Depression and anxiety among children and adolescents during the COVID-19 pandemic in Europe: A systematic review protocol

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Abstract

Some studies point to a high mental health burden among children and adolescents (CA) during the COVID-19 pandemic, particularly concerning depression and anxiety (DA). However, the quality of existing studies and some results are heterogeneous. Research gaps exist regarding (1) a high-quality summarizing overview on studies with (2) a pre-pandemic baseline on the impact of the COVID-19 pandemic on DA among CA in Europe. Therefore, the planned systematic review (SR) aims to close these gaps.

SR was registered in the Prospective Register of Systematic Reviews (PROSPERO) and the protocol was prepared in accordance to the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) statement. Search strategy was peer reviewed. Systematic search was conducted in six databases (MEDLINE, EMBASE, PsycINFO, Cochrane Central Register of Controlled Trials, Web of Science and WHO COVID-19 database). Risk of bias (RoB) will be assessed using the RoB instrument for non-randomized studies of exposures. Certainty of evidence will be evaluated by using the GRADE approach adapted to the use of non-randomized studies. Also, subgroup analysis, sensitivity analysis, and publication bias will be performed.

Results of this SR could contribute to determine the actual overall prevalence of DA among CA in European countries with an expert opinion on the clinical relevance and extrapolation of DA in CA in the next years. In addition, it aims identifying geographic and pandemic-policy differences and designate particularly vulnerable risk groups within European CA.

What Is Known

- Global and primary studies point to the COVID-19 pandemic impacting depression and anxiety among children and adolescents.

What Is New

- Addressing the research gap regarding the impact of the COVID-19 pandemic on depression and anxiety among children and adolescent in Europe compared to a pre-pandemic baseline with a high-quality systematic review.
- Effect pooling within particular European countries and comparison among them.
- Outline clinical relevance and extrapolation of DA in CA in the next years.
- Stratified analyses regarding relevant demographic, social status and methodological determinants.

Background

The COVID-19 pandemic affects many public health (PH) fields. Besides disease rates, persistent symptoms (Long-COVID) and death, impacts on mental health aspects are essential with regard to short-

term and long-term well-being [1]. To keep incidence rates as low as possible, governments used various combinations of social isolation strategies. However, compared to adults, children and adolescents (CA) represent a particularly vulnerable group and tend to be affected differently by the pandemic and social distancing policies. The short-term health effects of COVID-19 infections on CA without comorbidities seemed to generally be mild, e.g. clinically mild disease or asymptomatically infection [2]. However, a growing number of studies point to a high mental health burden among the youth during the pandemic, particularly regarding depression and anxiety (DA) [3].

In studies of earlier pandemics and disease-related quarantine, associations between loneliness and isolation with mental health problems such as DA are already well described in CA [4, 5]. Also, according to UNICEF estimates, the prevalence of mental disorders for boys and girls aged 10–19 in Europe was 16.3% in 2019; thus, DA were the most common mental health disorders and accounted for 55% within CA mental disorders [5].

Within the ongoing COVID-19 pandemic, the number of primary studies on the effects of the pandemic on DA among CA is rapidly increasing. Up to now existing systematic reviews primarily focus on the general population [6], the global prevalence of DA among CA [3] or the situation in China [7]. So far, two research gaps exist: First, regarding methodologically high-quality analysis e.g. considering a pre-pandemic baseline. Second, regarding the impact of the COVID-19 pandemic on DA among CA in European countries, taking pandemic-specific national context variables into account. Thereby, it remains unclear which vulnerable groups exist among CA in the European context, which clinical relevance a changed DA prevalence may have, and which influence certain determinants could have on the DA in CA.

As mental health is an essential predictor for health over the life course of CA [1], a comprehensive, systematic and differentiated analysis of the COVID-19 impact on DA among CA in Europe is of particular PH interest.

Therefore, the planned SR aims to

1. Estimate the change in overall prevalence of DA among CA in Europe before versus during the COVID-19 pandemic.
2. Conduct an effect pooling within particular European countries and comparison with other European countries (a quasi-experimental design), if possible.
3. Outline the clinical relevance of the available results and extrapolation of DA in CA in the next years, if possible.
4. Perform stratified analyses regarding relevant factors: demographic (e.g. age, sex), social status (e.g. education) and methodological (e.g. pandemic time point, study quality) determinants, if possible.

In this protocol of the planned SR, the used methods will be described.

Materials And Methods

The SR was registered on the International Prospective Register of SR (PROSPERO) (CRD42022303714) (**Appendix 1**). This protocol is prepared in accordance with the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) statement [8] (**Appendix 2**); the PROSPERO record will be updated regularly.

The final SR will be conducted according to updated PRISMA statement [9] and will follow the guidelines of the actual Cochrane Handbook for SR, if applicable [10].

Eligibility criteria and information sources

Based on the examination of an environmental exposure, namely the COVID-19 pandemic, the research question was formulated within a Population-Exposure-Comparison-Outcome (PECO) scheme [11]:

- **P**opulation: General population ≤19 years in Europe
- **E**xposure: COVID-19 pandemic
- **C**omparison: Pre-pandemic baseline
- **O**utcome: Depression or anxiety

The eligibility criteria were conducted in accordance to the PECO scheme and are presented in Table 1. Also, further categories were defined, e.g. effect measure, study design, language, time frame and publication status.

