

PROSPERO
International prospective register of systematic reviews

NHS
National Institute for
Health Research

UNIVERSITY of York
Centre for Reviews and Dissemination

Systematic review

1. * Review title.

Give the title of the review in English

Antenatal Corticosteroids for Reducing Adverse Maternal and Child Outcomes in Special Populations of Women at Risk of Imminent Preterm Birth: A Systematic Review and Meta-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.

Antenatal Corticosteroids for Reducing Adverse Maternal and Child Outcomes in Special Populations of Women at Risk of Imminent Preterm Birth: A Systematic Review and Meta-Analysis

3. * Anticipated or actual start date.

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

06/06/2021

4. * Anticipated completion date.

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

31/12/2021

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: Yes

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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.

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.

Kana Saito

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

Dr Kana Saito

7. * Named contact email.

Give the electronic email address of the named contact.

kana988@saitama-med.ac.jp

8. Named contact address

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

1981, Kamoda, Kawagoe-city, Saitama, Japan

9. Named contact phone number.

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

81-49-228-3400

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.

Saitama Medical University

Organisation web address:

<http://www.saitama-med.ac.jp/>

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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.**

Dr KANA SAITO. Saitama Medical University, Neonatology Department
Ms Etsuko Nishimura. St. Luke's International University

12. * Funding sources/sponsors.

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

Non funded research

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.**

Dr Toshiyuki Swa. Osaka University Graduate School of Medicine
Dr Fumihiko Namba. Saitama Medical University
Dr Erika Ota. St. Luke's International University
Dr Joshua P. Vogel. Child and Adolescent Health Program, Burnet Institute, Melbourne
Dr Jenny Ramson. Child and Adolescent Health Program, Burnet Institute, Melbourne
Dr Jenny Cao. Child and Adolescent Health Program, Burnet Institute, Melbourne

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.

This study aims to synthesize available evidence on antenatal corticosteroid (ACS) use among specific subgroups of women at risk of imminent preterm birth.

The primary objective is to determine the effects of ACS administration for four subgroups of pregnant women at risk of imminent preterm birth on maternal and child outcomes. These subgroups are as follows.

- 1) women with pregestational or gestational diabetes mellitus
- 2) women undergoing elective CS in the late preterm period (from 34 weeks 0 days to 36 weeks 6 days)
- 3) women with an intrapartum inflammation, infection, or both (eg: chorioamnionitis)
- 4) women with growth-restricted fetuses

16. * Searches.

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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.)

We will search electronic databases (e.g. MEDLINE, EMBASE, CINAHL, Cochrane Library, POPLINE, and Global Index medicus for publications). Our search is not limited by language or geographic restrictions.

Relevant unpublished material will be identified through key term searches of the following databases:

Cochrane Register of Controlled Trials (CENTRAL), ClinicalTrials.gov, International Standard Randomised Controlled Trial Number Register (ISRCTN), and the International Clinical Trial Registry Platform (ICTRP).

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**.

We will search electronic databases (i.e. MEDLINE, EMBASE, CINAHL, Cochrane Library, POPLINE, and Global Index medicus for publications). Our search is not limited by language or geographic restrictions.

Relevant unpublished material will be identified through key term searches of the following databases:

Cochrane Register of Controlled Trials (CENTRAL), ClinicalTrials.gov, International Standard Randomised Controlled Trial Number Register (ISRCTN), and the International Clinical Trial Registry Platform (ICTRP).

Search terms include “adrenal cortex hormones”, “pregnancy”, “pregnancy outcome”, “fetal death”, “maternal death”, “obstetric labor complications”, “obstetric labor, premature”, “pregnancy, prolonged”, “fetus”, “infant, newborn”, “prenatal care”, “fetal development”, “birth weight”, “prenatal exposure delayed effects”, “diabetes mellitus”, “hyperglycemia”, “diabetes, gestational”, “pregnancy in diabetics”, “cesarean section”, “bacterial infections and mycoses”, “chorioamnionitis”, “pregnancy complications, infectious”, “fetal development”.

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.

Pregnancy

19. * Participants/population.

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

Exclusion: Pregnant women with a population at risk of preterm birth who are not at least 20 weeks gestation at the start of the study.

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.

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We will include women who received at least one dose of antenatal corticosteroid, either betamethasone, dexamethasone, or hydrocortisone after 20 weeks of gestation.

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.

Women and babies who did not receive antenatal corticosteroids.

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.

We will include all published, unpublished, and ongoing randomized or quasi-randomized controlled trials, controlled before-and-after studies, interrupted-time-series studies, historical controlled studies, cohort studies, and cross-sectional studies comparing ACS administration (betamethasone, dexamethasone, or hydrocortisone), given parenterally or enterally, compared with placebo or no treatment in women at risk of imminent preterm birth as a result of either spontaneous preterm labor, preterm rupture of the membranes, or elective preterm delivery, and where all (or at least a well-defined sub-sample) of the women under study also fulfil the gestational age of gestation and conditions:

1. having a gestational age of gestation and conditions
2. undergoing elective caesarean birth in late preterm (from 34 weeks 0 days to 36 weeks 6 days);
3. having intrauterine inflammation, infection, or both; or
4. having a growth-restricted infant (or, more broadly, one that was at least small for gestational age).

23. Context.

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

We aim to establish the existing evidence that examines the implications of using or not using ACS in cases of imminent preterm birth in these subgroups of women. This evidence-based effort will be the source for the World Health Organization's (WHO) updated recommendations on interventions to improve preterm birth outcomes.

