

## Systematic review

### 1. \* Review title.

Give the working title of the review, for example the one used for obtaining funding. Ideally the title should state succinctly the interventions or exposures being reviewed and the associated health or social problems. Where appropriate, the title should use the PI(E)COS structure to contain information on the Participants, Intervention (or Exposure) and Comparison groups, the Outcomes to be measured and Study designs to be included.

Accuracy of testing for serious bacterial infections in the immunocompromised in ambulatory care: diagnostic accuracy review

### 2. Original language title.

For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

### 3. \* Anticipated or actual start date.

Give the date when the systematic review commenced, or is expected to commence.

15/06/2020

### 4. \* Anticipated completion date.

Give the date by which the review is expected to be completed.

31/10/2020

### 5. \* Stage of review at time of this submission.

Indicate the stage of progress of the review by ticking the relevant Started and Completed boxes. Additional information may be added in the free text box provided.

Please note: Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. Should evidence of incorrect status and/or completion date being supplied at the time of submission come to light, the content of the PROSPERO record will be removed leaving only the title and named contact details and a statement that inaccuracies in the stage of the review date had been identified.

This field should be updated when any amendments are made to a published record and on completion and publication of the review. If this field was pre-populated from the initial screening questions then you are not able to edit it until the record is published.

The review has not yet started: Yes

Review stage	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	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

Provide any other relevant information about the stage of the review here (e.g. Funded proposal, protocol not yet finalised).

### 6. \* Named contact.

The named contact acts as the guarantor for the accuracy of the information presented in the register record.

Julie McLellan

### Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Mrs McLellan

### 7. \* Named contact email.

Give the electronic mail address of the named contact.

julie.mclellan@phc.ox.ac.uk

### 8. Named contact address

Give the full postal address for the named contact.

Department of Primary Care Health Sciences, University of Oxford, Radcliffe Observatory Quarter,  
Woodstock Road, Oxford, OX2 6GG

### 9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

01865 289667

### 10. \* Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

Evidence synthesis working group within NIHR School for Primary Care Research  
University of Oxford

### Organisation web address:

<https://www.spcr.nihr.ac.uk/eswg>

### 11. \* Review team members and their organisational affiliations.

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country are now mandatory fields for each person.**

Mrs Julie McLellan. Nuffield Department of Primary Care Health Sciences, University of Oxford  
Professor Carl Heneghan. Nuffield Department of Primary Care Health Sciences, University of Oxford  
Dr Annette Plüddemann. Nuffield Department of Primary Care Health Sciences, University of Oxford  
Dr Oghenekome Gbinigie. Nuffield Department of Primary Care Health Sciences, University of Oxford

### 12. \* Funding sources/sponsors.

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Include any unique identification numbers assigned to the review by the individuals or bodies listed.

National Institute for Health Research School for Primary Care Research (NIHR SPCR)

### Grant number(s)

Project Number 390

### 13. \* Conflicts of interest.

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

Yes

Julie McLellan reports funding from the NIHR School of Primary Care Research, and occasionally receives expenses for teaching Evidence-Based Medicine from NIHR School of Primary Care Research, during the conduct of the study; and occasionally receives expenses for teaching Evidence-Based Medicine.

Dr Gbinigie's time is funded by the Wellcome Trust.

Dr. Heneghan reports receiving expenses and fees for his media work. He has received expenses from the WHO and holds grant funding from the NIHR, the NIHR School of Primary Care Research, The Wellcome Trust and the WHO. He has received financial remuneration from an asbestos case. He has also received income from the publication of a series of toolkit books published by Blackwells. On occasion, he receives expenses for teaching EBM and is also paid for his GP work in NHS out of hours. CEBM jointly runs the EvidenceLive Conference with the BMJ and the Overdiagnosis Conference with some international partners which are based on a non-profit making model.

#### 14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country are now mandatory fields for each person.**

#### 15. \* Review question.

State the question(s) to be addressed by the review, clearly and precisely. Review questions may be specific or broad. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS where relevant.

Using evidence from observational studies, what is the diagnostic accuracy of symptoms, signs and/or tests for serious bacterial infections in immunocompromised adults, in the ambulatory setting, compared to established reference standards?

#### 16. \* Searches.

State the sources that will be searched. Give the search dates, and any restrictions (e.g. language or publication period). Do NOT enter the full search strategy (it may be provided as a link or attachment.)

