Oral hygiene care for critically ill patients to prevent ventilator associated pneumonia (Protocol)

Shi Z, Xie H, Wang P, Wu Y, Chen E, Ng L, Worthington HV, Singer M, Needleman I

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[Intervention Protocol]

Oral hygiene care for critically ill patients to prevent ventilator associated pneumonia

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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 effect of oral hygiene care on ventilator associated pneumonia (VAP) in critically ill patients receiving mechanical ventilation in hospital settings.

BACKGROUND

Critically ill patients who are mechanically ventilated are dependent on others for their oral hygiene. As a result these patients are at risk of deterioration in oral health if effective oral care is not provided. The effects of this may include increased dental plaque accumulation and drying of oral tissues (Fourrier 1998; Franklin 2000; Munro 2006; Prendergast 2009) accompanied by colonisation of dental plaque by microbial pathogens that may be causative of respiratory infections (Heo 2008). This situation is exacerbated by the placement of an endotracheal tube and possible injury of the oral and pharyngeal mucosa by intubation. Such trauma might impair the patient's normal defence mechanisms against infection (Gibbons 1989; Terpenning 2005).

Ventilator associated pneumonia (VAP) is defined as nosocomial pneumonia among patients receiving mechanical ventilation (Tantipong 2008).The prevalence of VAP in critically ill patients has ranges from 9% to 68% (Fagon 1993; Apostolopoulou 2003). A prospective European survey involving 107 general intensive care units (ICU) in 18 countries estimated a crude incidence of pneumonia as 8.9% and 7-day and 14-day pneumonia rates as 15.8% and 23.4% respectively (Chevret 1993). Patients with VAP had significantly longer stays in ICUs and possibly high mortality rates (Jimenez 1989; Fagon 1993; Mehta 2002), even as high as a 60% increase (Patel 2002). It is considered to be one of the leading causes of death from nosocomial infections in the United States (Craven 1991). Multiple antibiotics are used in treating respiratory tract infections for intubated patients, and the cost of antibiotics attributed to individual VAP patients was USD 11,897 and USD 15,893 in America and Europe respectively (Warren 2003; van Nieuwenhoven 2004).

There is increasing evidence in the literature to suggest a link between colonisation of dental plaque with respiratory pathogens and VAP (Scannapieco 1996; Fourrier 1998). Scannapieco et al conducted a survey in an ICU and dental clinic and found respiratory pathogen colonisation in the patients' plaque and/or oral mucosa being differently, in 65% of 34 ICU patients and 16% of 25 dental patients respectively (Scannapieco 1992). Treloar and co-workers reported that 37.5% of oropharyngeal cultures taken from orally intubated patients had the same pathogens as sputum specimens (Treloar 1995). In another study, pathogens from the respiratory tract of patients with hospital acquired pneumonia genetically matched those from dental plaque (El-Solh 2004; Heo 2008). Didilescu et al assessed supragingival plaque colonisation of 34 hospitalised chronic lung-diseased patients by checkerboard DNA-DNA hybridisation. Respiratory pathogens were detected in plaque from 29 of the 34 (85.3%) hospitalised patients, but in only 12 of the 31(38.7%) healthy dental outpatients who served as reference population. Furthermore, it was found that dental plaque samples of hospitalised patients harboured higher frequencies of the following organisms compared with dental outpatients without lung diseases: *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Enterobacter cloacae* ($P < 0.05$) (Didilescu 2005).

Scannapieco concluded in his systematic review that there is a potential association between poor oral hygiene and nosocomial pneumonia (Scannapieco 2003). Microaspiration may occur in patients with a depressed conscious level and reduced cough reflex, or around an imperfect seal of the endotracheal tube cuff in a ventilated patient. Many studies have shown that microaspiration contributes to the development of nosocomial pneumonia (Bentley 1984; Heyland 1992; Scannapieco 1992; Estes 1995; Meduri 1995; Garrouste-Orgeas 1997; Mojon 2002; Sole 2002; Azoulay 2006). It has also been suggested that the major cause of VAP might be aspiration of either microorganisms from the oropharynx or fragments of biofilm (Klarin 2008). In a prospective cohort study involving 16 ICUs, aspiration was recognised to be an independent risk factor for the development of VAP (Cook 1998).

