OR “mechanical ventilation”) AND (“disability” or “physical disability” OR “mental disability” OR “people with disability”). Two reviewers (AAS and AWT) will independently screen titles and abstracts of the studies, and any disagreement between the reviewers will be resolved by consensus or by another third reviewer (AAH). The search strategy of PubMed database is presented in table 1.

Table 1. PubMed search strategy

Search number	Search detail
#1	"COVID-19"[MeSH Terms]
#2	"disability"[MeSH Terms]
#3	"COVID-19"[Title/Abstract] OR "novel coronavirus 2019"[Title/Abstract] OR "novel coronavirus disease 2019"[Title/Abstract] OR "2019-nCoV"[Title/Abstract] OR "SARS-CoV"[Title/Abstract] OR "SARS-CoV-2"[Title/Abstract] OR "corona virus 2019"[Title/Abstract] OR "covid 19 disease"[Title/Abstract] OR "mortality"[Title/Abstract] OR "mortality rate"[Title/Abstract] OR "severity"[Title/Abstract] OR "rate of hospitalization"[Title/Abstract] OR "ICU admission"[Title/Abstract] OR "mechanical ventilation"[Title/Abstract] OR "disability"[Title/Abstract] OR "physical disability"[Title/Abstract] OR "mental disability"[Title/Abstract] OR "people with disability"[Title/Abstract]
#4	#1 AND #2
#5	#3 AND #4

Inclusion criteria

Only observational studies (cohort, case-control and cross-sectional studies) that focused on adult peoples with disabilities (aged over 18 years) and investigate the association between severity, hospitalization, ICU admission and need for mechanical ventilation, hospital stay and mortality due to COVID-19 will be included. The following types of studies will be excluded: (1) studies that included infants and children; (2) studies that did not classify COVID-19 severity; (3) studies with very small sample size; (4) studies that did not have enough statistical information to be extracted; and (5) descriptive reviews, randomized controlled trials, systematic review, meta-analysis, opinion, editorial, comments, and conference abstracts will be excluded. Excluded studies will be documented with reasons for their exclusion. Only full text published studies in English language will be included.

Outcome measures

The primary outcome measures will be the risk/ratio of COVID-19 severity and mortality in people with disabilities. Secondary outcome measures will include rate of hospitalization, ICU admission and the need for mechanical ventilation, viral load, hospital stay and others variables where data are available.

Data extraction

Two reviewers (AAS and AWT) will initially screen titles and abstracts of all identified articles for eligibility. After initially screening articles for inclusion based on titles and abstracts, full-text articles will be screened. Disagreements will be resolved by discussion or a third reviewer (AAH) will be consulted in order to reach a consensus. We will develop a standard data extraction form and use it to extract data to reflect the characteristics of each included study. The included studies might vary in their classification of COVID-19 disease severity, ranging from mild, moderate, severe, to critical severe. We will categorize mild and moderate cases into the non-severe group and severe and critical severe cases into the severe group.[12] We will extract the following information: year of publication, date of the study, type of study, the sample size of participant, severity and mortality of COVID-19, rates of hospitalization and other relevant clinical symptoms and laboratory findings.

Methodological quality assessment

Two reviewers (AAS and AAH) will independently assess the risk of bias of the included studies using the 9-star Newcastle-Ottawa Scale (NOS).[19] NOS scale rates observational studies based on 3 parameters: selection, comparability between the exposed and unexposed groups, and exposure/outcome assessment. the scale assigns a maximum of 4 stars for selection, 2 stars for comparability, and 3 stars for exposure/outcome assessment. Studies with less than 5 stars were considered low quality, 5–7 stars of moderate quality, and more than 7 stars of high quality.[9] Only studies with moderate and above quality score will be included in this systematic review and meta-analysis. When conflicts related to bias scores arise, the final decision will be taken by a consensus.

Data synthesis

Review Manager V.5.4 (Cochrane Collaboration) and Stata version 16.0 (STATA Corporation, College Station, TX, USA) software will be used to conduct the meta-analysis. We will calculate pooled estimates of odds ratio (OR) with 95% confidence interval (CI) by the generic inverse variance method. Heterogeneity among included studies will be assessed using the I^2 test. First a fixed-effect model will be used for data analysis. If $I^2 > 0.5$ or $p < 0.1$ it is considered that there is a significant heterogeneity among the included studies,[20] and random-effect model with the inverse variance method will be used in this case. To determine the source of heterogeneity sensitivity

analysis will be conducted by excluding studies one by one. Subgroup analyses will be performed on age, gender, type of disability and other variables depending on the data available. Publication bias across studies will be examined using funnel plot method, Egger's test and Begg's test.[21] If the funnel plot is symmetrical and the P value of Egger's and Begg's tests are >0.05, no significant publication bias will be considered to exist in the meta-analysis.[11] If publication bias is found, a trim and fill analysis will be used to evaluate the number of missing studies and recalculate the pooled odds ratio with the addition of those missing hypothetical studies.

Patient and public involvement: No patient involved.

Acknowledgement: Not applicable.

Funding: Not applicable.

Conflict of interest: No conflict of interest to disclose.

Author contributions: All authors have made significant contributions to this study protocol. AAS developed the research question, wrote the first draft, designed the search strategy, and edited and approved the final version of the manuscript. AAH revised the search strategy of databases, developed the data extraction form, and edited and approved the final version of the manuscript. AWT revised the data extraction form and edited and approved the final version of the manuscript.

Data availability statement: This is a study protocol of observational studies and no data is available to be shared.

Ethics approval: Ethics approval and informed consent are not required as this study is a literature review which only involve the use of previously published data and does not include any patient. The final results of this systematic review and meta-analysis will be published in a peer-reviewed journal and presented at relevant conferences and events.