Searches will be conducted in multiple electronic databases from inception onwards, including: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science for conference proceedings, dissertations, and theses, World Health Organization International Clinical Trials Registry Platform (ICTRP), ClinicalTrials.gov, and Database of Abstracts of Reviews of Effect (DARE).

Hand searches of the reference lists of relevant publications will also be conducted.

No language restrictions will be applied.

#### 17. URL to search strategy.

Give a link to a published pdf/word document detailing either the search strategy or an example of a search strategy for a specific database if available (including the keywords that will be used in the search strategies), or upload your search strategy. Do NOT provide links to your search results.

[https://www.crd.york.ac.uk/PROSPEROFILES/190362\\_STRATEGY\\_20200604.pdf](https://www.crd.york.ac.uk/PROSPEROFILES/190362_STRATEGY_20200604.pdf)

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Yes I give permission for this file to be made publicly available

#### 18. \* Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

Serious bacterial infections: Sepsis (including bacteraemia), pneumonia (excluding infective exacerbations of COPD and Asthma) and urinary tract infection. Skin and soft tissue infection (including cellulitis), intra-abdominal infection (cholecystitis, appendicitis, diverticulitis and abscesses), bacterial meningitis, bacterial infective endocarditis and active tuberculosis will be excluded.

## PROSPERO

### International prospective register of systematic reviews

#### 19. \* Participants/population.

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

All adults (? 18 years of age) who are immunocompromised. No gender restriction will be applied.

Immunocompromised patients with non-congenital conditions (existing at or before birth or acquired at birth) will be included.

#### 20. \* Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the nature of the interventions or the exposures to be reviewed.

Patient symptoms, signs, and/or tests for predicting serious bacterial infections in ambulatory care.

Ambulatory care will include general practice, hospital outpatient and emergency department settings.

#### 21. \* Comparator(s)/control.

Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Established reference standards, undertaken by a healthcare practitioner, to confirm diagnosis of a serious bacterial infection.

#### 22. \* Types of study to be included.

Give details of the types of study (study designs) eligible for inclusion in the review. If there are no restrictions on the types of study design eligible for inclusion, or certain study types are excluded, this should be stated. The preferred format includes details of both inclusion and exclusion criteria.

Retrospective and prospective observational studies

#### 23. Context.

Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

#### 24. \* Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

Data to enable completion of two by two tables allowing calculation of diagnostic accuracy parameters.

#### \* Measures of effect

Please specify the effect measure(s) for you main outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

Sensitivity and specificity.

## 25. \* Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

None.

## \* Measures of effect

Please specify the effect measure(s) for you additional outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

Not applicable.

## 26. \* Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

The title and abstract of each reference will be reviewed independently by two reviewers, using the predetermined inclusion criteria. Potentially relevant references will be identified. The full text of these references will be obtained and two reviewers will independently select studies to be included in the review. In all cases, disagreements about study inclusion will be resolved by consensus and a third reviewer will be consulted if disagreements persist.

Two reviewers will independently extract information from selected studies into a data extraction sheet. Disagreements will be resolved by discussion, or if necessary with the help of a third reviewer. The following data will be extracted, if available, from the included studies: Study details (author, year, location, research question, design, setting, definition for serious bacterial infection, target condition definition/diagnostic criteria, index test, reference standard, timing of tests, source of funding, author conflicts), participant details (baseline characteristics, number of participants, study inclusion and exclusion criteria), and outcome data (flow of participants through study including losses to follow-up, absolute counts of true positive (TP), false positive (FP), false negative (FN) and true negative (TN) diagnoses, statistical analyses that were performed, including whether all participants were included in analyses, additional summary information).

If there is insufficient or unclear information, and there is an email address provided, the authors will be contacted via email for clarification

## 27. \* Risk of bias (quality) assessment.

Describe the method of assessing risk of bias or quality assessment. State which characteristics of the studies will be assessed and any formal risk of bias tools that will be used.

To assess methodological quality, we will use the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool. Two reviewers will independently assess studies' methodological quality; disagreements will be resolved by discussion, or if necessary, by a third reviewer. The QUADAS-2 tool facilitates assessment of bias in four areas: patient selection; index test; reference standard; flow and timing; and also

facilitates assessment of applicability of the studies to the review research question.

### 28. \* Strategy for data synthesis.

Provide details of the planned synthesis including a rationale for the methods selected. This **must not be generic text** but should be **specific to your review** and describe how the proposed analysis will be applied to your data.