The search plan includes the following databases: MEDLINE (Pubmed), EMBASE, PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science and WHO COVID-19 database (also including pre-prints). Also, study registries (e.g. PROSPERO), relevant grey literature (e.g. government reports), related articles, reference lists of included articles and previous published reviews will be screened. Translating the research question into a search string was performed in accordance with the guideline for Peer Review of Electronic Search Strategies (PRESS) [12] and with the use of validated or recommended search filters where possible. The search strategy was peer reviewed before the searches were run by an expert in conducting SR in health sciences according to the evidence-based checklist PRESS Evidence-Based Checklist [12] to ensure a high-quality search strategies (search submission and peer review assessment are attached in **Appendix 3 and 4**). The draft search strategy for Pubmed is presented in **Appendix 5**.

The literature search was performed on March 18, 2022. Study selection will be conducted in three steps: (1) duplicates removal; (2) screening at title and abstract level; and (3) screening the full text. Several publications with the equal or similar study population will be considered once; duplicates with e.g. smaller sample sizes will be excluded. Any discrepancies between the two reviewers will be discussed and, if necessary, resolved by a third author. The reasons for study exclusion in step 3 will be reported in the Appendix of the final study. All screening procedures will be presented using the PRISMA flow diagram [9].

Data extraction

Data extraction will be conducted by two authors using specially developed (pilot tested) tabular data collection forms [10]. Any discrepancies between the two reviewers will be discussed extensively and, if necessary, resolved by a third author.

Risk of bias assessment

The risk of bias (RoB) will be assessed using the RoB instrument for non-randomized studies of exposures [13]. This instrument contains seven RoB items; the defined criteria for each category to assess the included studies will be described in the Appendix of the final study. Judgments for each RoB item and the overall study-judgement could be: “Low RoB”, “Moderate RoB”, “Serious RoB”, or “Critical RoB”.

The certainty of evidence for each outcome will be evaluated by using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach adapted to the use of non-randomized studies [14]. GRADE assessments are determined through eight domains for study downgrading or upgrading. The use of the RoB instrument for non-randomized studies will allow to start at “high” initial certainty of evidence within GRADE [13]. The GRADE approach finally specifies four levels of the certainty for a body of evidence for each outcome: high, moderate, low and very low.

The ratings for RoB and GRADE will be separately conducted by two reviewers, and disagreement will be resolved by discussion with involvement of a third author where necessary.

Data synthesis

In accordance with the Cochrane Handbook [10] the characteristics of each study will first be summarized in a “Characteristics of included studies” table. Second data will be checked which studies are similar enough to be grouped within a comparison by comparing the characteristics across studies and it will be determined what data are available for synthesis. If appropriate, a statistical synthesis (meta-analysis) will be performed using the statistical software *Stata*. If a statistical pooling (meta-analysis) appears to be inappropriate, e.g. if data are highly heterogeneous or if study designs differ considerably, a tabular, graphical or narrative synthesis will be provided [15].

Sensitivity analysis

To determine whether the pooled results are robust, sensitive analysis will be conducted. This includes the repetition of the primary analysis or meta-analysis with different comparison categories [10] e.g. for different study types, different pandemic time points and RoB [13].

Publication bias

The SR will also address RoB due to missing results in a synthesis. Graphical and statistical methods will be used to provide information about the extent of missing results. Funnel plots will be generated and visually interpreted for signs of asymmetry, which could indicate that publication bias is present [10].

When at least 10 studies of different sample size will be included in meta-analysis, statistical tests will also be used to test for funnel plot asymmetry [10].

Conclusion

This protocol aims to provide a description of the approach and used methods of the SR addressing the real impact of the COVID-19 pandemic on DA among CA in Europe in contrast to the percived impact of many clinical and epidemilogical observations without pre-pandemic baseline. The results of the SR will provide relevant evidence in order to address the gap in the literature with a high-quality methodological approach.

Abbreviations

CA	children and adolescents
COVID-19	coronavirus disease 2019
DA	depression and anxiety
GRADE	Grading of Recommendations Assessment, Development and Evaluation
PECO	Population-Exposure-Comparison-Outcome
PH	public health
PRESS	Peer Review of Electronic Search Strategies
PRISMA-P	Preferred Reporting Items for Systematic review and Meta-Analysis Protocols
PROSPERO	Prospective Register of Systematic Reviews
RoB	risk of bias
SR	systematic review

Declarations

Author Contributions

MB is the project leader. HLW and MB formulated the research question with clinical feedback from JMF. All authors contributed to the study conception and design. Material preparation, data collection and analysis were/will be performed by HLW, ID and LP. The first draft of the manuscript was written by HLW and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets used and analyzed during this study are available from the corresponding author on reasonable request.

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Declarations

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Ethics approval

Not applicable.

Consent to participate

Not applicable.

Consent for publication

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

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Table

Table 1. Inclusion and exclusion criteria of the systematic review according to the PECO scheme

Category	Inclusion criteria	Exclusion criteria
Population	General population ≤19 years of both sexes and of any ethnicity in Europe Europe will be defined as European continent according to the definition of WHO Regional Office for Europe [16]	Studies with population samples with >19 years or mixed population samples of children, adolescents and/or adults Studies with any population group outside of Europe Samples of children with preexisting psychiatric diagnoses Countries that are not included in the WHO overview [16]
Exposure	Data collection within Covid-19 pandemic	Previous pandemics Studies that analyzed depression and anxiety due to the use of alcohol or other drugs
Comparison	Pre-pandemic baseline (numerically recorded)	No comparison Comparisons of two time points within the Covid-19 pandemic
Outcome	Depression or anxiety, based on self-reports or (validated) measurements	Other outcomes
Effect measures	All effect measures	-
Study design	All study designs	-
Language	English, German	Other languages
Time frame	1.11.2019 – 18.3.2022	Other time frames
Publication status	Published studies, grey literature, pre-prints	Other publication status
Species	Human studies	Animals studies

Supplementary Files

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- 20220502AppendixProtocolCovid19MentalHealthChildAdol.docx