# Systematic review

A list of fields that can be edited in an update can be found here

## 1. * Review title.

Give the title of the review in English

Drug Therapies for Treatment of Idiopathic Pulmonary Fibrosis: Systematic Review, Bayesian Network Meta-analysis and Cost-Effectiveness Analysis

## 2. Original language title.

For reviews in languages other than English, give the title in the original language. This will be displayed with the English language title.

## 3. * Anticipated or actual start date.

Give the date the systematic review started or is expected to start.

26/06/2022

## 4. * Anticipated completion date.

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

31/07/2022

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

**This field uses answers to initial screening questions. It cannot be edited until after registration.**

Tick the boxes to show which review tasks have been started and which have been completed.

Update this field each time any amendments are made to a published record.

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 | 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.

## 6. * Named contact.

The named contact is the guarantor for the accuracy of the information in the register record. This may be any member of the review team.

Jiayi Cai

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

Dr Cai

## 7. * Named contact email.

Give the electronic email address of the named contact.

caijiayi_syphu@163.com

## 8. Named contact address

Give the full institutional/organisational postal address for the named contact.

No.77 Puhe Road, Shenyang, 110122, China.

## 9. Named contact phone number.

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

+8613840063930

## 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.

College of Pharmaceutical Science, China Medical University

## Organisation web address:

## 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 now MUST be entered for each person, unless you are amending a published record.**

Assistant/Associate Professor Jiayi Cai. College of Pharmaceutical Science, China Medical University
Dr Chunyang Zhao. Department of Pharmacy, the First Affiliated Hospital of China Medical University

## 12. * Funding sources/sponsors.

Details of the individuals, organizations, groups, companies or other legal entities who have funded or sponsored the review.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

## Grant number(s)

State the funder, grant or award number and the date of award

## 13. * Conflicts of interest.

List actual or perceived conflicts of interest (financial or academic).

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 must be completed for each person, unless you are amending a published record.**

## 15. * Review question.

State the review question(s) clearly and precisely. 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 or similar where relevant.

We plan to conduct a network meta-analysis cost-effectiveness analysis to compare and rank relative efficacy and safety for treatment of idiopathic pulmonary fibrosis among all available drug therapies, and provide evidence for clinical decision makers which treatment is the cost-effective choice.

## 16. * Searches.

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

To identify eligible RCT, we plan to perform literature searches on MEDLINE, Embase, Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), Chinese National Knowledge Infrastructure (CNKI), ClinicalTrials.gov, World Health Organization International Clinical Trials Registry Platform (WHO ICTRP), and International Standard Randomized Controlled Trial Number (ISRCTN) Registry published from 1 January 1992 to 1 January 2022 (last 30 years), that investigating the efficacy and/or tolerability of drug therapies for treatment of idiopathic pulmonary fibrosis (IPF).

## 17. URL to search strategy.

Upload a file with your search strategy, or an example of a search strategy for a specific database, (including the keywords) in pdf or word format. In doing so you are consenting to the file being made publicly accessible. Or provide a URL or link to the strategy. Do NOT provide links to your search **results**.

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.

Do not make this file publicly available until the review is complete

## 18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied in your systematic review.

Idiopathic Pulmonary Fibrosis

## 19. * Participants/population.

Specify the participants or populations being studied in the review. The preferred format includes details of both inclusion and exclusion criteria.

Subjects are individuals diagnosed with IPF, defined by individual authors in accordance with American Thoracic (ATS)/European Respiratory Society (ERS), without restrictions on sex, age and ethnicity.

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

Give full and clear descriptions or definitions of the interventions or the exposures to be reviewed. The preferred format includes details of both inclusion and exclusion criteria.

Interventions of interest for treatment of IPF include: ambrisentan; bosentan; colchicine; cyclophosphamide; etanercept; imatinib; interferon-? (INF-?); macitentan; N-acetylcysteine (NAC); nintedanib; pamrevlumab; pentraxin; pirfenidone; sildenafil; simtuzumab; warfarin; and their combinations when available.

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

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

Placebo, no treatment or usual care.

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

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

RCTs irrespective of design.

## 23. Context.

Give summary details of the setting or 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.

All-cause mortality, acute exacerbation rate, progression of disease, serious adverse events and any adverse events.