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Figure Legends:

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow chart

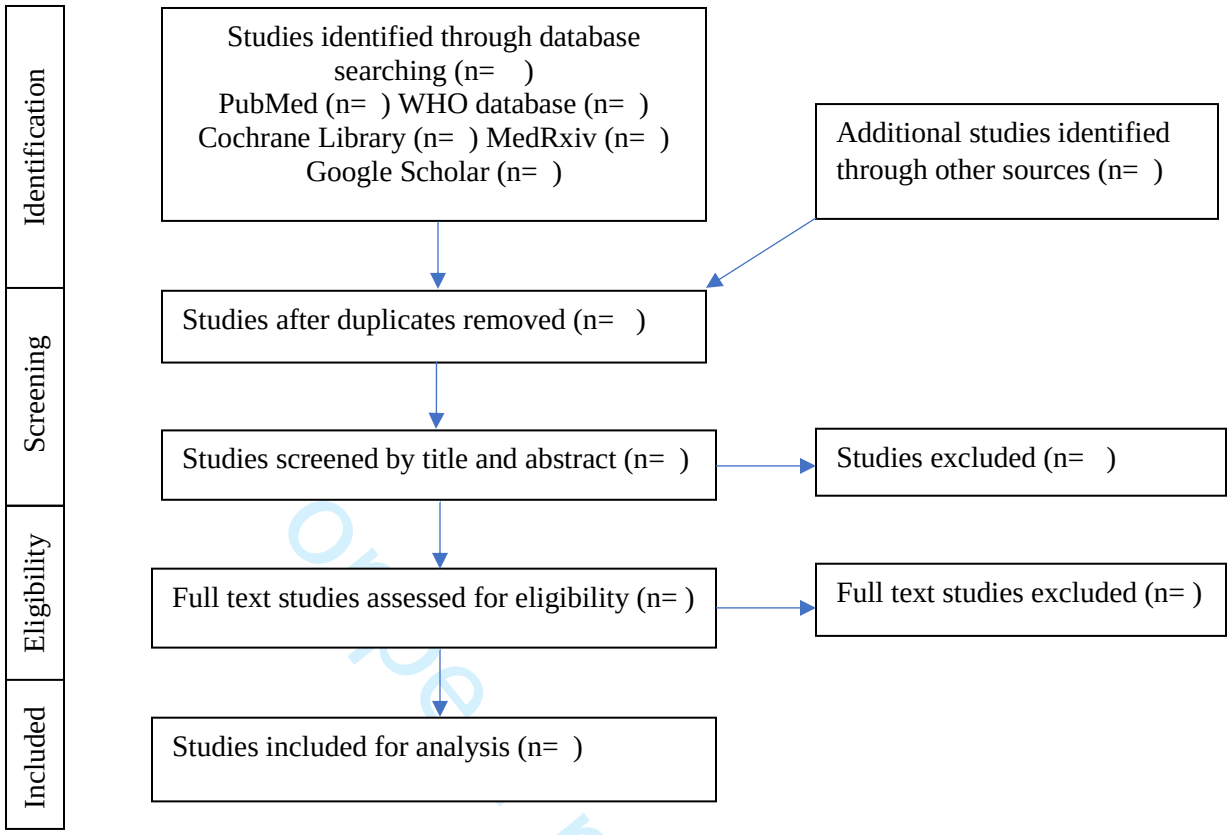

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow chart

Reporting checklist for protocol of a systematic review and meta-analysis.

Based on the PRISMA-P guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA-P reporting guidelines, and cite them as:

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Page Number
Title			
Identification	#1a	Identify the report as a protocol of a systematic review	1
Update	#1b	If the protocol is for an update of a previous systematic review, identify as such	n/a

Registration			
	#2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors			
Contact	#3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contribution	#3b	Describe contributions of protocol authors and identify the guarantor of the review	7
Amendments			
	#4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support			
Sources	#5a	Indicate sources of financial or other support for the review	7
Sponsor	#5b	Provide name for the review funder and / or sponsor	7
Role of sponsor or funder	#5c	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	7
Introduction			
Rationale	#6	Describe the rationale for the review in the context of what is	3

		already known	
Objectives	#7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	3-4
Methods			
Eligibility criteria	#8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	4
Information sources	#9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	#10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5, Table 1.
Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6
Study records - selection process	#11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	4
Study records - data collection	#11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any	5

process		processes for obtaining and confirming data from investigators	
Data items	#12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	n/a
Outcomes and prioritization	#13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5
Risk of bias in individual studies	#14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	6
Data synthesis	#15a	Describe criteria under which study data will be quantitatively synthesised	6
Data synthesis	#15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I2, Kendall's τ)	6
Data synthesis	#15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	n/a
Data synthesis	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned	n/a-.
Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within	7

		studies)	
Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	6

Notes:

- 4: n/a- this is a new protocol
- 15d: n/a-quantitative analysis is possible. The PRISMA-P elaboration and explanation paper is distributed under the terms of the Creative Commons Attribution License CC-BY. This checklist was completed on 20. January 2022 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

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Secondary Subject Heading:	Global health, Health services research, Public health
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ABSTRACT

Introduction: As the COVID-19 pandemic and the subsequent global healthcare crisis continues, people with disabilities may face greater health risks than their non-disabled peers in a wide range of aspects. This systematic review and meta-analysis aimed to determine the severity and mortality of people with different types of disabilities due to COVID-19.

Methods and analysis: We will search PubMed, HINARI, ScienceDirect, PEDro and Cochrane Library databases. Gray literature search will also be conducted on MedRxiv and Google Scholar to identify studies available from inception to date. Cohort, case-control and cross-sectional studies assessing the severity and mortality of people with disabilities due to COVID-19 will be included. Only full text studies in English language will be included. The outcomes of interest include the risk of COVID-19 infection, rate of hospitalization, severity, hospital stay, mortality and others variables where data are available. Two reviewers will extract data and perform risk of bias assessment independently. The Newcastle-Ottawa Scale will be used to assess risk of bias. Review Manager V.5.4 and Stata version 16.0 software will be used for statistical analysis. Heterogeneity will be analyzed using I^2 statistics. Pooled odds ratio with 95% CI will be used to calculate the pooled results for outcome variables.

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- The absence of sufficient high-quality studies focusing on disability and COVID-19, heterogeneity in severity of COVID-19 measures and small sample size might be the limitations for this systematic review and meta-analysis.

