Routine neonatal circumcision for the prevention of urinary tract infections in infancy (Protocol)

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TABLE OF CONTENTS

HEADER 1
ABSTRACT 1
BACKGROUND 2
OBJECTIVES 3
METHODS 3
ACKNOWLEDGEMENTS 6
REFERENCES 6
HISTORY 7
CONTRIBUTIONS OF AUTHORS 7
DECLARATIONS OF INTEREST 8

[Intervention Protocol]

Routine neonatal circumcision for the prevention of urinary tract infections in infancy

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To assess the effectiveness and safety of routine neonatal circumcision for the prevention of urinary tract infections (UTIs) in infancy.

BACKGROUND

Routine neonatal circumcision is a fairly common surgical procedure (To 1998) that may be carried out for medical or religious reasons. The potential medical benefits include reduced occurrence of urinary tract infections (UTI) in infancy and a reduced risk of sexually transmitted diseases (STD) like HIV, penile cancer, phimosis, and human papilloma virus-related cervical cancer in female sexual partners in later life (Alanis 2004). Circumcision is a relatively simple procedure and is in general associated with minimal complications when carried out in neonates rather than in later life (Wiswell 1990).

It has been suggested that newborn circumcision can be a valuable preventive health measure for UTI in infancy (Schoen 2000). A systematic review and meta-analysis (Amato 1992) of newborn circumcision concluded that the risk of UTI may decrease with circumcision but, given that the risk of UTI during the first year of life is itself low, a recommendation for routine circumcision may not be justified. The conclusions from a more recent review (Singh-Grewal 2005) indicated that although circumcision reduces the risk of UTI there was an attendant risk of complications and that the net clinical benefits are only achievable in boys at high risk of UTI. Regular foreskin hygiene is important for all males to prevent UTI (Robson 1992) but there is no evidence that many of the potential medical benefits of circumcision can be achieved by simple daily penile hygiene (Wiswell 1990). While the procedure appears to be beneficial in the prevention of UTI, a number of studies have shown that UTI may itself present as a complication of circumcision (Cohen 1992).

Neonatal circumcision continues to be a controversial subject. The American Academy of Pediatrics has revised its earlier policy, stating that newborn circumcision has potential benefits as well as risks, and emphasizes the need to explain these issues to parents who are considering the procedure such that an informed decision can be made (American Academy of Pediatrics 1999).

Parents of newborn boys are often faced with a dilemma when trying to decide whether to subject their child to this procedure. Many of the paediatric societies (Canadian Pediatric Society 1996; Royal Australasian College of Physicians 2002) oppose routine circumcision but consider it an acceptable intervention for recurrent balanitis, true phimosis, and UTI. The American Academy of Pediatrics 1999 noted that although there is scientific evidence to demonstrate the advantage of neonatal circumcision, the available data has not clearly shown advantages of routine neonatal circumcision. Hence they have left the onus on parents to weigh up the pros and cons of the procedure and make an informed decision accordingly. The latest revision in the position statement of the American Urological Association 2007 suggests that an explanation of the health benefits of neonatal circumcision should be presented to parents to help inform decision making.

Description of the condition

Urinary tract infections occur in 1% to 2% of neonates with a female:male ratio of 1:5 during infancy. Predisposing factors during infancy include anatomic abnormalities and obstructions of the urinary tract, prematurity, indwelling catheters, and possibly lack of circumcision (Barnett 1997). Most UTIs are caused by *Escherichia coli*, and gram negative enterobacteria like *Klebsiella, Proteus mirabilis*, and *Pseudomonas aeruginosa* (Barnett 1997).
Antibiotics are the main stay of treatment (Rubin 1992). With careful management UTI rarely progresses to complications. However repeated infections, especially in those with underlying tract abnormalities, may cause renal scarring, hypertension, and more rarely lead to renal failure.

