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Demographic factors and COVID-19: a rapid and living systematic review and meta-analysis

Anique Atherley, Raissa Derckx, Janna Dijkstra, Gregor Franssen, Stevie Hendriks, Shahab Jolani, Bart Pijls, Anke Richters, Annemarie Venemans, Saurabh Zalpuri, Maurice Zeegers

Citation

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Review question

What is the association between demographic factors* and COVID-19 in:
1) patients diagnosed with COVID-19 compared to patients not diagnosed with COVID-19?
2) COVID-19 patients admitted to hospital compared to COVID-19 patients not admitted to hospital?
3) Patients with severe COVID-19 (clinical / radiological) compared to patients with non-severe COVID-19?
4) COVID-19 patients admitted to ICU compared to COVID-19 patients not admitted to ICU?
5) COVID-19 patients who died compared to COVID-19 patients who survived?
*demographic factors include: age, sex, social economic status (education level), pregnancy and ethnicity.
Rationale for the rapid and living systematic review design: in the midst of a pandemic there is an urgent need for the most up-to-date evidence while maintaining scientific rigor and quality. Additionally, studies relevant for these research questions will likely be continuously published in the foreseeable future. Moreover, traditional systematic reviews risk becoming rapidly outdated when new evidence is published almost on a daily basis and it is not an option to wait untill the pandemic is over to publish a systematic review on the full body of evidence. Hence a rapid systematic review that is continuously updated (aka living) is necessary.

Searches

The search strategy will be devised with an information specialist and the following databases will be searched from 2019-12 onwards: PubMed, EMBASE and Web of Science. Additionally, EPPI Centre (COVID-19: a living systematic map of the evidence) will be consulted.
We will also search preprint repositories medRxiv and bioRxiv from 2019-12 onwards.
No language restrictions will be applied during the search strategy. Studies reported in languages spoken by the research team will be included. These are at least English, Dutch, German, French and Russian. Studies published in any other language will be excluded and listed seperately in the appendix.

Types of study to be included

Studies that provide information on the 5 research questions mentioned above.
Inclusion criteria:
1) Human study on COVID-19 or SARS-CoV-2 coronavirus
2) Comparison of patients diagnosed with COVID-19 with patients not diagnosed with COVID-19 regarding age, sex, social economic status, pregnancy or ethnicity
3) Comparison of COVID-19 patients admitted to hospital to COVID-19 patients not admitted to hospital regarding age, sex, social economic status, pregnancy or ethnicity
4) Comparison of patients with severe COVID-19 (clinically / radiologically) to patients with non-severe COVID-19 regarding age, sex, social economic status, pregnancy or ethnicity
5) Comparison of COVID-19 patients admitted to ICU to COVID-19 patients not admitted to ICU regarding age, sex, social economic status, pregnancy or ethnicity
6) Comparison of COVID-19 patients who died to COVID-19 patients whu survived, regarding age, sex, social economic status, pregnancy or ethnicity

Exclusion criteria:
1) No reporting/evaluation of demographic factors (age, sex, social economic status, pregnancy or ethnicity)
2) No comparison of diagnosis-positive versus diagnosis-negative, admitted to hospital versus not admitted to hospital, severe COVID-19 versus not severe COVID-19, admitted to ICU versus not admitted to ICU, deaths versus alive

Condition or domain being studied
COVID-19 or the disease caused by SARS-CoV-2 coronavirus.

Participants/population
Patients or individuals subjected to diagnosis of COVID-19.

Intervention(s), exposure(s)
The exposure is COVID-19 or the disease caused by the SARS-CoV-2 coronavirus. As cases we consider:
1) patients diagnosed with COVID-19
2) COVID-19 patients admitted to hospital
3) COVID-19 patients with severe COVID-19 (clinically / radiologically)
4) COVID-19 patients admitted to the ICU
5) COVID-19 patients who died
demographic factors for the analysis include age, sex, social economic status (education level), pregnancy and ethnicity.

Comparator(s)/control
As the controls we consider:
1) patients not diagnosed with COVID-19
2) COVID-19 patients not admitted to hospital
3) COVID-19 patients with non-severe COVID-19 (clinically / radiologically)
4) COVID-19 patients not admitted to ICU
5 COVID-19 patients who survived

Main outcome(s)
1) COVID-19 diagnosis
2) hospital admittance due to COVID-19
3) severity of COVID-19 (clinically / radiologically)
4) ICU admittance due to COVID-19
5) mortality as a result of COVID-19

* Measures of effect

These outcomes are expressed as the number of patients or individuals for each outcome or the ratio of the probabilities of the 5 outcomes between the exposed and unexposed groups regarding demographic factors, mentioned above, expressed as Relative Risk, Odds Ratio, Hazard Ratio or Risk Difference.