INTRODUCTION

The number of globally registered coronavirus disease 2019 (COVID-19) cases exceeded 320 million, with more than 5.5 million deaths (as of January 14, 2022).[1] There is a growing concern that people with disability might be more exposed to severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) infection, more likely to present with severe COVID-19 outcomes and having poorer health during and after the outbreak depending on their disability status.[2,3,4] According to the International Classification of Functioning, Disability and Health (ICF), disability is the umbrella term for impairments, activity limitations and participation restrictions, and it happens when difficulties encountered in any or all three areas of functioning.[5] It is not easy to practice COVID-19 prevention measures such as social distance in most disable people with visual impairment and walking problems. It is relevant to notice that many people with disabilities are financially dependent on others for their daily lives, so it is difficult to afford COVID-19 prevention measures as well as to practice quarantine and stay home. In addition, people with disabilities were systemically vulnerable for COVID-19 due to inaccessible health information and marginalization.[6,7]

Previous studies have outlined that older age and presence of underlying comorbidities such as cancer, diabetes, cardiovascular disease, hypertension, heart failure, chronic kidney disease, HIV/AIDS and obesity, increased the risk of infection and mortality from COVID-19.[8,9,10,11,12,13] There are also ongoing and newly published review studies investigating the severity and mortality of COVID-19 in patients with sleep disorder and mental disorders.[14,15] Studies have identified that people with intellectual and developmental disabilities have higher prevalence of co-morbidities, such as hypertension, heart disease, respiratory disease, diabetes, and depression, which are in-turn identified as risk factors for poor outcomes from COVID-19.[2] Even though, there exist limitations in data collection, recent studies have highlighted that COVID-19 related disease severity and death rate in people with intellectual and developmental disabilities were higher than the general population.[2,3] Thus, intellectual and developmental disability and COVID-19 infection seems to be closely associated. A systematic review and meta-analysis conducted on COVID-19 in Parkinson's disease (PD) peoples reported 5%, 49% and 12% prevalence, hospitalization and mortality rates respectively.[16] Another study reported that the prevalence of dementia was 10% (7-

13%) with an increased mortality rate (adjusted odds ratio 1.80, 95% CI 1.45-2.24, P<0.001; I^2=72.9%) in COVID-19 patients.[17]

With nearly 1 billion (15% of the world's population) people with disabilities across the globe,[18] it remains urgent to characterize the outcomes of COVID-19 among this group. International definition and statistics of disability is very wide and general (disability is perceived and defined differently in different contexts). In this study we will focus on the most common types of disabilities like intellectual and developmental disability (such as autism, Down syndrome and fragile x syndrome), sensory disability (such as visual and hearing impairments), physical disability (such as cerebral palsy, multiple sclerosis and absence or deformities of limbs), mental/neurologic related disability (such as schizophrenia, obsessive-compulsive disorder (OCD), bipolar disorder, Alzheimer's disease and Parkinson's disease) and other types of disability where data are available. This study aimed to explore the associations between different types of disabilities and the mortality and severity of COVID-19. We will also explore the rate of hospitalization, rate of Intensive Care Unit (ICU) admission, hospital stay, laboratory findings and other relevant clinical symptoms as well as long term impacts due to COVID-19. To our knowledge, this will be the first systematic review and meta-analysis to investigate the mortality and severity of people with disabilities due to COVID-19 pandemic in the literature.

METHODS AND ANALYSIS

This systematic review and meta-analysis protocol is reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P)[19] statement. The reporting flow chart is presented in figure 1.

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow chart

Search strategy

Literature search will be conducted in PubMed, HINARI, ScinceDirect, PEDro, Cochrane Library, MedRxiv and Google Scholar databases supplemented by manual search of references of included studies will be carried out. Articles published from inception to date will be included. Observational studies (cohort, case-control and cross-sectional studies) assessing the severity and mortality of people with disabilities due to COVID-19 will be considered. The predefined search

terms determined by the Medical Subject Headings (MeSH) and keywords including multiple combinations of COVID-19 and disabled persons (MeSH Terms and entry terms for each) as well as severity and mortality related terms will be used. Two reviewers (AAS and AWT) will independently screen titles and abstracts of the studies, and any disagreement between the reviewers will be resolved by consensus or by another third reviewer (AAH). The search strategy of PubMed database is presented in table 1. The search strategy of other databases was presented in the supplementary file (supplementary file 1).

Table 1. PubMed search strategy

Search number	Search detail
#1	"COVID-19"[MeSH Terms]
#2	"disabled persons"[MeSH Terms]
#3	"COVID-19"[Title/Abstract] OR "sars coronavirus 2"[Title/Abstract] OR "coronavirus 2 sars"[Title/Abstract] OR "coronavirus disease 2019 virus"[Title/Abstract] OR "2019 novel coronavirus"[Title/Abstract] OR "2019 novel coronaviruses"[Title/Abstract] OR "coronavirus 2019 novel"[Title/Abstract] OR "novel coronavirus 2019"[Title/Abstract] OR "wuhan seafood market pneumonia virus"[Title/Abstract] OR "sars cov 2 virus"[Title/Abstract] OR "sars cov 2 viruses"[Title/Abstract] OR "virus sars cov 2"[Title/Abstract] OR "2019-nCoV"[Title/Abstract] OR "covid 19 virus"[Title/Abstract] OR "severe acute respiratory syndrome coronavirus 2"[Title/Abstract] OR "wuhan coronavirus"[Title/Abstract]
#4	"prevalence"[Title/Abstract] OR "rate of infection"[Title/Abstract] OR "mortality"[Title/Abstract] OR "death"[Title/Abstract] OR "severity"[Title/Abstract] OR "hospitalization"[Title/Abstract] OR "icu admission"[Title/Abstract] OR "mechanical ventilation"[Title/Abstract] OR "disabled persons"[Title/Abstract] OR "disabled person"[Title/Abstract] OR "persons disabled"[Title/Abstract] OR "Handicapped"[Title/Abstract] OR "people with disabilities"[Title/Abstract] OR "persons with disabilities"[Title/Abstract] OR "persons with disability"[Title/Abstract] OR "physically handicapped"[Title/Abstract] OR "handicapped physically"[Title/Abstract] OR "physically disabled"[Title/Abstract] OR "physically challenged"[Title/Abstract] OR "Amputees"[Title/Abstract] OR "mentally ill persons"[Title/Abstract] OR "persons with hearing impairments"[Title/Abstract] OR "persons with mental disabilities"[Title/Abstract] OR "visually impaired persons"[Title/Abstract] OR "psychosocial disability"[Title/Abstract] OR "intellectual disability"[Title/Abstract] OR "developmental disability"[Title/Abstract] OR "autism spectrum disorder"[Title/Abstract] OR "cerebral palsy"[Title/Abstract] OR "Autism"[Title/Abstract] OR "Down syndrome"[Title/Abstract] "fragile x syndrome"[Title/Abstract] OR "epilepsy"[Title/Abstract] OR "multiple sclerosis"[Title/Abstract] OR "schizophrenia"[Title/Abstract] OR "obsessive-compulsive disorder"[Title/Abstract] OR "bipolar disorder"[Title/Abstract] OR "Alzheimer's disease"[Title/Abstract] OR "sensory disability"[Title/Abstract] OR "Parkinson's disease"[Title/Abstract]
#5	#1 OR #3
#6	#2 OR #4
#7	#5 AND #6