Description of the intervention

Circumcision is a surgical procedure in which the foreskin is removed from the penis, which can decrease microbial colonisation in the periurethral area and hence reduce the incidence of UTI (Wiswell 1988). It may also remove the protective subpreputial moisture and antibacterial lysozyme (Fleiss 1998) and thereby expose infants to hospital strains of *E. coli*, which makes the procedure a potential iatrogenic cause of UTI (Winberg 1989).
Neonatal circumcision rates vary widely at the global level, with rates as high as 64% in North America (American Academy of Pediatrics 1999), between 10% and 20% in Australia (Royal Australasian College of Physicians 2002), and much lower rates in Europe and Asia (American Academy of Pediatrics 1999).
The overall complication rate of circumcision is between 2% and 10% (Kaplan 1983; Williams 1993), with most complications being categorised as minor (Griffiths 1985). Haemorrhage is the most frequent acute complication followed by infection, glandular ulceration, urethral fistula formation, and even penile amputation. Long-term complications include meatal stenosis and poor cosmetic results (Williams 1993).

How the intervention might work

The urethral meatus of uncircumcised male infants has been found to harbour more uropathogenic organisms than that of circumcised male infants, although this tends to decrease in both groups after the first six months. This would appear to be a biologically plausible explanation for a relationship between an intact foreskin and increased UTI during infancy (Wiswell 1988). These bacteria have also been shown to be more adherent to the mucosal surface of the foreskin than the keratinized surface (Fussell 1988). Circumcision could therefore help in reducing the incidence of UTI by reducing periurethral bacterial colonization, which is accepted as a potential risk factor in UTI.

Why it is important to do this review

Male circumcision is a surgical procedure that has been performed for cultural, religious, social, and medical reasons for a long time and whilst it continues to receive some attention the perceived benefits are still very much in dispute. There is a lack of clear consensus on the magnitude of the benefits or the cost effectiveness of circumcision when carried out routinely in neonates (Ganiats 1991). Although there appear to be many benefits and a low risk of major complications with elective circumcision carried out during the neonatal period, some have argued that the complications outweigh the benefits (Pieretti 2010). A number of position statements have been developed on circumcision which conclude that there is insufficient evidence to recommend routine neonatal circumcision but suggest that parents should be involved in the decision making process.

The policies and recommendations on this topic have transformed over time with accumulating evidence to support both the relative merits as well as demerits. As the most frequently suggested benefit of neonatal circumcision is prevention of UTI we aim to evaluate this aspect in this systematic review.

OBJECTIVES

To assess the effectiveness and safety of routine neonatal circumcision for the prevention of urinary tract infections (UTIs) in infancy.

METHODS

Criteria for considering studies for this review

Types of studies

We will consider randomised controlled trials (RCT), quasi-randomised controlled trials, and cluster randomised trials as eligible for this study.

Types of participants

All male newborns with or without urogenital anomalies.

Types of interventions

Medical circumcision performed at the time of birth or within the first four weeks of life compared with no circumcision or uncircumcised but following penile hygiene instructions provided by a healthcare provider as control.

If trial data are available, to compare:

- safety and effectiveness if the timing of the circumcision procedure is before three days and after three days of life (prior to or after maternal discharge after delivery);
- effectiveness between groups defined by the presence or absence of urogenital anomalies;
- safety and effectiveness between different techniques of the circumcision procedure.

Types of outcome measures

Primary outcomes

Urinary tract infection (UTI): a positive urine culture from a bag or clean-catch specimen in the presence of urinary symptoms or, for asymptomatic UTI, from a sample collected during the regular well baby visits for vaccination.

1. Proportion of babies with UTI.
2. Total number of episodes of UTI.
3. Proportion of babies with more than one episode of UTI.

Secondary outcomes

1. Complications of the intervention: proportion of babies who had complications (bleeding, infection, or other).
2. Complications of UTI, proportion of babies who exhibited any of the complications of UTI:

- renal scarring (renal parenchymal defects assessed with intravenous pyelogram (IVP) or dimercaptosuccinic acid (DMSA) scan);
- renal failure (reported based on serum creatinine levels, glomerular filtration rate, or urine output);
- renal stones;
- renal hypertension defined as an average systolic or diastolic blood pressure, or both, > 95th percentile for gender, age, and height on three or more separate occasions (Falkner 2004); and
- others, if any, in the follow up of infants with UTI.

All outcome measures will be considered at three months, six months, and one year end points, while the complications of surgery will be considered at or before three days, and later.