Additional outcome(s)
None.

* Measures of effect

Not applicable.

Data extraction (selection and coding)
For this rapid and living systematic review design we consider two phases which may alternate periodically when new evidence becomes available: rapid phase and quality assurance phase.
During the rapid phase emphasis is put on timely availability of up-to-date analyses, so one reviewer (from a pool of reviewers) will perform study selection and data extraction. During the quality assurance phase, a

second reviewer (from a pool of reviewers) will re-do the full study selection procedure. Both reviewers will record their findings in an electronic database. Any disagreements will be resolved by either consensus or by consulting a referee.
During the rapid phase one reviewer (from a pool of reviewers) will extract data from included studies regarding the outcomes, patient demographics, and study characteristics. During the quality assurance phase, a second reviewer (from a pool of reviewers) will re-do the data extraction for at least 20 studies (randomly selected). Both reviewers will record their findings in an electronic database. Any disagreements will be resolved by either consensus or by consulting a referee. In case the data extraction from the second reviewer leads to more than 10% change in the results from the meta-analysis, the second reviewer will re-do the whole data extraction.

Risk of bias (quality) assessment

The risk of bias of the included studies will be appraised by one reviewer (from a pool of reviewers) during the rapid phase using the Newcastle Ottawa Scale (NOS) http:/www.ohri.ca/programs/clinical_epidemiology/oxford.asp. During the quality assurance phase, a second reviewer (from a pool of reviewers) will re-do the risk of bias assessment for at least 20 studies (randomly selected). Both reviewers will record their findings in an electronic database. Any disagreements will be resolved by either consensus or by consulting a referee. In case the risk of bias assessment from the second reviewer leads to a different quality score in more than 10% of the studies, the second reviewer will re-do the whole risk of bias assessment.

Strategy for data synthesis

The data from the included studies will be pooled in a meta-analysis with the random effects model according to DerSimonian and Laird to determine the pooled effect sizes with corresponding 95% confidence intervals and (in case of heterogeneity) corresponding 95% prediction intervals. The amount of statistical heterogeneity will be assessed through visual inspection of the Forest plots and by calculating the $?^2$ statistics and I^2 statistics. In case of statistical heterogeneity and if data allow, potential sources of statistical heterogeneity will be explored through subgroup analyses (e.g. geographical region/countries and items from NOS) and with random effects meta-regression (e.g. study size, inclusion period or publication data).
To assess for publication bias we will construct a funnel plot. In case of asymmetry in the funnel plot, a trim-and-fill method and cumulative meta-analyses will be used to explore the magnitude and direction of publication bias.

Analysis of subgroups or subsets

See also strategy for data synthesis. Subgroup analyses will be performed, if data permit, on pre-defined factors:
* geographical region/country\
* items from NOS (separately, not total score)
* study size
* start inclusion period
* publication date
* diagnostic modality (e.g. PCR test, CT signs, clinical symptoms and their combinations that led to the diagnosis of COVID-19)
* clinical setting (e.g. nursing home, home, hospital, GP cohort)
If considered appropriate sensitivity analyses will explore the effect of other non pre-defined items/factors. These will be labellled as "non pre-defined" in the results.

Contact details for further information

Dr. Bart G Pijls
b.g.c.w.pijls@lumc.nl

Organisational affiliation of the review

Maastricht University, the Netherlands

Review team members and their organisational affiliations

Dr Anique Atherley. School of Health Professions Education, Dept of Educational Research and

Development, Maastricht University
Ms Raissa Derckx. Care and Public Health Research Institute (CAPHRI), Dept of General Practice, Maastricht University
Ms Janna Dijkstra. Amsterdam University Medical Centers, location VUmc
Mr Gregor Franssen. Maastricht University Library
Ms Stevie Hendriks. School of Mental Health and Neuroscience (MNeNS), Maastricht University
Dr Shahab Jolani. Maastricht University, Dept of Methodology and Statistics
Dr Bart Pijls. Leiden University Medical Center, Dept of Orthopaedics
Dr Anke Richters. The Netherlands Comprehensive Cancer Organisation, Dept of Research and Development
Dr Annemarie Venemans. De Onderzoekerij
Dr Saurabh Zalpuri. Real World Evidence, UCB Pharmaceutical BV
Dr Maurice Zeegers. Care and Public Health Research Institute (CAPHRI), Maastricht University

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Review Ongoing

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Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

20 April 2020