Inclusion criteria

Only observational studies (cohort, case-control and cross-sectional studies) that focused on adult peoples with disabilities (aged over 18 years) and investigate the association between severity, hospitalization, ICU admission and need for mechanical ventilation, hospital stay, mortality, other complications and long-term effects due to COVID-19 will be included. The following types of studies will be excluded: (1) studies that included infants and children; (2) studies with very small sample size; (3) studies that did not have enough statistical information to be extracted; and (4) descriptive reviews, randomized controlled trials, systematic review, meta-analysis, opinion, editorial, comments, and conference abstracts will be excluded. Excluded studies will be documented with reasons for their exclusion. Only full text published studies in English language will be included.

Outcome measures

The primary outcome measures will be the risk/ratio of COVID-19 severity and mortality in people with disabilities. Secondary outcome measures will include rate of hospitalization, ICU admission and the need for mechanical ventilation, viral load, hospital stay and others variables where data are available.

Data extraction

Two reviewers (AAS and AWT) will initially screen titles and abstracts of all identified articles for eligibility. After initially screening articles for inclusion based on titles and abstracts, full-text articles will be screened. Disagreements will be resolved by discussion or a third reviewer (AAH) will be consulted in order to reach a consensus. We will develop a standard data extraction form and use it to extract data to reflect the characteristics of each included study. The included studies might vary in their classification of COVID-19 disease severity, ranging from mild, moderate, severe, to critical severe. We will categorize mild and moderate cases into the non-severe group and severe and critical severe cases into the severe group.[12] We will extract the following information: year of publication, date of the study, type of study, the sample size of participant, severity and mortality of COVID-19, rates of hospitalization and other relevant clinical symptoms and laboratory findings.

Methodological quality assessment

Two reviewers (AAS and AAH) will independently assess the risk of bias of the included studies using the Newcastle-Ottawa Scale (NOS).[20] NOS scale rates observational studies based on 3 parameters: selection, comparability between the exposed and unexposed groups, and exposure/outcome assessment. the scale assigns a maximum of 4 stars for selection, 2 stars for comparability, and 3 stars for exposure/outcome assessment. Studies with less than 5 stars were considered low quality, 5–7 stars of moderate quality, and more than 7 stars of high quality.[9] Only studies with moderate and above quality score will be included in this systematic review and meta-analysis. When conflicts related to bias scores arise, the final decision will be taken by a consensus.

Data synthesis

Review Manager V.5.4 (Cochrane Collaboration) and Stata version 16.0 (STATA Corporation, College Station, TX, USA) software will be used to conduct the meta-analysis. We will calculate pooled estimates of odds ratio (OR) with 95% confidence interval (CI) by the generic inverse variance method. Heterogeneity among included studies will be assessed using the I^2 test. First a fixed-effect model will be used for data analysis. If $I^2 > 0.5$ or $p < 0.1$ it is considered that there is a significant heterogeneity among the included studies,[21] and random-effect model with the inverse variance method will be used in this case. To determine the source of heterogeneity sensitivity analysis will be conducted by excluding studies one by one. Subgroup analyses will be performed on age, gender, type of disability and other variables depending on the data available. Publication bias across studies will be examined using funnel plot method, Egger's test and Begg's test.[22] If the funnel plot is symmetrical and the P value of Egger's and Begg's tests are >0.05, no significant publication bias will be considered to exist in the meta-analysis.[11] If publication bias is found, a trim and fill analysis will be used to evaluate the number of missing studies and recalculate the pooled odds ratio with the addition of those missing hypothetical studies.

Patient and public involvement: No patient involved.

Ethics and dissemination: Ethics approval and informed consent are not required as this study is a systematic review which only involve the use of previously published data and does not include any patient. The final results of this systematic review and meta-analysis will be published in a peer-reviewed journal and presented at relevant conferences and events.

Funding: Not applicable.

Competing interests: No conflict of interest to disclose.

Contributors: All authors have made significant contributions to this study protocol. AAS developed the research question, wrote the first draft, designed the search strategy, and edited and approved the final version of the manuscript. AAH revised the search strategy of databases, developed the data extraction form, and edited and approved the final version of the manuscript. AWT revised the data extraction form and edited and approved the final version of the manuscript.

