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.

Whole blood mycobacterial growth assays for assessing human tuberculosis susceptibility: a systematic review and meta-analysis

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.

01/09/2019

4. * Anticipated completion date.

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

20/08/2020

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: No

Review stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	Yes	No
Data extraction	No	No
Risk of bias (quality) assessment	Yes	No
Data analysis	Yes	No

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

We have piloted of these activities in an exploratory manner. After PROSPERO registration we will formally and definitively commence all of these activities, aiming to complete them within 2 months.

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6. * Named contact.

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

Carlton Evans

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

Carlton

7. * Named contact email.

Give the electronic mail address of the named contact.

Carlton.Evans@ifhad.org

8. Named contact address

Give the full postal address for the named contact.

Dept Infectious Disease, Commonwealth Building level 8, Imperial College London Hammersmith Hospital campus, 150 Du Cane Rd, London W12 0NN, UK

9. Named contact phone number.

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

+51 997942800

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.

Imperial College London, UK

Organisation web address:

https://www.imperial.ac.uk/people/carlton.evans

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.**

Professor Carlton Evans. Imperial College London
Mr Jeroen Bok. University Medical Centre Utrecht
Dr Regina Hofland. University Medical Center Utrecht

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.

The Wellcome Trust (awards 057434/Z/99/Z, 070005/Z/02/Z, 078340/Z/05/Z, 105788/Z/14/Z and 201251/Z/16/Z); DFID-CSCF; the Joint Global Health Trials consortium (MRC, DFID, & Wellcome Trust award MR/K007467/1); the STOP TB partnership's TB REACH initiative funded by the Government of Canada and the Bill & Melinda Gates Foundation (awards W5_PER_CDT1_PRISMA and OPP1118545); and the charity IFHAD: Innovation For Health And Development

Grant number(s)

057434/Z/99/Z, 070005/Z/02/Z, 078340/Z/05/Z, 105788/Z/14/Z, 201251/Z/16/Z); MR/K007467/1; W5_PER_CDT1_prisma; OPP1118545

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.

None

None

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.

In whole blood mycobacterial growth assays (WBMGA), mycobacterial growth in vitro in blood is quantified over 72-96 hours, assuming that this predicts tuberculosis susceptibility in vivo. Our objective was to assess

the evidence for this assumption.

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.)

PubMed and EMBASE

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.

http://www.ifhad.org/data-repository/

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.

Tuberculosis susceptibility

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.

Any people at risk of tuberculosis infection or disease, without exclusion

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

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

Any people who have a whole blood mycobacterial growth assays (WBMGA), without exclusion

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.

Any people without or before or after the potential tuberculosis risk factor, without exclusion

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.

No restriction

23. Context.

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

Not relevant to this study.

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.

Whole blood mycobacterial growth assays (WBMGA) association with human susceptibility to tuberculosis infection or disease

* 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.

Comparing the ratio of whole blood mycobacterial growth assay (WBMGA) results

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

Not applicable

* 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.

Studies will be selected for inclusion as follows: PubMed and EMBASE searched to identify relevant studies using the following search terms: (“mycobacterial” or “mycobacterium” or “mycobacteria” or “tuberculosis” or “BCG”); (“growth inhibition” or “mycobacterial immunity” or “antimycobacterial immunity” or “MGIA”) and (“assay” or “in vitro” or “whole blood”). References cited by these publications searched to find other relevant articles. For inclusion in this study, peer-reviewed, English-language publications will be selected that describe cross-sectional, case-control, or cohort studies using WBMGA to study mycobacterial growth in human blood samples in relation to: risk of TB infection; risk of TB disease; established or possible TB risk factors. All available literature will be studied without the restrictions of language or date.

Data will be extracted as follows: reviewers will independently review potentially relevant publication titles, then abstracts and finally full-text publications for eligibility, with discrepancies being resolved by discussion

and potentially resolved by another reviewer. WBMGA results, study characteristics and methodological characteristics will be extracted from each publication and categorised by factors known to decrease or likely to affect TB susceptibility. Heterogeneity of data will also be assessed.

This will be done and recorded using a shared cloud-based spreadsheet that logs all edits and who they made them.

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.

A quality assessment tool from National Heart, Lung, and Blood Institute (NHLBI), leading to an overall rating for the quality of each study of “good”, “fair”, or “poor”: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, leading to an overall rating for the quality of each study of “good”, “fair”, or “poor”

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.

Whole blood mycobacterial growth assays (WBMGA) results presented as statistically significant or not. Additionally, ratios of one study group versus the other calculated for each of the main findings of the publications, representing relative growth, and presented in figures. Meta-analyses pool relative growth ratios of comparable studies calculating the respective weighted means of these ratios, including weighted confidence intervals.

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.

Comparable studies will be analysed as groups. No other subgroup analyses are planned.

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
No

Epidemiologic
No

Individual patient data (IPD) meta-analysis
No

Intervention
No

Meta-analysis
Yes

Methodology
Yes

Narrative synthesis
No

Network meta-analysis
No

Pre-clinical
No

Prevention
No

Prognostic
Yes

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
Yes

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)
No

Rehabilitation
No

Respiratory disorders
Yes

Service delivery
No

Skin disorders
No

Social care

No

Surgery
No

Tropical Medicine
Yes

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 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
Peru

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.

Not applicable

34. Reference and/or URL for published protocol.

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

Not applicable

Give the link to the published protocol.

http://www.ifhad.org/wp-content/uploads/2019/03/WBMGA_review_protocol.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.

No I do not make this file publicly available until the review is complete

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.

Presentation at conferences and publication in an international peer-reviewed open access journal

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.

Tuberculosis; TB; whole blood mycobacterial growth assay; whole blood mycobacterial growth inhibition assay

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.

Not applicable

38. * Current review status.

Review status should be updated when the review is completed and when it is published. For newregistrations 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.

Not applicable

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.