Summary tables will detail study information including the patient sample, condition, study design, the test used and test, Review Manager will be used to produce paired forest plots to explore the between-study variability of sensitivity and specificity across the included studies. For each study estimate of sensitivity and specificity, corresponding 95% confidence intervals will be shown to illustrate the uncertainty related to each study estimate.

Meta-analysis will be conducted where possible, but may not be appropriate due paucity of data and/or anticipated high heterogeneity between studies.

### 29. \* Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

If substantial heterogeneity is observed, given sufficient data, we will perform subgroup analysis to further

investigate the immunocompromised patient:

- Chronic inflammatory diseases maintained on immunosuppressive medications
- HIV-infected
- Cancer
- Transplant recipients
- Asplenia or sickle cell

2. Age

3. Study setting

Sensitivity analyses

Where there is sufficient data, sensitivity analyses will be performed to ensure the findings are not sensitive to the quality of the studies, or the definition of the collective terms serious bacterial infections or immunocompromised. Sensitivity analyses will further be considered to remove a study where it uses a clinically weak reference standard. Finally, if there appear to be any outliers in the data, these studies will be removed from the analysis to evaluate the impact on the overall pooled estimates.

### 30. \* Type and method of review.

Select the type of review and the review method from the lists below. Select the health area(s) of interest for

your review.

### Type of review

Cost effectiveness

No

Diagnostic

Yes

Epidemiologic

No

Individual patient data (IPD) meta-analysis

No

Intervention

No

Meta-analysis

No

Methodology

No

Narrative synthesis

No

Network meta-analysis

No

Pre-clinical

No

Prevention

No

Prognostic

No

Prospective meta-analysis (PMA)

No

Review of reviews

No

Service delivery

No

Synthesis of qualitative studies

No

Systematic review

Yes

Other

No

### Health area of the review

Alcohol/substance misuse/abuse

No

Blood and immune system

No

Cancer

No

Cardiovascular

No

Care of the elderly

No



Child health

No

Complementary therapies

No

COVID-19

No

Crime and justice

No

Dental

No

Digestive system

No

Ear, nose and throat

No

Education

No

Endocrine and metabolic disorders

No

Eye disorders

No

General interest

No

Genetics

No

Health inequalities/health equity

No

Infections and infestations

Yes

International development

No

Mental health and behavioural conditions

No

Musculoskeletal

No

Neurological

No

Nursing

No

Obstetrics and gynaecology

No

Oral health

No

Palliative care

No

Perioperative care

No

Physiotherapy

No

Pregnancy and childbirth

No

Public health (including social determinants of health)

## PROSPERO

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No

Rehabilitation

No

Respiratory disorders

No

Service delivery

No

Skin disorders

No

Social care

No

Surgery

No

Tropical Medicine

No

Urological

No

Wounds, injuries and accidents

No

Violence and abuse

No

### 31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.  
English

There is not an English language summary

### 32. \* Country.

Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved.

England

### 33. Other registration details.

Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. (N.B. Registration details for Cochrane protocols will be automatically entered). If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

### 34. Reference and/or URL for published protocol.

Give the citation and link for the published protocol, if there is one

Give the link to the published protocol.

[https://www.crd.york.ac.uk/PROSPEROFILES/190362\\_PROTOCOL\\_20200611.pdf](https://www.crd.york.ac.uk/PROSPEROFILES/190362_PROTOCOL_20200611.pdf)

Alternatively, upload your published protocol to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Yes I give permission for this file to be made publicly available

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Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

#### 35. Dissemination plans.

Give brief details of plans for communicating essential messages from the review to the appropriate audiences.

#### Do you intend to publish the review on completion?

Yes

#### 36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords will help users find the review in the Register (the words do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

~~Serious bacterial infection~~

Diagnostic accuracy review

Ambulatory care

#### 37. Details of any existing review of the same topic by the same authors.

Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

#### 38. \* Current review status.

Review status should be updated when the review is completed and when it is published. For new registrations the review must be Ongoing.

Please provide anticipated publication date

Review\_Ongoing

#### 39. Any additional information.

Provide any other information the review team feel is relevant to the registration of the review.

#### 40. Details of final report/publication(s) or preprints if available.

This field should be left empty until details of the completed review are available OR you have a link to a preprint.

Give the link to the published review.