As a result of the association between microaspiration and VAP, a number of interventions have been investigated in order to reduce VAP incidence. These include selective oropharyngeal decontamination (SOD) with topically applied antibiotics and antiseptics, toothbrushing and dental prophylaxis, etc (Yoshida 2001; Coleman 2002; Loeb 2003; Seguin 2006; Chan 2007). Antibiotics have been used as a tool for selective digestive tract decontamination (SDD) and/or selective oropharyngeal decontamination (SOD) (Abele-Horn 1997; de Smet 2009) aiming at reducing microbial colonisation and VAP of ventilated patients. Results from three randomised controlled trials (Pugin 1991; Abele-Horn 1997; de Smet 2009) showed that SDD and/or SOD reduced the rate of microbial colonisation as well as VAP incidence with a lesser requirement for systemic antibiotics during care. Such an approach has also shown evidence of cost-effectiveness (van Nieuwenhoven 2004). Nevertheless a recent systematic review indicated that oral decontamination with antibiotics did not show evidence of a statistically significant reduction of VAP rates, with risk ratio (RR) = 0.69, 95% confidence interval (CI) 0.41 to 1.18 (Chan 2007). However, the same review suggested that decontamination with oral antiseptics can show a statistically significant reduction of VAP rates, with RR = 0.56, 95% CI 0.39 to 0.81 (Chan 2007).

Oral hygiene and a subsequent reduction in the colonisation of dental plaque is increasingly considered to be an important strategy in preventing VAP. The Center for Disease Control and Prevention of the USA recommended the development and implementation of a comprehensive oral hygiene programme for patients at risk of hospital-acquired pneumonia (Tablan 2004). The evidence-based practice suggested that standardisation of oral hygiene care practices could improve the oral health of critically ill patients (DeRiso 1996; Stiefel 2000; Houston 2002; O' Reilly 2003). However, research-based protocols for providing oral care in ICUs are still rare (Abbott 2006; O'keefe-McCarthy 2006).

A systematic review in Chinese showed that some mechanical oral hygiene care methods, antiseptics and nursing educational programmes in China had greater effectiveness than routine oral care in improving health status of dependent patients (Bai 1995; Lai 1997; Zhao 1998; Chen 2001; Hong 2001; Hou 2001; Li 2001; Xue 2001; Cao 2002; Huang 2003; Li 2003; Sun 2003; Wang 2003; Jiang 2004; Shi 2004). Fundamental nursing practices such as hand hygiene, semi-recumbent positioning of patients, subglottal suctioning and reducing dental plaque colonised with respiratory pathogens are thought to play a critical role in minimizing the incidence of VAP.

Therefore, whilst a number of oral interventions have been studied, their effectiveness is not clear. The goal of this review is therefore to systematically review all relevant publications concerning oral care to determine the best evidence for prevention of VAP.

OBJECTIVES

To assess the effect of oral hygiene care on ventilator associated pneumonia (VAP) in critically ill patients receiving mechanical ventilation in hospital settings.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled clinical trials on this topic will be included in the review.

Types of participants

Critically ill patients receiving mechanical ventilation in hospital.

Types of interventions

Oral care interventions, such as nurse-assisted toothbrushing, oral and pharyngeal cavity rinse, decontamination with antibiotics or antiseptics. These will be compared with no oral care or different types of oral care interventions.

Types of outcome measures

Primary outcomes

1. Incidence or prevalence of ventilator associated pneumonia (VAP).
2. Mortality.

Secondary outcomes

1. Colonisation of dental plaque, saliva, oropharyngeal mucosa or endotracheal aspirates by VAP-associated organisms.
2. Oral health indices such as gingival index, plaque index, bleeding index, periodontal index etc.
3. Systemic antibiotic use.
4. Economic data.
5. Duration of mechanical ventilation and/or intensive care unit stay.
6. Any adverse outcomes of the interventions.
7. Care-givers preferences for oral hygiene care.