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Figure Legends:

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow chart

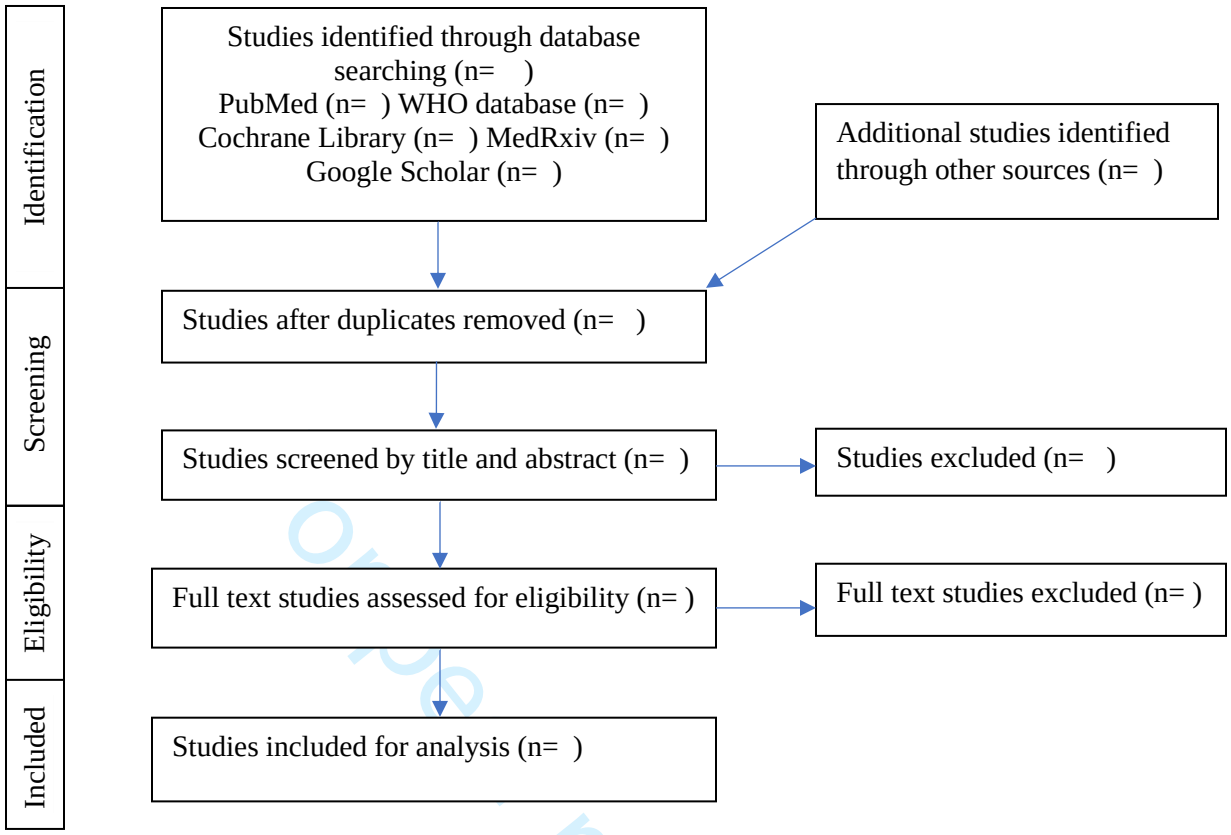

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow chart

Supplementary file 1: Search string for HINARI, ScienceDirect, PEDro, Cochrane Library, MedRxiv and Google Scholar databases

Search number	Search term
#1	COVID-19 OR Coronavirus disease 2019 OR SARS CoV-2
#2	disabled persons OR Handicapped OR people with disabilities OR persons with disability OR physically handicapped OR physically disabled OR physically challenged OR amputees OR mentally ill persons OR persons with mental disabilities OR psychosocial disability OR intellectual disability OR developmental disability OR autism OR autism spectrum disorder OR down syndrome OR fragile x syndrome OR sensory disability OR visual impairment OR hearing impairments OR physical disability OR cerebral palsy OR multiple sclerosis OR absence of limb OR deformities of limbs OR mental disability OR neurologic disability OR schizophrenia OR obsessive-compulsive disorder OR bipolar disorder OR Alzheimer's disease OR Parkinson's disease OR epilepsy
#3	#1 AND #2
#4	prevalence OR rate of infection OR mortality OR death OR severity OR case fatality OR hospitalization OR ICU admission OR mechanical ventilation OR effect OR impact OR long-term impact OR complication OR sequela
#5	#3 AND #4
#6	Limit to December, 2019 to date
#7	Limit to Humans
#8	Limit to observational studies
#9	Limit to cohort OR case-control OR cross-sectional studies
#10	#5 AND #6 OR #7 OR #8 OR #9

Reporting checklist for protocol of a systematic review and meta-analysis.

Based on the PRISMA-P guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA-P reporting guidelines, and cite them as:

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Page Number
Title			
Identification	#1a	Identify the report as a protocol of a systematic review	1
Update	#1b	If the protocol is for an update of a previous systematic review, identify as such	n/a

Registration			
	#2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors			
Contact	#3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contribution	#3b	Describe contributions of protocol authors and identify the guarantor of the review	7
Amendments			
	#4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support			
Sources	#5a	Indicate sources of financial or other support for the review	7
Sponsor	#5b	Provide name for the review funder and / or sponsor	7
Role of sponsor or funder	#5c	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	7
Introduction			
Rationale	#6	Describe the rationale for the review in the context of what is	3

		already known	
Objectives	#7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	3-4
Methods			
Eligibility criteria	#8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	4
Information sources	#9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	#10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5, Table 1.
Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6
Study records - selection process	#11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	4
Study records - data collection	#11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any	5

process		processes for obtaining and confirming data from investigators	
Data items	#12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	n/a
Outcomes and prioritization	#13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5
Risk of bias in individual studies	#14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	6
Data synthesis	#15a	Describe criteria under which study data will be quantitatively synthesised	6
Data synthesis	#15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I2, Kendall's τ)	6
Data synthesis	#15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	n/a
Data synthesis	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned	n/a-.
Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within	7

		studies)	
Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	6

Notes:

- 4: n/a- this is a new protocol
- 15d: n/a-quantitative analysis is possible. The PRISMA-P elaboration and explanation paper is distributed under the terms of the Creative Commons Attribution License CC-BY. This checklist was completed on 20. January 2022 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

BMJ Open

Severity and mortality of COVID-19 among people with disabilities: protocol for a systematic review and meta-analysis

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Secondary Subject Heading:	Global health, Health services research, Public health
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Severity and mortality of COVID-19 among people with disabilities: protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction: As the COVID-19 pandemic and the subsequent global healthcare crisis continue, people with disabilities may face greater health risks than their non-disabled peers. This systematic review and meta-analysis aims to determine the severity and mortality of COVID-19 among people with different types of disabilities.