Search methods for identification of studies

Electronic searches

We will use the standard search strategy of the Cochrane Neonatal Review Group, as outlined in *The Cochrane Library*. We will consider unpublished studies to be eligible for review. The search of MEDLINE and PreMEDLINE (via the Ovid interphase) will include the following MeSH terms and text-words: bleeding, circumcision, infant, newborn, neonate, routine, renal failure, renal

scars, and urinary tract infections. We will limit searches to "randomised and quasi-randomised clinical trials". We will not apply language restrictions. For the identification of studies included or considered for inclusion in this review, detailed search strategies will be developed for each database to be searched. These strategies will be based on the search strategy developed for MEDLINE but revised appropriately for each database.
We will search the following databases:

- Cochrane Neonatal Group Trials Register;
- Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*, current issue);
- MEDLINE (from 1950 to current);
- EMBASE (from1980 to current).

For the MEDLINE search, we will run the subject search with the Cochrane highly sensitive search strategy (CHSSS) for identifying randomised trials in MEDLINE, sensitivity maximising version (2009 revision) as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of the Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.2 (updated September 2009) (Higgins 2009).
Detailed search strategies applied to each of the other databases will be provided in the completed review.

Searching other resources

The reference lists of relevant articles will be examined and we will contact the investigators of included studies by electronic mail to ask for details of additional published and unpublished trials. We will handsearch any journals in accordance with the recommendations of the Cochrane Neonatal Group.
Clinical trials registries were also searched for ongoing or recently completed trials (clinicaltrials.gov; controlled-trials.com; and who.int/ictrp)

Language

There will be no language restriction on included studies and we will arrange to translate any studies not in the English language.

Data collection and analysis

Selection of studies

Two review authors [Zbys Fedorowicz (ZF) and Vikas Sud (VS)] will independently assess the abstracts of studies resulting from the searches. We will obtain full copies of all relevant and potentially relevant studies, those appearing to meet the inclusion criteria and for which there were insufficient data in the title and abstract to make a clear decision. If only abstracts are available, the full texts will be sought from the contact authors for analysis.The full text papers will be assessed independently by the two review authors and any disagreement on the eligibility of included studies will be resolved through discussion and consensus or, if necessary, through a third author Vanitha Jagannath (VJ). We will exclude all irrelevant study reports and note the details and the reasons for their exclusion in the table 'Characteristics of excuded studies' section of this review.

Data extraction and management

We will enter study details into the table 'Characteristics of included studies' in the review and collect outcome data using a predetermined form designed for this purpose.
Data will be extracted independently and in duplicate by two review authors (ZF and VS) and only included if there is a consensus; any disagreements will be resolved by consulting with a third review author (VJ).
The following details will be extracted.

1. Trial methods: (a) method of allocation; (b) allocation concealment (adequate, unclear, inadequate or not used); (c) masking of participants, trialists, and outcome assessors; (d) exclusion of participants after randomisation and proportion and reasons for losses at follow up.
2. Participants: (a) country of origin and study setting; (b) sample size; (c) breast feeding history; (d) urogenital anomalies; (e) inclusion and exclusion criteria.
3. Intervention: (a) type of surgery; (b) day of life when surgery done; (c) duration of intervention in follow up.
4. Control: (a) If any blinding procedure is done.
5. Outcomes: (a) primary and secondary outcomes mentioned in the Types of outcome measures section of this review, to include any reported adverse effects.

The review authors will use this information to help them assess heterogeneity and the external validity of any included trials.

Assessment of risk of bias in included studies

Each review author will grade the selected trials using a simple contingency form and follow the domain-based evaluation described in Chapter 8 of the Cochrane Handbook for Systematic Reviews of Interventions 5.0.2 (Higgins 2009). The evaluations will be compared and any inconsistencies in these evaluations between the review authors will be discussed and resolved.
The following domains will be assessed as 'low risk', 'unclear risk', or 'high' risk of bias:

1. sequence generation;
2. allocation concealment;
3. blinding (of participants, personnel and outcome assessors);
4. incomplete outcome data addressed;
5. free of selective outcome reporting;
6. free of other bias.