Search methods for identification of studies

Electronic search

A range of related information including indexed published articles, grey literature, conference abstracts and unpublished data relevant to this topic will be searched by Huixu Xie and Ping Wang in China, checked and supplemented by Zongdao Shi and other authors of the review. If it is necessary, assistance will be applied for from Anne Littlewood who is the trials search co-ordinator of the Cochrane Oral Health Group.

The following electronic databases will be searched:

- Cochrane Oral Health Group's Trials Register
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* current issue)
- MEDLINE via OVID (1950 to present)
- EMBASE via OVID (1980 to present)
- CINAHL via EBSCO (1958 to present)
- LILACS (1982 to present)
- Chinese Biomedical Literature Database (1978 to present)
- China National Knowledge Infrastructure (1994 to present)
- Chinese Medical Library (1995 to present)
- OpenSIGLE (1990 to 2005).

Full search strategies for each database will be developed accordingly. For general databases such as MEDLINE, the search strategy will include three sets of terms: the target population, i.e. critically ill patients receiving mechanical ventilation, the target disease i.e. VAP, and the target intervention(s) i.e. oral hygiene care. A combination of subject terms selected from the controlled vocabulary or thesaurus with a wide range of free-text terms will be used to ensure all relevant records will be included.

The search strategy will combine the subject search with the Cochrane Highly Sensitive Search Strategy for identifying randomised controlled trials in MEDLINE (as published in chapter 6.4.11, box 6.4.c in the *Cochrane Handbook for Systematic Reviews of Interventions*, version 5.0.2, updated September 2009, Higgins 2009). The search strategy for MEDLINE is presented in Appendix 1.

Handsearching

Medical, dental, critical care and nursing journals which may contain possibly relevant articles will be handsearched by Huixu Xie and Ping Wang in China, and by Linda Ng in Australia. In addition, the trial search co-ordinators of the Cochrane Oral Health and Acute Respiratory Infections Groups will be contacted regarding handsearching already performed of journals or conference proceedings relevant to this topic. The following medical, dental and nursing journals in Chinese will be handsearched:

- *Chinese Journal of Stomatology* (1953 to present issue)
- *Journal of Stomatology* (1981 to present issue)
- *West China Journal of Stomatology* (1983 to present issue)
- *Journal of Practical Stomatology* (1985 to present issue)
- *Journal of Clinical Stomatology* (1985 to present issue)
- *Journal of Comprehensive Stomatology* (1985 to present issue)
- *Journal of Modern Stomatology* (1987 to present issue)
- *Chinese Journal of Conservative Dentistry* (1991 to present issue)
- *Journal of Maxillofacial Surgery* (1991 to present issue)
- *SHSngHSi Journal of Stomatology* (1992 to present issue)
- *Chinese Journal of Dental Material and Devices* (1992 to present issue)
- *Beijing Journal of Stomatology* (1993 to present issue)
- *Chinese Journal of Dental Prevention and Treatment* (1993 to present issue)
- *Chinese Journal of Orthodontics* (1994 to present issue)
- *Chinese Journal of Implantology* (1996 to present issue)
- *Journal of Qilu Nursing* (1995 to present issue)
- *Journal of Nursing* (1995 to present issue)
- *Journal of Practical Medical Techniques* (1994 to present issue)
- *Modern Nursing* (1995 to present issue)
- *Journal of Nurses Training* (1986 to present issue)
- *Chinese Journal of Nursing* (1954 to present issue)
- *Chinese Journal of Practical Nursing* (1985 to present issue)
- *International Journal of Nursing* (1980 to present issue).

Reference lists

Reference lists of relevant original articles and systematic reviews will be used to supplement the search.

Language

All relevant publications will be included, irrespective of language. Articles in languages other than English and Chinese will have methodology and results sections translated using local resources and assistance from the Cochrane Oral Health Group.

Unpublished studies

An online search will be made for unpublished studies from the International Standard Randomised Controlled Trial Number Register (ISRCTN Register), the World Health Organization International Clinical Trials Registry Platform Search Portal (WHO ICTRP), and Current Controlled Trials (*meta*Register of Controlled Trials (*m*RCT)). Letters will be sent to the first author of the included studies, other experts well-known in this field, and pharmaceutical companies of oral hygiene products requesting unpublished relevant information.

