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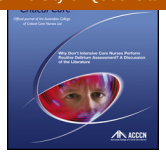

Best nursing review paper

Efficacy and safety of normal saline instillation and paediatric endotracheal suction: An integrative review

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ABSTRACT

Objective: To synthesise research findings regarding the efficacy and safety of normal saline instillation (NSI) during endotracheal suction in the paediatric intensive care unit.
Data sources: The Cochrane Library, PROSPERO, the National Health Service Centre for Reviews and Dissemination, PubMed and Cumulative Index to Nursing and Allied Health (CINAHL) databases were systematically searched. Subject headings included "suctioning, endotracheal", "suction", "sodium chloride", "normal saline" and "paediatrics". Additional references were sourced from hand searches of journal article reference lists and Google Scholar.
Method: An integrative, systematic approach was used to qualitatively synthesise study results in the context of paediatric intensive care nursing practice. Data were extracted using a standardised data extraction form. Quality assessment was performed independently by two reviewers.
Results: Three studies met pre-defined inclusion criteria. Quality of all study methods was 75% on the Mixed Method Appraisal Tool, although reporting quality varied. Overall, there was a scarcity of high quality evidence examining NSI and paediatric endotracheal suction. Outcome measures included oxygen saturation (SpO_2), serious adverse events (author/s defined) and ventilation parameters (author/s defined). Endotracheal suction with NSI was associated with a transient decrease in blood oxygen saturation; research protocols did not include interventions to mitigate alveolar derecruitment. Studies were not powered to detect differences in endotracheal tube (ETT) occlusion or ventilator associated pneumonia (VAP).
Conclusion: NSI was associated with a transient decrease in oxygen saturation. In children with obstructive mucous, NSI may have a positive effect. Practices which maximise secretion removal and mitigate the negative physiological interactions of ETS have been poorly evaluated in the paediatric population. High quality, powered, clinical trials are needed to determine the safety and efficacy of normal saline instillation and to inform clinical practice.

1. Introduction

Each year 50% of children (<18years) admitted to Australian and New Zealand intensive care units require intubation and mechanical ventilation.[1,2] Placement of the endotracheal tube (ETT), to facilitate mechanical ventilation impairs mucociliary clearance.[3] In combination with humidification of inspired gas, endotracheal suction (ETS) is a key secretion management technique in the

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paediatric intensive care unit (PICU).[4] Performed to maintain airway patency and prevent retained respiratory secretions,[5] ETS is not without complications. The adverse clinical effects of ETS may include hypoxia and atelectasis due to pulmonary derecruitment; hypotension related to increased intrathoracic pressure and reduced cardiac output; and bradycardia associated with vagal nerve stimulation.[6–8]

The effectiveness of ETS is impacted upon by the hydration of the airway mucous. If there is insufficient humidification of ventilator gas or obstructive mucous plugs the efficacy of ETS is reduced.[9] Normal saline instillation (NSI) with paediatric ETS is a long standing nursing intervention which has been practised for more than two decades.[10–12] NSI as an intervention is postulated to have several effects including: hydrating and mobilising airway secretions, stimulating the cough response and lubricating the suction catheter.[13,14] NSI is thought to enhance the removal of mucous plugs and reduce surface tension in the distal airways.[10,15] However, the majority of these claims are untested and effect of NSI on secretion rheology and airway mucosa is not clearly articulated in the literature.

2. Problem identification

In general, the prevalence of NSI use as an intervention with ETS in the PICU is largely unknown. Data obtained from a 1996 cross-sectional survey found more than 96% of PICU nurses used NSI as an intervention with ETS.[10] However, current usage rates are not published. Newer research has found NSI usage to be significantly associated with open suction when compared with closed suction (1397 vs 572, $p < 0.01$).[5] However given open suction is associated with improved secretion clearance,[16] and thick secretions are a key indication for NSI in the PICU,[17] the findings of this research are not surprising.

In adults, a number of studies explore NSI efficacy in patients without lung disease. In these studies researchers argue that NSI has a deleterious effect on oxygen saturation and does not increase secretion yield.[18–20] Consequently current ETS guidelines recommend the discontinuation of NSI,[13,21] however the application of these guidelines in the clinical environment have been poorly explored.

In paediatrics the benefits of NSI with ETS is uncertain and widely debated.[22] The generalisability of adult recommendations to the PICU population is problematic. Mechanically ventilated children have different diagnoses to adults, specifically a high incidence of respiratory disease and ETTs with small internal diameters which may be easily occluded by obstructive mucous.[17] In this population NSI may be both warranted and beneficial. The aim of this review was to synthesise research findings regarding the efficacy and safety of NSI as an intervention to improve pulmonary outcomes in intubated paediatric patients undergoing ETS.

3. Method

Due to the lack of randomised clinical trials (RCT) and the variability of study design an integrative approach was used to qualitatively synthesise research findings. The integrative method allows for the combination of diverse study methodologies, providing a comprehensive review of the topic as it pertains to clinical practice. The format for the review was based on Whittemore and Knafl's[23] five stage integrative review process of: problem identification, literature search, data evaluation, data analysis and presentation of findings. The use of this systematic process enhances review rigor.