Methods and analysis: We will search PubMed, HINARI, ScienceDirect, PEDro and Cochrane Library databases. Gray literature search will also be conducted on MedRxiv and Google Scholar. Searches will be without date restrictions. Cohort, case-control and cross-sectional studies assessing the severity and mortality of COVID-19 among people with disabilities will be included. Only full text studies in the English language will be included. The outcomes of interest include the risk of COVID-19 infection, rate of hospitalization, severity, hospital stay, mortality and others variables where data are available. Two reviewers will extract data and perform risk of bias assessment independently. The Newcastle-Ottawa Scale will be used to assess risk of bias. Review Manager V.5.4 and Stata version 16.0 software will be used for statistical analysis. Heterogeneity will be analyzed using I^2 statistics. Pooled odds ratio with 95% CI will be used to calculate the pooled results for outcome variables.

Ethics and dissemination: Ethical approval and informed consent are not required as this is a systematic review of existing publications. The final results will be published in a peer reviewed journal and presented at national and international conferences.

PROSPERO registration number: CRD42022306361.

Strengths and limitations of this study

- Data extraction and risk of bias assessment will be performed by two reviewers independently.
- The Newcastle-Ottawa Scale will be used to assess the risk of bias of the included studies.
- The risk of publication bias and sensitivity analysis for outcomes will be assessed.
- The absence of sufficient high-quality studies focusing on disability and COVID-19, heterogeneity in severity of COVID-19 measures and small sample size might be the limitations for this systematic review and meta-analysis.

INTRODUCTION

The number of globally registered coronavirus disease 2019 (COVID-19) cases exceeded 320 million, with more than 5.5 million deaths (as of January 14, 2022).[1] There is a growing concern that people with disability might be more exposed to severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) infection, more likely to present with severe COVID-19 outcomes and having poorer health during and after the outbreak depending on their disability status.[2,3,4] According to the International Classification of Functioning, Disability and Health (ICF), disability is the umbrella term for impairments, activity limitations and participation restrictions, and it happens when difficulties encountered in any or all three areas of functioning.[5] It is not easy to practice COVID-19 prevention measures such as social distance in most disable people with visual impairment and walking problems. It is relevant to notice that many people with disabilities are financially dependent on others for their daily lives, so it is difficult to afford COVID-19 prevention measures as well as to practice quarantine and stay home. In addition, people with disabilities were systemically vulnerable for COVID-19 due to inaccessible health information and marginalization.[6,7]

Previous studies have outlined that older age and presence of underlying comorbidities such as cancer, diabetes, cardiovascular disease, hypertension, heart failure, chronic kidney disease, HIV/AIDS and obesity, increased the risk of infection and mortality from COVID-19.[8,9,10,11,12,13] There are also ongoing and newly published review studies investigating the severity and mortality of COVID-19 in patients with sleep disorder and mental disorders.[14,15] Studies have identified that people with intellectual and developmental disabilities have higher prevalence of co-morbidities, such as hypertension, heart disease, respiratory disease, diabetes, and depression, which are in-turn identified as risk factors for poor outcomes from COVID-19.[2] Even though, there exist limitations in data collection, recent studies have highlighted that COVID-19 related disease severity and death rate in people with intellectual and developmental disabilities were higher than the general population.[2,3] Thus, intellectual and developmental disability and COVID-19 infection seems to be closely associated. A systematic review and meta-analysis conducted on COVID-19 in Parkinson's disease (PD) peoples reported 5%, 49% and 12% prevalence, hospitalization and mortality rates respectively.[16] Another study reported that the prevalence of dementia was 10% (7-

13%) with an increased mortality rate (adjusted odds ratio 1.80, 95% CI 1.45-2.24, P<0.001; I^2=72.9%) in COVID-19 patients.[17]

With nearly 1 billion (15% of the world's population) people with disabilities across the globe,[18] it remains urgent to characterize the outcomes of COVID-19 among this group. International definition and statistics of disability is very wide and general (disability is perceived and defined differently in different contexts). In this study we will focus on the most common types of disabilities like intellectual and developmental disability (such as autism, Down syndrome and fragile x syndrome), sensory disability (such as visual and hearing impairments), physical disability (such as cerebral palsy, multiple sclerosis and absence or deformities of limbs), mental/neurologic related disability (such as schizophrenia, obsessive-compulsive disorder (OCD), bipolar disorder, Alzheimer's disease and Parkinson's disease) and other types of disability where data are available. This study aimed to explore the associations between different types of disabilities and the mortality and severity of COVID-19. We will also explore the rate of hospitalization, rate of Intensive Care Unit (ICU) admission, hospital stay, laboratory findings and other relevant clinical symptoms as well as long term impacts due to COVID-19. To our knowledge, this will be the first systematic review and meta-analysis to investigate the mortality and severity of COVID-19 among people with disabilities.

METHODS AND ANALYSIS

This systematic review and meta-analysis protocol is reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P)[19] statement. The reporting flow chart is presented in figure 1.

Search strategy

Literature search will be conducted in PubMed, HINARI, ScinceDirect, PEDro, Cochrane Library, MedRxiv and Google Scholar databases supplemented by manual search of references of included studies will be carried out. Articles published from inception to date will be included. Observational studies (cohort, case-control and cross-sectional studies) assessing the severity and mortality of COVID-19 among people with disabilities will be considered. The predefined search terms determined by the Medical Subject Headings (MeSH) and keywords including multiple combinations of COVID-19 and disabled persons (MeSH Terms and entry terms for each) as well

as severity and mortality related terms will be used. Two reviewers (AAS and AWT) will independently screen titles and abstracts of the studies, and any disagreement between the reviewers will be resolved by consensus or by another third reviewer (AAH). The search strategy of PubMed database is presented in table 1. The search strategy of other databases was presented in the supplementary file (supplementary file 1).