### 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.

## 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

Lung function decline, survival analysis index, and health-related quality of life assessments.

### 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.

## 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.

Teams of two reviewers independently screen papers by titles and abstracts for possible inclusion. If either

reviewer considers a study potentially eligible, full text will be retrieved and assessed criteria in duplicate for final inclusion. After pilot testing our standardized form, two authors independently extract and summarize relevant information from main reports and supplementary materials of the enrolled trials, including study characteristics (e.g. first author, year of publication, region, study design and setting, sample size), participant characteristics (e.g. sex ratio, mean age, ethnicity), and treatment characteristics (e.g. intervention and dose, comparator and dose, duration, follow up, outcome parameters reported), etc.

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

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

Risk of bias of randomized trials is planed to be appraised in seven specified domains by two independent investigator with the Cochrane Collaboration' tool. Each domain is scored as high risk, some concerns or low risk.

## 28. * Strategy for data synthesis.

Describe the methods you plan to use to synthesise data. This **must not be generic text** but should be **specific to your review** and describe how the proposed approach will be applied to your data. If meta-analysis is planned, describe the models to be used, methods to explore statistical heterogeneity, and software package to be used.

Data for pooling are calculated as rate ratio (RR) for dichotomous outcomes, mean difference (MD) for continuous outcomes, and hazard ratio (HR) for survival analysis indexes, with corresponding 95% confidence intervals (CIs). For available direct associations across interventions and outcomes, conventional pairwise random-effects model is imposed. Cochran' Q test and $I^2$ statistic are applied to assess the heterogeneity in treatment effects. Heterogeneity variance is estimated based on restricted maximum likelihood (REML) approach in both direct and indirect comparisons. We plan a Bayesian NMA to simultaneously compare all relevant drug therapies for each parameter, and pooled data are synthesized within random effects models. We plan to appraise the ranking probabilities of drug therapies for treatment of IPF, and offered a relative hierarchy grounded on surface under the cumulative ranking curve (SUCRA). Comparison adjusted funnel plots are planed to examine small study effect bias by visual inspection of asymmetry. Key trial and participant characteristics within treatment comparisons are compared to assess whether effect modifiers are similarly distributed across trials, and to identify potential sources of clinical and methodological heterogeneity. Node-spitting approach and Higgins mode are adopted for evaluating network consistency assumption for primary endpoints.

Data synthesis is conducted using STATA (version15.1, TX, USA), WinBUGS (version1.4.3, Cambridge, UK), Review manager software (RevMan, version5.4, Copenhagen, Denmark) and GRADEprofiler

(version3.6, Hamilton, Canada).

## 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.

Subgroup analysis is not currently planned

## 30. * Type and method of review.

Select the type of review, review method and health area from the lists below.

### Type of review

Cost effectiveness

Yes

Diagnostic

No

Epidemiologic

No

Individual patient data (IPD) meta-analysis

No

Intervention

No

Living systematic review

No

Meta-analysis

No

Methodology

No

Narrative synthesis

No

Network meta-analysis

Yes

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
No

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

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 an English language summary.

## 32. * Country.

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

China

## 33. Other registration details.

Name any other organisation where the systematic review title or protocol is registered (e.g. Campbell, or The Joanna Briggs Institute) together with any unique identification number assigned by them. 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.

If the protocol for this review is published provide details (authors, title and journal details, preferably in Vancouver format)

Add web link to the published protocol.

Or, upload your published protocol here in pdf format. Note that the upload will be 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.

Do you intend to publish the review on completion?

Yes

Give brief details of plans for communicating review findings.?

## 36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords help PROSPERO users find your review (keywords 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.

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

If you are registering an update of an existing review give details of the earlier versions and include a full bibliographic reference, if available.

## 38. * Current review status.

Update review status when the review is completed and when it is published.New registrations must be ongoing so this field is not editable for initial submission.

Please provide anticipated publication date

Review_Ongoing

## 39. Any additional information.

Provide any other information relevant to the registration of this review.

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

Leave empty until publication details are available OR you have a link to a preprint (NOTE: this field is not editable for initial submission). List authors, title and journal details preferably in Vancouver format.

Give the link to the published review or preprint.