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.

maternal outcomes severe morbidity (e.g. organ dysfunction, intensive care unit admission, chorioamnionitis)
-maternal morbidity(e.g. puerperal sepsis, pregnancy-induced hypertension, gestational diabetes mellitus, placental abruption, postpartum haemorrhage, or as defined by the author)

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- route of delivery
- side effects of therapy
- b) neonatal outcomes
 - perinatal mortality
 - fetal mortality
 - neonatal mortality
 - respiratory distress syndrome (RDS) and moderate/severe RDS
 - surfactant use
 - interventricular haemorrhage (IVH)
 - periventricular leukomalacia (PVL)
 - sepsis; early onset sepsis
 - necrotizing enterocolitis (NEC)
 - mechanical ventilation use and mean duration
 - patent ductus arteriosus (PDA)
 - chronic lung disease (CLD)/ bronchopulmonary dysplasia (BPD)
 - Apgar scores seven at 5 minutes
 - neurodevelopment
 - anthropometric status; birth weight, height, and head circumference
 - NICU admission and mean duration
 - side effects of therapy

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.

Aggregate odds ratios (ORs) and 95% confidence intervals (CIs) will be calculated for dichotomous data using Mantel-Haenszel analysis (fixed-effect model). Where between-study clinical or methodological heterogeneity will undermine the compatibility of the quantitative results, or if substantial statistical heterogeneity is detected, random-effect meta-analysis will be used. Data will be pooled using ORs when the number of events is available and using logarithms of the ORs weighted by the inverse variance when the event is not available. For continuous data, mean difference (MDs) with 95% CIs will be used.

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

We will conduct the sub-group analysis; extremely preterm (less than GA 28weeks), very preterm (GA28 to 32weeks) and moderate to late preterm (GA 32 to 37weeks) on each predetermined outcome.

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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.

Aggregate odds ratios (ORs) and 95% confidence intervals (CIs) will be calculated for dichotomous data using Mantel-Haenszel analysis (fixed-effect model). Where between-study clinical or methodological heterogeneity will undermine the compatibility of the quantitative results, or if substantial statistical heterogeneity is detected, random-effect meta-analysis will be used. Data will be pooled using ORs when the number of events is available and using logarithms of the ORs weighted by the inverse variance when the event is not available. For continuous data, mean difference (MDs) with 95% CIs will be used.

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.

At least two researchers will work independently to assess each title and abstract for eligibility. Disagreement will yield automatic inclusion into the next level of screening. After the initial screening of titles and abstracts, full-text publications of studies with the potential for inclusion will be obtained and assessed. The same reviewers will independently evaluate studies under consideration for inclusion without consideration of their results. Any disagreement will be resolved through discussion to reach a consensus. Finally, the reviewers independently will extract baseline and outcome data and assess the quality of the included studies. Any discrepancies will be resolved through discussion to reach a consensus.

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.

Study quality will be assessed independently by the aforementioned reviewers at the outcome level using the Risk of Bias Assessment tool for Non-randomized Studies (RoBANS). Randomized control trials will be assessed with Risk of Bias 2 (RoB2). Potential publication bias will be assessed by visual inspection of funnel plots for asymmetry, subject to a sufficient number of included studies. Any disagreement will be resolved by discussion to reach a consensus.

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.

Aggregate odds ratios (ORs) and 95% confidence intervals (CIs) will be calculated for dichotomous data using Mantel-Haenszel analysis (fixed-effect model). Where between-study clinical or methodological heterogeneity will undermine the compatibility of the quantitative results, or if substantial statistical heterogeneity is detected, random-effect meta-analysis will be used. Data will be pooled using ORs when the

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number of events is available and using logarithms of the ORs weighted by the inverse variance when the event is not available. For continuous data, mean difference with 95% CIs will be used.

The heterogeneity of studies will be assessed using both qualitative and quantitative measures. Statistical heterogeneity will be determined for each meta-analysis using T^2 , I^2 , and τ^2 statistics.

Heterogeneity will be deemed substantial if T^2 will be greater than zero and either I^2 will be greater than 50% or $p < 0.10$ in the τ^2 test for heterogeneity. To further assess potential heterogeneity, both fixed- and random-effects models will be compared for each outcome, where possible.

All statistical analyses will be performed using RevMan 5. Existing meta-analyses will be reviewed for relevance and completeness, and new meta-analyses will be performed where deemed necessary.

Statistical significance will be set at an alpha level of 0.05 for all analyses, except when testing study heterogeneity, where $p < 0.10$ will be regarded as significant.

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.

None

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

No

Diagnostic

No

Epidemiologic

No

Individual patient data (IPD) meta-analysis

No

Intervention

Yes

Living systematic review

No

Meta-analysis

Yes

Methodology

No

Narrative synthesis

No

Network meta-analysis

No

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Pre-clinical
No

Prevention
Yes

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

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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

Yes

Public health (including social determinants of health)

No

Rehabilitation

No

Respiratory disorders

No

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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.

Japan

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.

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

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?

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Yes

Give brief details of plans for communicating review findings.?

We will disseminate the finding with a relevant medical journal.

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.

Antenatal corticosteroid

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.

Amiya RM, Mlunde LB, Ota E, Swa T, Oladapo OT, Mori R. Antenatal corticosteroids for reducing adverse maternal and child outcomes in special populations of women at risk of imminent preterm birth: a systematic review and meta-analysis. PLoS ONE. 2016; 11(2): e0147604.

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.