Table 1. PubMed search strategy

Search number	Search detail
#1	"COVID-19"[MeSH Terms]
#2	"disabled persons"[MeSH Terms]
#3	"COVID-19"[Title/Abstract] OR "sars coronavirus 2"[Title/Abstract] OR "coronavirus 2 sars"[Title/Abstract] OR "coronavirus disease 2019 virus"[Title/Abstract] OR "2019 novel coronavirus"[Title/Abstract] OR "2019 novel coronaviruses"[Title/Abstract] OR "coronavirus 2019 novel"[Title/Abstract] OR "novel coronavirus 2019"[Title/Abstract] OR "wuhan seafood market pneumonia virus"[Title/Abstract] OR "sars cov 2 virus"[Title/Abstract] OR "sars cov 2 viruses"[Title/Abstract] OR "virus sars cov 2"[Title/Abstract] OR "2019-nCoV"[Title/Abstract] OR "covid 19 virus"[Title/Abstract] OR "severe acute respiratory syndrome coronavirus 2"[Title/Abstract] OR "wuhan coronavirus"[Title/Abstract]
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#5	"prevalence"[Title/Abstract] OR "impact"[Title/Abstract] OR "rate of infection"[Title/Abstract] OR "mortality"[Title/Abstract] OR "death"[Title/Abstract] OR "severity"[Title/Abstract] OR "hospitalization"[Title/Abstract] OR "ICU admission"[Title/Abstract] OR "mechanical ventilation"[Title/Abstract]
#6	#1 OR #3
#7	#2 OR #4
#8	#5 AND #6 AND #7

Inclusion criteria

Only observational studies (cohort, case-control and cross-sectional studies) that focused on adult peoples with disabilities (aged over 18 years) and investigate the association between severity, hospitalization, ICU admission and need for mechanical ventilation, hospital stay, mortality, other complications and long-term effects due to COVID-19 will be included. The following types of studies will be excluded: (1) studies that included infants and children; (2) studies with very small sample size; (3) studies that did not have enough statistical information to be extracted; and (4) descriptive reviews, randomized controlled trials, systematic review, meta-analysis, opinion, editorial, comments, and conference abstracts will be excluded. Excluded studies will be documented with reasons for their exclusion. Only full text published studies in English language will be included.

Outcome measures

The primary outcome measures will be the risk ratio for COVID-19 severity and mortality in people with disabilities. Secondary outcome measures will include rate of hospitalization, ICU admission and the need for mechanical ventilation, viral load, hospital stay and others variables where data are available.

Data extraction

Two reviewers (AAS and AWT) will initially screen titles and abstracts of all identified articles for eligibility. After initially screening articles for inclusion based on titles and abstracts, full-text articles will be screened. Disagreements will be resolved by discussion or a third reviewer (AAH) will be consulted in order to reach a consensus. We will develop a standard data extraction form and use it to extract data to reflect the characteristics of each included study. The included studies might vary in their classification of COVID-19 disease severity, ranging from mild, moderate, severe, to critical severe. We will categorize mild and moderate cases into the non-severe group and severe and critical severe cases into the severe group.[12] We will extract the following information: year of publication, date of the study, type of study, the sample size of participant, severity and mortality of COVID-19, rates of hospitalization and other relevant clinical symptoms and laboratory findings.

Methodological quality assessment

Two reviewers (AAS and AAH) will independently assess the risk of bias of the included studies using the Newcastle-Ottawa Scale (NOS).[20] NOS scale rates observational studies based on 3 parameters: selection, comparability between the exposed and unexposed groups, and exposure/outcome assessment. the scale assigns a maximum of 4 stars for selection, 2 stars for comparability, and 3 stars for exposure/outcome assessment. Studies with less than 5 stars were considered low quality, 5–7 stars of moderate quality, and more than 7 stars of high quality.[9] Only studies with moderate and above quality score will be included in this systematic review and meta-analysis. When conflicts related to bias scores arise, the final decision will be taken by a consensus.

Data synthesis

Review Manager V.5.4 (Cochrane Collaboration) and Stata version 16.0 (STATA Corporation, College Station, TX, USA) software will be used to conduct the meta-analysis. We will calculate pooled estimates of odds ratio (OR) with 95% confidence interval (CI) by the generic inverse variance method. Heterogeneity among included studies will be assessed using the I^2 test. First a fixed-effect model will be used for data analysis. If $I^2 > 0.5$ or $p < 0.1$ it is considered that there is a significant heterogeneity among the included studies,[21] and random-effect model with the inverse variance method will be used in this case. To determine the source of heterogeneity sensitivity analysis will be conducted by excluding studies one by one. Subgroup analyses will be performed on age, gender, type of disability and other variables depending on the data available. Publication bias across studies will be examined using funnel plot method, Egger's test and Begg's test.[22] If the funnel plot is symmetrical and the P value of Egger's and Begg's tests are >0.05, no significant publication bias will be considered to exist in the meta-analysis.[11] If publication bias is found, a trim and fill analysis will be used to evaluate the number of missing studies and recalculate the pooled odds ratio with the addition of those missing hypothetical studies.

Patient and public involvement

There was no patient or public involvement in the study.

Ethics and dissemination

Ethics approval and informed consent are not required as this study is a systematic review which only involve the use of previously published data and does not include any patient. The final results

of this systematic review and meta-analysis will be published in a peer-reviewed journal and presented at relevant conferences and events.

Contributors: All authors have made significant contributions to this study protocol. AAS developed the research question, wrote the first draft, designed the search strategy, and edited and approved the final version of the manuscript. AAH revised the search strategy of databases, developed the data extraction form, and edited and approved the final version of the manuscript. AWT revised the data extraction form and edited and approved the final version of the manuscript.

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Competing interests: No conflicts of interest to disclose.