Data collection and analysis

Study selection

The title and abstract of each article obtained from the searches will be examined independently by two review authors (Ping Wang and Huixu Xie). If they disagree with the inclusion of any study, a group discussion with Zongdao Shi and E Chen will be held to resolve the problem. If there is still disagreement, Linda Ng, Mervyn Singer and Ian Needleman will be contacted to reach consensus. The extra duplicate reports of the same studies and other irrelevant reports will be excluded. Multiple reports of the same study will be linked and only the one with complete follow-up data will be selected.

Full text of any potentially relevant reports will be gathered and examined in detail to determine whether the study fulfils eligibility criteria. Any queries will be raised with the lead authors for clarification.

Data extraction

Two review authors (Huixu Xie and Ping Wang) will independently and in duplicate extract data from the included studies and complete the data extraction forms. Data extraction will include the following items:

(1) General characteristics of the study:

Authors, year of publication, country where the study was performed, funding, language of publication, total study duration, citation, contact details for the authors and identifier.

(2) Specific trial characteristics:

Basic study design characteristics: sequence generation, allocation sequence concealment, blinding and outcome data will be collected and presented in the 'Characteristics of included studies' table. Verbatim quotes on these issues from original reports will be adopted.

Participants: total number, setting, age, sex, country, ethnicity, socio-demographic details (e.g. education level), diagnostic criteria of VAP and the presence of co-morbid conditions will be collected.

Interventions: details of all experimental and control interventions, such as routes of delivery, dosages of the drugs being used, format for oral hygiene care, timing and duration of the oral care procedures, etc will be collected. In addition, information on co-interventions will also be collected.

Outcomes: incidence of pneumonia or other respiratory diseases, mortality (directly and indirectly attributable), adverse outcomes resulting from the interventions, changes of the quantities of pathogenic microorganisms from culture of oral materials, changes of the indices measuring plaque, inflammation of the gum or periodontal pathology, etc will be collected. All outcome variables will be specified in terms of definition, timing, units and scales.
Other results: summary statistics, sample size, key conclusions, comments and any explanations provided for unexpected findings by the study authors will also be collected. If data are unclear, the lead authors will be contacted for clarification.

Assessment of risk of bias and validity assessment of included studies

Judgement of validity of included studies

Each included study will be initially assessed by two review authors (Huixu Xie and Ping Wang) according to the criteria suggested by the *Cochrane Handbook for Systematic Reviews of Interventions* (version 5.0.2, updated September 2009, Higgins 2009). In particular, the study's validity will be judged on the basis of the following:

- Method of sequence generation and allocation concealment
- Blindness of the outcome assessment
- Completeness of follow-up and details of how drop outs or withdrawals were managed and reported
- Whether a sample size calculation was reported and the means used to calculate sample size
- Whether groups were treated identically other than the named intervention
- Whether diagnostic criteria/methods for the VAP were clearly defined and appropriate
- Whether confounders related to medical status and medical care were evaluated and managed (if necessary, an expert in this field will be consulted)
- Whether the outcomes were fully reported
- The level of care-giver training on how to provide the intervention
- The level of outcome assessor training and calibration.

Risk of bias assessment of included studies

Risk of bias assessment will be made according to the following items.

(1) Was the allocation sequence adequately generated?

- Low risk of bias: a random component in the sequence generation process was reported.
- High risk of bias: a random component in the sequence generation process was not reported, or sequence generated by odd or even date of birth, or allocation by judgement of the clinician.
- Uncertain risk of bias: insufficient information about the sequence generation process to permit judgement of 'Yes' or 'No'.

(2) Was allocation adequately concealed?

- Low risk of bias: concealed allocation was completed by clearly described methods so that either participants or investigators could not foresee assignment.
- High risk of bias: participants or investigators could possibly foresee assignments on enrolling participants.
- Uncertain risk of bias: insufficient information to permit judgement of 'Yes' or 'No' of concealment.

(3) Was knowledge of the allocated intervention(s) adequately prevented during the study?

- Low risk of bias: blinding of participants and key study personnel, or the outcome measurement was not likely to be influenced by lack of blinding.
- High risk of bias: no blinding of participants and key study personnel, or the outcome measurement was likely to be influenced by lack of blinding.
- Uncertain risk of bias: insufficient information to permit judgement of 'Yes' or 'No' of blinding.

