Systematic Review Process

CDC-led investigations of underlying medical conditions

Updated Feb. 15, 2022

Since May 2021, CDC conducted systematic reviews of evidence about associations between various underlying conditions and severe COVID-19. These reviews are ongoing. As we complete a review and new information becomes available, we will update the list of underlying conditions that are associated with higher risk of severe infection. CDC-conducted systematic reviews prioritizing topics that were not reviewed at the time that systematic reviews began. The information below is provided to describe the methods used in the Science Brief.

Methods

The aim of these reviews is to identify and synthesize the best available evidence on the associations between various underlying conditions and severe COVID-19 to update the CDC's list of underlying conditions and enable the creation of an evidence-based resource page with more rigorous information.

1 Literature Search

A list of search terms was developed to identify the literature most relevant to each population, exposure, comparator, and outcome-based (PECO) question. Clinical experts and library scientists were consulted to develop a robust list of search terms for each relevant condition. These terms were then incorporated into search strategies, and these searches were performed in OVID (a search engine for peer-reviewed articles) using the COVID-19 filter from the end of the previous literature search (December 2020). In the cases of new underlying conditions of interest, the searches are performed using the OVID COVID-19 filter from November 2019 to present.

The detailed search strategies for identifying primary literature and the search results are provided in each systematic review summary of findings. Subject matter experts supplemented the literature search results by recommending relevant references published before December 2020. References were included if retrieved by the literature searches and reported exposures and outcomes relevant to these reviews.

More details on each summary of findings: Scientific Evidence for Conditions Associated with Higher Risk for Severe COVID-19

2 Study Selection

Titles and abstracts from references were screened by dual review, and reviewers are indicated in each summary of findings for each relevant condition. Full-text articles were retrieved if they were:

1. Relevant to the PECO question,
2. Primary research, and
3. Written in English.

The summary of findings present the full list of exclusion criteria for each underlying condition, or condition category. The full texts of selected articles were then screened by two independent reviewers, and disagreements were resolved by discussion. For each review, studies with a comparator group were considered the optimal evidence to answer the PECO question. For underlying conditions and outcomes where this level of evidence was not available, studies with no comparator group, or descriptive evidence was included. Reviewers are indicated in the summary of findings for each relevant condition.

After the full-text screening was complete, a bibliography of the articles selected for inclusion was vetted with subject matter experts. Additional studies suggested by the subject matter experts were screened for inclusion as described above. The results of the study selection process are depicted in each summary of findings.

3 Data Extraction

Methodologic data and results of relevant outcomes from the studies meeting inclusion criteria were extracted into standardized evidence tables. Data and analyses were extracted as presented in the studies. For the purposes of this review, statistical significance was defined as p-value less than 0.05 ($p < 0.05$).

4 Internal Validity Assessment

The internal validity associated with each study was assessed using a tool developed by CDC's Division of Healthcare Quality Promotion. This tool contains questions to guide the identification of systematic bias within the evidence. Internal validity assessment scores were recorded in the evidence tables. Each summary of findings includes the questions used to assess the quality of each study included in this review.

5 Aggregation of the Evidence

The total evidence strength, direction, precision, consistency, and applicability of results were assessed using the available evidence for each potential association. The language used in aggregations was specific to the strength and direction of the evidence. The word "indicated" is used when results were overwhelmingly statistically significant or unified in directionality. The word "suggested" is used when the strength and direction of the results are unified but results do not achieve statistical significance. The overall confidence in the evidence base is reported in the aggregation tables in each summary of findings.

6 Reviewing and Finalizing the Systematic Review

Draft findings, aggregation tables, and evidence tables, are presented to CDC subject matter experts for review and input. Following further revisions, summaries of findings are published on the CDC website. When the evidence indicates or suggests an association between an underlying condition and at least one severe COVID-19 outcome of interest, this underlying condition is added to the list of underlying conditions on the Science Brief page called Scientific Evidence for Conditions Associated with Higher Risk for Severe COVID-19.

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