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Figure Legends:

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow chart

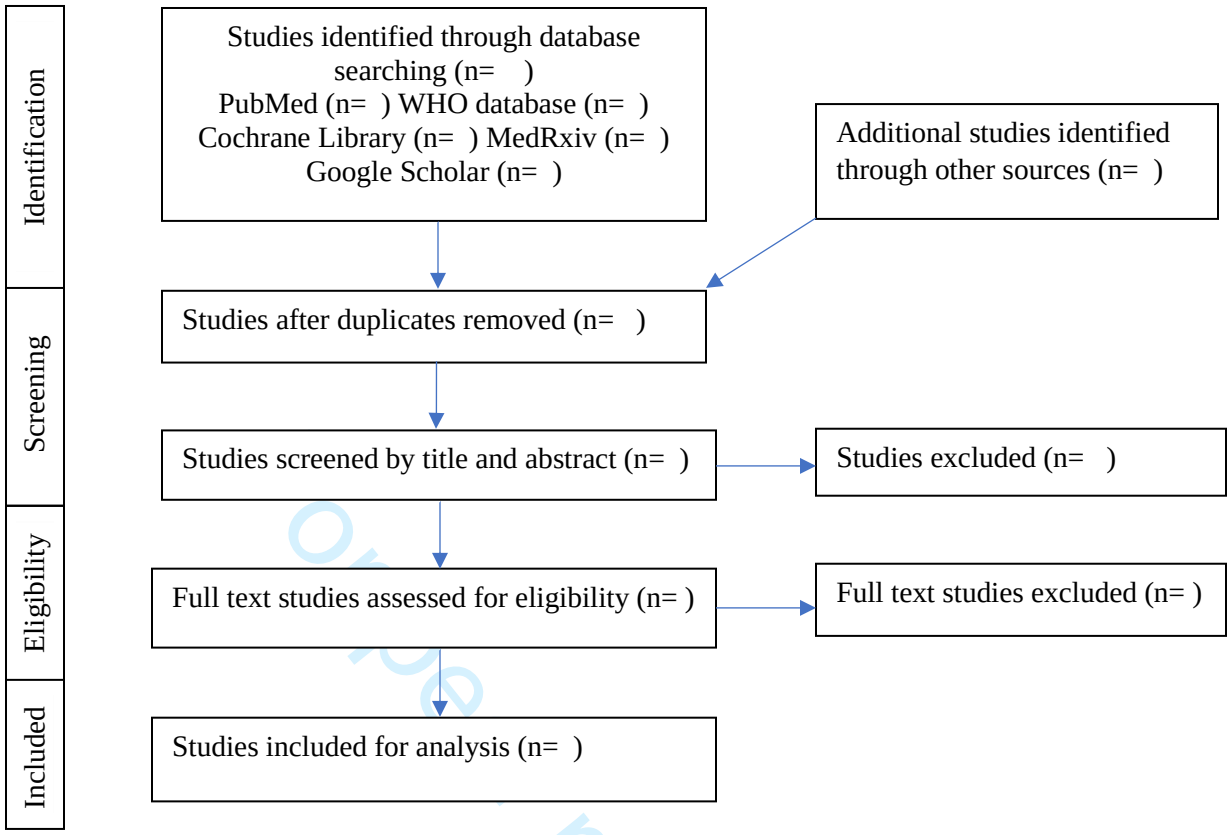

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow chart

Supplementary file 1: Search string for HINARI, ScienceDirect, PEDro, Cochrane Library, MedRxiv and Google Scholar databases

Search number	Search term
#1	COVID-19 OR Coronavirus disease 2019 OR SARS CoV-2
#2	disabled persons OR Handicapped OR people with disabilities OR persons with disability OR physically handicapped OR physically disabled OR physically challenged OR amputees OR mentally ill persons OR persons with mental disabilities OR psychosocial disability OR intellectual disability OR developmental disability OR autism OR autism spectrum disorder OR down syndrome OR fragile x syndrome OR sensory disability OR visual impairment OR hearing impairments OR physical disability OR cerebral palsy OR multiple sclerosis OR absence of limb OR deformities of limbs OR mental disability OR neurologic disability OR schizophrenia OR obsessive-compulsive disorder OR bipolar disorder OR Alzheimer's disease OR Parkinson's disease OR epilepsy
#3	#1 AND #2
#4	prevalence OR rate of infection OR mortality OR death OR severity OR case fatality OR hospitalization OR ICU admission OR mechanical ventilation OR effect OR impact OR long-term impact OR complication OR sequela
#5	#3 AND #4
#6	Limit to December, 2019 to date
#7	Limit to Humans
#8	Limit to observational studies
#9	Limit to cohort OR case-control OR cross-sectional studies
#10	#5 AND #6 OR #7 OR #8 OR #9

Reporting checklist for protocol of a systematic review and meta-analysis.

Based on the PRISMA-P guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA-P reporting guidelines, and cite them as:

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Page Number
Title			
Identification	#1a	Identify the report as a protocol of a systematic review	1
Update	#1b	If the protocol is for an update of a previous systematic review, identify as such	n/a

Registration			
	#2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors			
Contact	#3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contribution	#3b	Describe contributions of protocol authors and identify the guarantor of the review	7
Amendments			
	#4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support			
Sources	#5a	Indicate sources of financial or other support for the review	7
Sponsor	#5b	Provide name for the review funder and / or sponsor	7
Role of sponsor or funder	#5c	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	7
Introduction			
Rationale	#6	Describe the rationale for the review in the context of what is	3

		already known	
Objectives	#7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	3-4
Methods			
Eligibility criteria	#8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	4
Information sources	#9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	#10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5, Table 1.
Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6
Study records - selection process	#11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	4
Study records - data collection	#11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any	5

process		processes for obtaining and confirming data from investigators	
Data items	#12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	n/a
Outcomes and prioritization	#13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5
Risk of bias in individual studies	#14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	6
Data synthesis	#15a	Describe criteria under which study data will be quantitatively synthesised	6
Data synthesis	#15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I2, Kendall's τ)	6
Data synthesis	#15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	n/a
Data synthesis	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned	n/a-.
Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within	7

		studies)	
Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	6

Notes:

- 4: n/a- this is a new protocol
- 15d: n/a-quantitative analysis is possible. The PRISMA-P elaboration and explanation paper is distributed under the terms of the Creative Commons Attribution License CC-BY. This checklist was completed on 20. January 2022 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai