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England

Protecting and improving the nation's health

# Summary: An Umbrella Review on Cardiovascular Risk Factors, Cardiovascular Disease and COVID-19

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## 1. Purpose

Public Health England (PHE) collaborated with the Liverpool Centre for Cardiovascular Science, University of Liverpool to conduct an umbrella review, which is a review of systematic reviews or meta-analyses.<sup>1</sup> This paper summarises the key findings.

The aim of the umbrella review was to systematically examine the associations between cardiovascular risk factors, cardiovascular disease (CVD), and COVID-19 by addressing the following research questions:

1. What is the association between cardiovascular risk factors and health outcomes, hospitalisation, mechanical ventilation and mortality caused by COVID-19?
2. What is the impact of COVID-19 on cardiovascular health?

The findings from this work may be of interest to policy teams addressing CVD risk factors, and commissioners and providers of CVD prevention and management programmes, i.e. the NHS Health Check (NHS HC) programme. The evidence helps consider the contribution that tackling CVD can make to mitigating against poor COVID-19 health outcomes.

## 2. Method

In November 2020, PHE's Knowledge and Library Services team conducted a search of electronic databases for systematic reviews and meta-analyses relevant to the two research questions. The time limit on the search was from January 1, 2020 to November 5, 2020. Researchers from the University of Liverpool screened the identified papers and carried out a quality assessment using A Measurement Tool to Assess Systematic Reviews (AMSTAR 2). The full methodology can be viewed elsewhere.<sup>1</sup>

## 3. Key Findings

Following the screening process, 84 systematic reviews or meta-analyses met the inclusion criteria. The quality of the identified reviews varied; one review was assessed as high quality, 31 reviews were assessed as moderate quality, and 52 were assessed as low or critically low quality. This low scoring may be due to reviews being conducted rapidly in the time limited period that was used to identify evidence. There was also duplication in the primary studies included in the reviews. Therefore, in this umbrella review, for each of the risk factors the researchers have highlighted the findings from the most recent, largest and highest quality reviews.

## What is the association between cardiovascular risk factors and health outcomes, hospitalisation, mechanical ventilation and mortality caused by COVID-19?

Findings from the most recent, largest and highest quality evidence reviews show:

- **Cardiovascular disease (CVD)** was associated with 3.9 times higher odds of severe COVID-19 and 2.7 times higher odds of mortality, although there were variations in the primary studies definition of CVD.<sup>2</sup>
- **Coronary heart disease** was associated with 2 times higher odds of severe COVID-19,<sup>3</sup> and 3.6 times higher odds of mortality.<sup>4</sup>
- **Hypertension** was associated with 2.6 times higher odds of severe COVID-19 and 2.5 times higher odds of mortality.<sup>2</sup>
- **Diabetes mellitus** was associated with 2.5 times higher odds of severe COVID-19 and 2.1 times higher odds of mortality.<sup>2</sup>
- **Renal disease** was associated with 2.2 times higher odds of severe COVID-19 and 3.1 times higher odds of mortality.<sup>2</sup>
- **Cerebrovascular disease** was associated with 2.8 times higher odds of severe COVID-19<sup>3</sup> and mortality<sup>4</sup>; however, it was not specified if stroke occurred prior to or following infection.
- **Liver disease** was associated with 2.8 times higher odds of mortality,<sup>5</sup> but was not significantly associated with severe COVID-19.<sup>6</sup>
- **Current smoking** was associated with 1.8 times higher risk of severe COVID-19 compared to former smoking and never smoking, but not mortality. Any **smoking history** was associated with 1.3 times higher risk of severe COVID-19 and mortality compared to never smoking.<sup>7</sup>
- **Obesity** was associated with 2.2 times higher odds of mortality,<sup>4</sup> but there was an absence of moderate or high-quality reviews to determine the association between obesity and severe COVID-19.
- **Any cardiovascular risk factor or cardiovascular co-morbidity** was a significant predictor of COVID-19 case fatality rate.<sup>8</sup>
- **Cholesterol levels, arrhythmias, diet, physical activity, alcohol consumption and dementia:** There was an absence of evidence examining these risk factors and outcomes with COVID-19.

Definitions for severe COVID-19 varied between the identified reviews, definitions typically included a composite of key outcomes such as respiratory distress, low oxygen saturation, mechanical ventilation, intensive care unit admission and / or mortality. Where available, the full report details the definitions used for severe COVID-19 in the identified reviews.<sup>1</sup>

## What is the impact of COVID-19 on cardiovascular health?

All of the reviews which examined the impact of COVID-19 on cardiovascular health were completed in the acute in-hospital phase, and the impact of COVID-19 on long-term cardiovascular health was not investigated.

The evidence in the largest moderate quality reviews which examined incident cardiac complications following COVID-19 showed that of those hospitalised with COVID-19:

- 2% experienced acute heart failure<sup>8</sup>

- 4% experienced myocardial infarction (heart attack)<sup>8</sup>
- 10% experienced myocardial injury<sup>8</sup>
- 10% experienced angina<sup>8</sup>
- 18% experienced arrhythmias<sup>8</sup>
- 25% experienced venous thromboembolism<sup>9</sup>
- 19% experienced pulmonary embolism<sup>9</sup>
- 7% experienced deep vein thrombosis.<sup>9</sup>

Acute cardiac injury was associated with 17 times higher odds of mortality.<sup>2</sup>

## 4. Limitations

The search of electronic databases was conducted in November 2020. The COVID-19 evidence base is rapidly emerging and there may be new terms available that were not included in the original search. Due to the pace of research publications over the time period of interest, there was duplication of studies included in the reviews, and the quality of reviews varied with many critically low and low-quality reviews identified. Additionally, as there was a wide range of study designs in the included studies, there was likely high variation in how the comorbidities and risk factors were established. Confounding factors such as age, sex and ethnicity may also impact the results of reviews, but it was not clear in many of the reviews if the studies included in meta-analyses adjusted for these factors.

A quarter of the reviews (n=21) reported that all of the included studies only used data from China. More recent reviews tended to include larger numbers of patients, greater numbers of cohort studies, and data from a wider variety of countries. Therefore, in this umbrella review researchers have highlighted the findings from the most recent, largest and highest quality reviews.

## 5. Conclusions

The evidence shows that pre-existing CVD, coronary heart disease, cerebrovascular disease, high blood pressure, obesity, diabetes, current and former smoking, and renal and liver disease were associated with a higher likelihood of more severe outcomes from COVID-19. Incidence of acute cardiovascular events following hospitalisation with COVID-19 were high and associated with higher odds of severe COVID-19 and mortality with COVID-19.

There was little or no evidence identified at the time of the search in November 2020 to determine associations between alcohol consumption, cholesterol levels, diet, physical activity and dementia with COVID-19 outcomes. Furthermore, no reviews examined the impact of cardiovascular health on long-COVID.

The evidence identified in this umbrella review clearly shows that CVD and COVID-19 severity are interconnected. There is also other evidence that shows both CVD and COVID-19 disproportionately affect the most deprived communities.<sup>10 11</sup> Therefore, prevention programmes which target CVD risk factors, such as the NHS Health Check programme, are more critical than ever in not only detecting and treating CVD risk and reducing health inequalities, but also mitigating against the severity of consequences from COVID-19.

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