Risk of bias in any included studies will be categorised according to the following:

- low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met;
- unclear risk of bias (plausible bias that raises some doubt about the results) if one or more criteria were assessed as unclear; or
- high risk of bias (plausible bias that seriously weakens confidence in the results) if one or more criteria were not met.

These assessments will be reported for each trial in the Risk of Bias table for included studies table in the review.

Measures of treatment effect

The authors will include the results from studies that meet the inclusion criteria in the review and data for any of the outcomes of interest in a subsequent meta-analysis.
We will analyse treatment effects in the individual trials using RevMan 5 (RevMan 2008).

Dichotomous data

We will report dichotomous data using relative risk (RR) and risk difference (RD), each with a 95% confidence interval (CI). If there is a statistically significant reduction in RD then we will calculate the number needed to treat (NNT) or number needed to harm (NNH) and associated 95% CI.

Continuous data

We will report continuous data as mean difference (when measures are in the same unit) or standardised mean difference, 'effect size', when different scales are used to evaluate the same outcome, with 95% CI.

Unit of analysis issues

The unit of randomisation is the intended unit of analysis and we expect this to be individual infants in the individually randomised studies.
Unit of analysis issues that might arise may be the result of recurrences or many episodes of UTI in a patient. If the studies report the proportion of participants with episodes of UTI or number of episodes of UTI per participant per unit time they will be compared and analysed accordingly. We will follow the advice provided in Section 16.3.4 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2009).
Cluster randomised controlled trials will be included.
We are planning to include cluster randomised trials in the analyses, along with individually randomised trials. We will analyse these using the methods described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2009) using an estimate of the intra-cluster correlation coefficient (ICC) derived from the trial (if possible) or from another source. If ICCs from other sources are used, we intend to report this and conduct sensitivity analyses to investigate the effect of variation in the ICC.
If we identify both cluster randomised trials and individually randomised trials, we plan to synthesise the relevant information accordingly. We will consider it reasonable to combine the results from both if there is limited heterogeneity between the studies and if we consider interaction between the effect of the intervention and the choice of randomisation unit to be unlikely.

Dealing with missing data

We will try to obtain missing data directly from the investigators of any of the included studies. If this is not possible, we will analyse the available data (that is ignoring the missing data) in addition to conducting further analyses by imputation (both best- and worst-case scenarios) and last observation carried forward (LOCF) to the final assessment, for dichotomous and continuous outcome data respectively.
For dichotomous outcomes we will conduct both best- and worst-case scenarios and intention-to-treat (ITT) analyses. We will compare results obtained from the two analysis options to enable a better understanding of the robustness of results relative to the different analytic approaches. We will consider an imputation approach of best-case scenarios (that is all missing participants in the intervention group did not experience poor outcomes (such as death, bronchopulmonary dysplasia (BPD) and all missing participants in the control group experienced poor outcomes) and worst-case scenarios (that is all missing participants in the intervention group experienced the event and all missing participants in the control condition did not). We will conduct sensitivity analyses to compare results based on different imputation assumptions (that is best- versus worst-case scenarios).
We will analyse missing continuous data on an end point basis, including only participants with a final assessment or analysed using LOCF if the trial authors reported any LOCF data.
If unsuccessful, or if the discrepancies are significant, we will provide a narrative synthesis of the data as presented in the individual reports.

Assessment of heterogeneity

We will assess clinical heterogeneity by examining the characteristics of the studies, the similarity between the types of participants, the interventions, and the outcomes as specified in the criteria for included studies. Statistical heterogeneity will be assessed using a Chi^2 test and the I^2 statistic, where I^2 values of 30% to 60% indicate moderate to high, 50% to 90% substantial, and 75% to 100% considerable heterogeneity. We will consider heterogeneity to be significant when the P value is less than 0.10 (Higgins 2003).

Assessment of reporting biases

If sufficient trials are identified for inclusion in this review, publication bias will be assessed according to the recommendations

on testing for funnel plot asymmetry (Egger 1997) as described in section 10.4.3.1 of the Cochrane Handbook for Systematic Reviews of Interventions 5.0.2 (updated September 2009) (Higgins 2009). If asymmetry is identified, we will try to assess other possible causes of asymmetry and these will be explored in the discussion, if appropriate.

