**Do blood biomarkers predict prognosis in COVID-19 infection?**

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Protocol for systematic review.

Background: Most people with COVID-19 infection have mild, self-limiting disease. Identifying people who are currently well but likely to go on to develop severe disease is clinically important. Some blood biomarkers are different in people with severe disease compared to those with mild disease, but it is not clear if they can be used to predict deterioration. We therefore plan a review of the current evidence to identify published information about how clinicians can use blood biomarkers to inform prognosis.

Structured question:

Population: Adults (>16 years) infected with COVID-19

Tests of interest: Blood biomarkers, including but not limited to CRP, D-Dimer, Full Bood Count, biochemistry.

Timing/flow: Biomarkers measured before the onset of severe disease, or longitudinal data starting before severe disease, or analyses taking into account severity of disease at measurement

Excluded tests: Radiology (e.g. CT), markers in other media (e.g. cerebro-spinal fluid), observations (e.g. blood pressure)

Outcomes of interest: Disease progression or deterioration, prediction of mild disease vs severe disease. Severe disease including published clinical scores for severity, intensive/critical care admission. ARDS, requirement for mechanical ventilation, supplementary Oxygen, hospital admission for treatment (recognising some admissions were for infection control purposes rather than the need for further healthcare) and death.

Study types excluded: Studies of biomarkers associations with severe disease, but without prognostic information, e.g. not taking into account different severity of disease at the time biomarkers were measured. Studies of biomarkers during recovery.

Screening: Single screening at the abstract and title stage, with double screening for studies where inclusion/exclusion is not immediately clear to the screener

Data extraction: single extraction, using a modified CHARMS checklist including reference standard, participants, outcomes, predictors, sample size, missing data, model development, performance and validation, results: <https://methods.cochrane.org/sites/methods.cochrane.org.prognosis/files/public/uploads/CHARMS%20checklist.pdf>

Bias assessment: We will assess the risk of bias of included studies with the QUIPS Tool (participation, attrition, prediction measures, outcome measures, confounding and analysis/reporting) (<https://annals.org/aim/fullarticle/1650776/assessing-bias-studies-prognostic-factors>)

Data synthesis: We will use random effects meta-analysis to pool results from studies reporting similar outcomes. We will use methods appropriate for the type of measure reported (e.g. for continuous or binary effect size measures) and report these in separate subgroups if different variable types cannot be pooled together. We will tabulate and summarise narratively results of studies that are highly heterogeneous in outcomes or effect size measures, unsuitable for pooling, or not reported in sufficient detail to allow meta-analysis.

Dissemination: Via CEBM website