(4) Were incomplete outcome data adequately addressed?

- Low risk of bias: there were no missing outcome data, or the missing data did exist but not have the impact to influence the observed clinical effects.
- High risk of bias: missing outcome data did exist and have an impact on observed clinical effects.
- Uncertain risk of bias: judgement of 'Yes' or 'No' of missing data and its effects could not be clearly determined.

(5) Are reports of the study free of any suggestion of selective outcome reporting?

- Low risk of bias: all outcomes of interest in the study have been reported in a pre-specified way by the authors.
- High risk of bias: not all outcomes of interest in the study have been reported in a pre-specified way by the authors.
- Uncertain risk of bias: insufficient information to permit judgement of 'Yes' or 'No' of this question.

(6) Was the study apparently free of other problems that could place it at risk of bias?

- Low risk of bias: the study appears to be free of other risk of bias.
- High risk of bias: there is at least one important risk of bias existing in the study.
- Uncertain risk of bias: insufficient information to assess whether other important risk of bias exists.

An explicit judgement about the risk of bias for important outcomes both within and across studies should be made according to the following criteria.

Summary assessments of risk of bias for each study

- Low risk of bias: there was a low risk of bias for all key domains or any plausible bias was unlikely to seriously alter the study results.
- Unclear risk of bias: there was an unclear risk of bias for one or more key domains or any plausible bias raised some doubt about the study results.
- High risk of bias: there was a high risk of bias for one or more key domains or any plausible bias might seriously weaken confidence on the results.

Summary assessments of risk of bias for important outcomes across studies

- Low risk of bias: all outcome information was from studies at low risk of bias.
- Unclear risk of bias: most outcome information was from studies at low risk and some from studies with unclear risk of bias.
- High risk of bias: the proportion of information from studies at high risk of bias did sufficiently affect the interpretation of results.

The agreement on rating scores in half of the included studies between two review authors (Huixu Xie and Ping Wang) will be evaluated using the Kappa statistic in the pilot study. Further discussion will be conducted between both review authors if there is any divergence on the judgement. If disagreement still exists, group discussion with Zongdao Shi and E Chen will be conducted. In case the discussion does not resolve the disagreement, an email consultation with Linda Ng, Mervyn Singer and Ian Needleman will be carried out.

Data analysis

Measures of treatment effect

This review will measure the effect of oral hygiene care on the incidence of VAP and other related clinical outcomes such as oral health status for critically ill patients with mechanical ventilation. Factors having a modifying role on the magnitude of the effects will be investigated, if possible, by further analyses.

For dichotomous data

For dichotomous outcomes the estimates of effect of an intervention will be expressed as risk ratios (RR) and their 95% confidence intervals.

For continuous data

For continuous outcomes the weighted mean difference will be used to estimate the effects of interventions. If different scales are used then standardised mean differences will be calculated.

Unit of analysis issues

The patient will be the unit of analysis. Indices such as those measuring status of plaque and gingivitis will be managed as mean values for the patient. Episodes of care will also relate back to individual patients.

Dealing with missing data

The lead author of the study with missing data will be contacted. If contact proves unsuccessful, this could be dealt with by making assumptions about the data using the methods described in the section for calculating missing standard deviations of the *Cochrane Handbook for Systematic Reviews of Interventions*, version 5.0.2, updated September 2009. An intention-to-treat analysis will be conducted wherever it is possible. The potential impact of missing data on the results will be addressed in the discussion section of the review.

Assessment of heterogeneity

To determine if there is heterogeneity among studies, the Chi^2 test for heterogeneity with a 10% level of significance as the cut-off will be applied. The impact of heterogeneity will be quantified using the I^2 statistic. The thresholds for interpretation, as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* (version 5.0.2, updated September 2009), will be used to evaluate the size of I^2. If heterogeneity is present, this will be investigated by undertaking a subgroup analysis based on such items as criteria for risk of bias, time of publication, baseline status, diagnostic criteria for VAP, methods and quality of interventions, dental training of the oral care-givers, etc.