Data synthesis

Two review authors (ZF and VS) will analyse the data and report them as specified in Chapter 9 of the Cochrane Handbook for Systematic Reviews of Interventions 5.0.2 (Higgins 2009). If sufficient numbers of studies investigating similar interventions are included, analysis will be conducted in RevMan (RevMan 2008). We will use the fixed-effect method for the synthesis and meta-analysis of any quantitative data. If we establish that there is heterogeneity between the studies, we may not undertake a meta-analysis. If there are too few clinically homogenous trials, or insufficient data for pooling, we will present the results of the individual trials and perform a descriptive analysis only.
If adequate data are available, we will calculate a pooled estimate of effect of specific interventions together with the corresponding 95% CIs.

Subgroup analysis and investigation of heterogeneity

We plan to carry out the following subgroup analyses if we identify moderate, substantial, or considerable heterogeneity (as defined above) and If sufficient studies are identified.

- Timing of circumcision: < 3 days or after 3 days.
- Presence or absence of urogenital anomalies.
- Technique of circumcision (Mogen clamp, Gomco clamp, or Plastibell device).
- Method of sample collection for urine analysis (bag, catheter, or suprapubic).

Sensitivity analysis

If sufficient studies are included, we plan to conduct sensitivity analyses to assess the robustness of our review results by repeating the analysis with the following adjustments: exclusion of studies with unclear or inadequate allocation concealment, unclear or inadequate blinding of outcomes assessment or completeness of follow up.

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REFERENCES

Additional references

Alanis 2004
Alanis MC, Lucidi, RS. Neonatal circumcision: a review of the world's oldest and most controversial operation. *Obstetrical and Gynecological Survey* 2004;**59**(5):379–95.

Amato 1992
Amato D, Garduno-Espinosa J. Circumcision in the newborn child and risk of urinary tract infection during the first year of life. A meta-analysis [Circuncision en el nino recien nacido y el riesgo de presentar infeccion de vias urinarias durante el primer ano de vida. Un meta–analisis.]. *Boletin medico del Hospital Infantil de Mexico* 1992;**49**(10):652–8. [PUBMED: 1449623]

American Academy of Pediatrics 1999
American Academy of Pediatrics. Task Force on Circumcision. Circumcision policy statement. *Pediatrics* 1999;**103**(3):686–93. [PUBMED: 10049981]

American Urological Association 2007
Circumcision Policy Statement. http://www.auanet.org/content/guidelines-and-quality-care/policy-statements/c/circumcision.cfm.

Barnett 1997
Barnett BJ, Stephens DS. Urinary tract infection: an overview. *American Journal of the Medical Sciences* 1997;**314**(4):245–9.

Canadian Pediatric Society 1996
Fetus and Newborn Committee, Canadian Paediatric Society. Neonatal circumcision revisited. *Canadian Medical Association Journal* 1996;**154**(6):769–80. [PUBMED: 8634956]

Cohen 1992
Cohen HA, Drucker MM, Vainer S, Ashkenasi A, Amir J, Frydman M, et al.Postcircumcision urinary tract infection. *Clinical Pediatrics* 1992;**31**(6):322–4. [PUBMED: 1628463]

Egger 1997
Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**(7109):629–34.

Falkner 2004
Falkner B, Daniels SR. Summary of the fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Hypertension* 2004;**44**(4):387–8. [PUBMED: 15353515]

Fleiss 1998
Fleiss PM, Hodges FM, Van Howe RS. Immunological functions of the human prepuce. *Sexually Transmitted Infections* 1998;**74**(5): 364–7. [PUBMED: 10195034]

Fussell 1988
Fussell EN, Kaack MB, Cherry R, Roberts JA. Adherence of bacteria to human foreskins. *Journal of Urology* 1988;**140**(5): 997–1001. [PUBMED: 2902235]

Ganiats 1991
Ganiats TG, Humphrey JB, Taras HL, Kaplan RM. Routine neonatal circumcision: a cost-utility analysis. *Medical Decision Making* 1991;**11**(4):282–93. [PUBMED: 1766331]

Griffiths 1985
Griffiths DM, Atwell JD, Freeman NV. A prospective survey of the indications and morbidity of circumcision in children. *European Urology* 1985;**11**(3):184–7. [PUBMED: 4029234]

Higgins 2003
Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**(7414):557–60.

