PROSPERO International prospective register of systematic reviews

Review title and timescale

1 Review title
Give the working title of the review. This must be in English. Ideally it should state succinctly the interventions or exposures being reviewed and the associated health or social problem being addressed in the review.
What factors predict the severity of neurodevelopmental outcome in infants born very preterm

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.
01/01/2013

4 Anticipated completion date
Give the date by which the review is expected to be completed.
31/12/2014

5 Stage of review at time of this submission
Indicate the stage of progress of the review by ticking the relevant boxes. Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. This field should be updated when any amendments are made to a published record.

The review has not yet started ×

Review stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
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.

Review team details

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

7 Named contact email
Enter the electronic mail address of the named contact.
louise.linsell@npeu.ox.ac.uk

8 Named contact address
Enter the full postal address for the named contact.
National Perinatal Epidemiology Unit (NPEU), Richard Doll Building, Old Road Campus, Headington, Oxford, OX3 7LF

9 Named contact phone number
Enter the telephone number for the named contact, including international dialing code.
01865 617922

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.

National Perinatal Epidemiology Unit (NPEU)

Website address:
https://www.npeu.ox.ac.uk/

11 Review team members and their organisational affiliations
Give the title, first name and last name of all members of the team working directly on the review. Give the organisational affiliations of each member of the review team.

Title	First name	Last name	Affiliation
Ms	Louise	Linsell	National Perinatal Epidemiology Unit (NPEU)
Professor	Jenny	Kurinczuk	National Perinatal Epidemiology Unit (NPEU)
Professor	Neil	Marlow	Institute of Women's Health, University College London
Professor	Joan	Morris	Queen Mary University of London
Dr	Reem	Malouf	National Perinatal Epidemiology Unit (NPEU)

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. Any unique identification numbers assigned to the review by the individuals or bodies listed should be included.
National Institute of Health Research (NIHR)

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.
Are there any actual or potential conflicts of interest?
None known

14 Collaborators
Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

Title	First name	Last name	Organisation details

Review methods

15 Review question(s)
State the question(s) to be addressed / review objectives. Please complete a separate box for each question.
What factors predict the severity of neurodevelopmental outcome in infants born very preterm?

16 Searches
Give details of the sources to be searched, and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.
MEDLINE, EMBASE and PSYCHINFO, all languages and publication date between 1st January 1990 and 26th March 2013.

17 URL to search strategy
If you have one, give the link to your search strategy here. Alternatively you can e-mail this to PROSPERO and we will store and link to it.
http://www.crd.york.ac.uk/PROSPEROFILES/6943_STRATEGY_20140020.pdf

I give permission for this file to be made publicly available
No

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.
Surviving infants born very preterm are at high risk of long term developmental problems, including cerebral palsy,

visual and auditory deficits, impairments in global and executive cognitive function, learning disabilities and behavioural problems. This risk is inversely related to birth weight and gestational age.

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.
Study population were born before 33 weeks gestation and/or had birth weight below 1250g.

20 Intervention(s), exposure(s)
Give full and clear descriptions of the nature of the interventions or the exposures to be reviewed
Multivariable risk prediction of at least one neurodevelopmental outcome assessed after the age of 18 months.

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).
Not applicable.

22 Types of study to be included initially
Give details of the study designs to be included in the review. If there are no restrictions on the types of study design eligible for inclusion, this should be stated.
No restriction.

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

24 Primary outcome(s)
Give the most important outcomes.
To identify risk factors that predict the severity of neurodevelopmental outcome and to assess the strength of evidence that supports this association.

Give information on timing and effect measures, as appropriate.

25 Secondary outcomes
List any additional outcomes that will be addressed. If there are no secondary outcomes enter None.
None.

Give information on timing and effect measures, as appropriate.

26 Data extraction, (selection and coding)
Give the procedure for selecting studies for the review and extracting data, including the number of researchers involved and how discrepancies will be resolved. List the data to be extracted.
Articles identified by the search strategies will be screened on title and abstract by one reviewer for definite exclusions and duplicates. The full text will be retrieved for remaining articles and will be screened by the same reviewer for the following eligibility criteria: 1. Contains original data 2. Study population born after 1st January 1990 3. Study population born before 33 weeks gestation or birth weight below 1250g 4. Study population is not a highly select group, and results can be applied to the general population of very preterm infants 5. An objective of the paper is to develop a multivariable risk prediction model (more than 2 variables) for a neurodevelopmental outcome assessed after the age of 18 months. If the reviewer is unsure of the eligibility of an article, it will be screened independently by a second reviewer and if a decision cannot be reached it will be referred to the rest of the review team. For all articles eligible for inclusion, both reviewers will complete a full data extraction form and risk of bias assessment. The following data will be extracted from each included article: study design, participant setting, centre selection, study location, year of birth, gestational age, birth weight, age at assessment, selection criteria of study population, control group recruited, sample size, completeness of data at follow-up, details of outcomes assessed, number of candidate risk factors assessed, variable selection, treatment of continuous variables, adjustment for confounders, method of analysis, model assumptions checked, missing data analysis, presentation of multivariable model, details of risk factors included in final model, strength of association, statistical validation and clinical validation. The data extraction forms will be cross-validated for discrepancies, and referred to the review team if the two reviewers cannot reach a resolution.

27 Risk of bias (quality) assessment

State whether and how risk of bias will be assessed, how the quality of individual studies will be assessed, and whether and how this will influence the planned synthesis.

The quality of studies will be assessed according to a standardised set of criteria recommended for use in reviews of prognosis. These criteria were modified slightly using suggested criteria from other sources. These guidelines focus on six areas of potential bias pertinent to studies of prognosis: study participation, study attrition, prognostic factor measurement, outcome measurement, confounding measurement and account, and analysis. The Cochrane Handbook for Systematic Reviews of interventions recognises four sources of potential systematic bias in randomised and non-randomised comparisons of healthcare interventions, including: selection bias, performance bias, attrition bias and detection bias. The six areas that will be evaluated in this review encompass the usual four sources of bias assessed, but have been adapted for use in studies of risk factor analysis or prognosis. Studies will be classified as acceptable quality if they at least partly satisfy all six areas of potential bias.

28 Strategy for data synthesis

Give the planned general approach to be used, for example whether the data to be used will be aggregate or at the level of individual participants, and whether a quantitative or narrative (descriptive) synthesis is planned. Where appropriate a brief outline of analytic approach should be given.

A narrative synthesis is planned, reporting the number and type of risk factors studied for each outcome domain: motor function, cognitive function, hearing, vision and behavioural/psychiatric. These domains will be further stratified by age of assessment: 1.5-2 years, 3-5 years, 6-12 years and above 13 years. The number and quality of studies examining each risk factor will be reported along with the strength and direction of association found. The level of evidence for each risk factor will be graded as high (multiple studies of acceptable quality), moderate (1 acceptable quality study and multiple lower quality studies), or low (1 study only or multiple lower quality studies).

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