Assessment of reporting biases

To detect publication bias, a funnel plot will be generated. If there are at least 10 studies in any comparison, additional tests for funnel plot asymmetry will be conducted (Egger M 1997).

Data synthesis

Meta-analysis

Meta-analysis will be attempted if the same comparison and same numerical outcomes are reported across studies. Risk ratios will be used for dichotomous data and weighted mean differences (or standardised mean differences for different scales) for continuous

data. Random-effects models will be used providing there are four or more trials.

Subgroup analysis

Subgroup analyses will be conducted if it is necessary, such as based on those characteristics as types of oral care methods or sorts of decontamination agents. Results of subgroup analyses will be interpreted cautiously.

Sensitivity analysis

To determine whether the conclusions concerning overall effects of oral hygiene care are robust, the following sensitivity analyses are planned: exclusion of studies with questionable diagnostic criteria for VAP, changing the arbitrarily defined thresholds for some selected variables, excluding studies with high risk of bias, changing assumptions about missing data, changing from a fixed-effect model to a random-effects model, or vice versa. Reporting of sensitivity analyses in the review will be presented in a summary table. If the results do not change substantially in sensitivity analyses, then the conclusion would be regarded as stable with a higher degree of certainty. Where sensitivity analyses identify particular factors that greatly influence the conclusions of the review, the plausible causes of the uncertainties will be explored, and the results of the review will be interpreted with caution.

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We are extremely grateful to Anne Littlewood, Trials Search Coordinator, Cochrane Oral Health Group for refining the search strategy in MEDLINE, providing search strategies for CINAHL via EBSCO, LILACS and OpenSIGLE, and assistance with literature searching. We would also like to acknowledge Luisa Fernandez Mauleffinch and Anne-Marie Glenny for their support and help with the protocol, and referees Michael Jan Shaw and Frank Scannapieco for their evaluation of the protocol.

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. MEDLINE via OVID search strategy

1 CRITICAL ILLNESS/
2 (critical$ adj5 ill$).mp.
3 ((dependent or dependant) adj5 patient$).mp.
4 INTENSIVE CARE/
5 ("intensive care" or intensive-care or "critical care" or critical-care).mp.
6 (ICU or VAP).ti,ab.
7 nosocomial infection.ti,ab.
8 PNEUMONIA, VENTILATOR-ASSOCIATED/
9 pneumonia.ti,ab.
10 ((intubated or ventilated) adj5 patient$).mp.
11 or/1-10
12 ORAL HEALTH/
13 exp ORAL HYGIENE/
14 exp DENTIFRICES/
15 MOUTHWASHES/
16 SALIVA ARTIFICIAL/
17 DECONTAMINATION/
18 ("oral care" or "oral health" or oral-health or "mouth care" or "oral hygien$" or oral-hygien$ or "dental hygien$or decontamination").ti,ab.
19 (mouthwash$ or mouth-wash$ or mouth-rinse$ or mouthrinse$ or "oral rinse$" or oral-rinse$ or "artificial saliva" or "saliva substitute$" or "denture clean$" or toothpaste$ or dentifrice$ or toothbrush$ or chlorhexidine$ or betadine$ or triclosan$).mp.
20 PERIODONTAL DISEASES/
21 periodont$.mp.
22 or/12-21
23 11 and 22

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CONTRIBUTIONS OF AUTHORS

Zongdao Shi: conceiving, designing and co-ordinating the review with primary responsibility for the statistics/methodology and writing draft of the review.

Huixu Xie and Ping Wang: undertaking searches, screening search results, appraising quality of papers, extracting data, entering data into RevMan and interpretation of data, writing results sections, participating in the discussion.

E Chen and Yan Wu: appraising quality of those papers for which Huixu Xie and Ping Wang disagree with some points, participating in the discussion.

Linda Ng: electronic and handsearching especially for the nursing journal articles and abstracts of nursing conference proceedings, providing consultation for screening search results, appraising quality of papers and interpretation of the meta-analysis, revising draft of the review.

Helen V Worthington, Mervyn Singer and Ian Needleman: providing professional expertise in all stages of the systematic review, revising drafts of the protocol and the review before submission.

DECLARATIONS OF INTEREST

None known.

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