Higgins 2009
Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions version 5.02 (updated September 2009). The Cochrane Collaboration, 2009. Available from www.cochrane-handbook.org.

Kaplan 1983
Kaplan GW. Complications of circumcision. *Urologic Clinics of North America* 1983;**10**(3):543–9. [PUBMED: 6623741]

Pieretti 2010
Pieretti RV, Goldstein AM, Pieretti-Vanmarcke R. Late complications of newborn circumcision: a common and avoidable problem. *Pediatric Surgery International* 2010;**26**(5):515–8.

RevMan 2008
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 5.0. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008.

Robson 1992
Robson WL, Leung AK. The circumcision question. *Postgraduate Medicine* 1992;**91**(6):237-42, 244. [PUBMED: 1579530]

Royal Australasian College of Physicians 2002
Paediatrics and Child Health Division. Policy statement on circumcision. www.racp.edu.au/hpu/paed/circumcision/index.htm#toc 2002.

Rubin 1992
Rubin RH, Shapiro ED, Andriole VT, Davis RJ, Stamm WE. Evaluation of new anti-infective drugs for the treatment of urinary tract infection. Infectious Diseases Society of America and the Food and Drug Administration. *Clinical Infectious Diseases* 1992;**15 Suppl**(1):216–27.

Schoen 2000
Schoen EJ, Colby CJ, Ray GT. Newborn circumcision decreases incidence and costs of urinary tract infections during the first year of life. *Pediatrics* 2000;**105**(4 Pt 1):789–93. [PUBMED: 10742321]

Singh-Grewal 2005
Singh-Grewal D, Macdessi J, Craig J. Circumcision for the prevention of urinary tract infection in boys: a systematic review of randomised trials and observational studies. *Archives of Disease in Childhood* 2005;**90**(8):853–8. [PUBMED: 15890696]

To 1998
To T, Agha M, Dick PT, Feldman W. Cohort study on circumcision of newborn boys and subsequent risk of urinary-tract infection. *Lancet* 1998;**352**(9143):1813–6. [PUBMED: 9851381]

Williams 1993
Williams N, Kapila L. Complications of circumcision. *The British Journal of Surgery* 1993;**80**(10):1231–6. [PUBMED: 8242285]

Winberg 1989
Winberg J, Bollgren I, Gothefors L, Herthelius M, Tullus K. The prepuce: a mistake of nature?. *Lancet* 1989;**1**(8638):598–9. [PUBMED: 2564120]

Wiswell 1988
Wiswell TE, Miller GM, Gelston HM Jr, Jones SK, Clemmings AF. Effect of circumcision status on periurethral bacterial flora during the first year of life. *Journal of Pediatrics* 1988;**113**(3):442–6. [PUBMED: 3411387]

Wiswell 1990
Wiswell TE. Routine neonatal circumcision: a reappraisal. *American Family Physician* 1990;**41**(3):859–63. [PUBMED: 2407075]

* *Indicates the major publication for the study*

HISTORY

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CONTRIBUTIONS OF AUTHORS

Vanitha Jagannath (VJ), Zbys Fedorowicz (ZF), Vikas Sud (VS), Abhishek Kumar Verma(AV), Sakineh Hajebrahimi (SH) will be responsible for:

- organising the retrieval of papers;
- writing to authors of papers for additional information;
- screening search results;
- screening retrieved papers against inclusion criteria;
- appraising the quality of papers;
- data collection for the review;
- extracting data from papers;
- obtaining and screening data on unpublished studies.

ZF and VJ will enter the data into RevMan and will be responsible for analysis and interpretation of the data.

All review authors will contribute to writing the review.

All review authors are responsible for designing and coordinating the review and for data management for the review.

ZF,VJ, and VS conceived the idea for the review and are the guarantors for the review.

DECLARATIONS OF INTEREST

There are no financial conflicts of interest and the review authors declare that they do not have any associations with any parties who may have vested interests in the results of this review.