3.1. Search strategy

A search of The Cochrane Library, PROSPERO and the National Health Service Centre for Reviews and Dissemination identified no reviews or registered protocols investigating the topic. A search of the National Institute of Health Clinical Trials, Australian and New Zealand Clinical Trials Registry and the World Health Organization International Clinical Trials Registry identified no clinical trials examining NSI and paediatric ETS. A systematic search was conducted in United States National Library of Medicine National Institutes of Health (PubMed), Cumulative Index to Nursing and Allied Health (CINAHL) and Google Scholar in February and repeated in April 2016. Following consultation with a Health Librarian, the review aim was broken into concepts which formed the basis of the search strategy. The PRESS guidelines were used to further refine the search strategy.[24] Search terms were developed for each concept and Boolean operators OR, AND and NOT were applied, Boolean operators were consistent across search services. Proximity operators were not applied. Subject headings (MeSH or CINAHL headings) were database specific and included "suctioning, endotracheal", "suction", "sodium chloride", "normal saline", "paediatrics" and "pneumonia, ventilator-associated"; some minor/subheadings were included. Key word and text word searching included pediatric; paediatric; infant; children; secretions and instillation. Truncation and wildcard symbols were database specific and included: CINAHL wildcard # (p#ediatric) and PubMed truncation * (paed* OR ped*). Truncation and wildcard symbols were not applied in google scholar searches. An English language limiter was applied to the search. Filter terms not applied within the search strategy included publication date and outcome measures. Database searches were supplemented by hand searches of article reference lists.

3.2. Selection criteria

Studies were included in the review upon satisfying predefined inclusion criteria: (1) paediatric patients aged 0–18years; (2) ETT airway in situ; and (3) investigated a clearly defined ETS solution intervention. Outcomes were not defined a priori due to the lack of evidence and desire for an inclusive review. A minimum level of acceptable study design was observational with no comparator as described by Merlin et al.[25] 'hierarchy of evidence for intervention studies'. No restrictions were placed on patients' principal diagnosis. Articles were excluded if: (1) study participants were adult or neonates; (2) paediatric data were not desegregated; (3) examined artificial airways other than ETT; (4) examined normal saline use in combination with another intervention; or (5) were not published in English.

3.3. Data extraction and assessment of study quality

Study data were extracted using a standardised data extraction form. Data extracted included study aim, setting, method, participant population, sample size, intervention and outcome measure and measure of effect (if empirical). The Mixed Methods Appraisal Tool (MMAT) as described by Pluye et al.[26] was used to appraise the methodological quality of each source. Comprised of screening questions and methodology specific criterion, the MMAT is a validated critical appraisal tool that facilitates systematic assessment for integrative reviews with studies using difference research methods.[27] Quality assessment for included studies was completed independently by JO and MM. Following discussion, any unresolved variances were resolved with the third author (MC) through discussion and consensus. Risk of bias assessment was performed on intervention and observational studies, guided by The Cochrane Collaboration's tool for assessing risk of bias.[28] No study was

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excluded based on minimum risk of bias or level of quality due to the lack of evidence and desire for an inclusive review.

4. Results

4.1. Search outcome

Fig. 1 outlines the flow of articles included in the review in accordance with thePreferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.[29] The systematic search yielded 551 citations. The potential relevance of each citation was examined, and 501 citations were excluded as irrelevant. The full papers of the remaining 50 citations were assessed to select articles directly concerned with NSI and paediatric ETS. Three articles were included and 47 articles were excluded based on the inclusion and exclusion criteria.

The studies reported on a combined total of 8781 ETS episodes, in 315 PICU patients, aged between 3.9 days and 18 years. Participants required intubation and ETS for postoperative care, respiratory disease and other medical/surgical conditions. Studies originated from Australia[5] and North America[17,30] and were published between 2003 and 2016. Two studies were prospective observational studies[5,17] and the remaining study was a randomised control trial (RCT).[30]

The volume of NSI interventions varied between study protocols. Two studies applied a predefined volume for all subjects: <0.5 mL[5] and 1–2 mL[17]; whilst Ridling et al.[30] used dose adjustment based on age—1 yr: 0.25–0.5 mL, 1–8yrs: 0.5 mL, >8yrs: 1–2 mL. One study outlined an ETS protocol with indications for NSI use.[17] Indications included thick secretions, medical officer request, suspected occlusion of endotracheal tube and no secretions yielded without NSI.[17] Suction methods included open suction[30] or a combination of both open and closed techniques.[5,17] Studies measured oxygenation and SAE as primary and secondary outcomes. Individual study summaries are outlined in Table 1.

4.2. Critical appraisal and assessment of risk of bias

All studies were single centre. Clinical trial registration numbers were not provided. No study undertook or was informed by feasibility work. Sample sizes ranged from 24 to 229. No study reported sample size calculations. One study defined the minimum clinically important difference as a 20% decrease in oxygen saturation from baseline.[5] All studies received a score of 75% for their methodological quality on the MMAT.[5,17,30] In all studies, participant eligibility criteria and outcome variables were clearly defined. Studies did not mask treatment allocation due to practicality constraints. No study discussed reporting frameworks such as the CONSORT (clinical trial) or STROBE (observational) checklists. A diagram of study flow was not included in the one RCT.[30]

A summary of studies risk of bias assessment is presented in Table 2.[28] Overall, studies had a high risk of bias, including selection and information bias. Further, there was a high risk of bias for data analysis with only two studies using an intention to treat approach.[5,30] Patient heterogeneity required control for a number of covariates including severity of illness, diagnosis, ETT size and age. Estimate of mortality scores were reported in two studies using the Paediatric Index of Mortality 2[17] and Pediatric Risk of Mortality (PRISMIII).[30] No study stratified patients according to diagnosis. One study included respiratory comorbidity as an explanatory variable in a regression analysis.[17] One study conducted subgroup analyses (cardiac and respiratory).[5] The RCT conducted multiple *t* test comparisons with no adjustment of alpha value.[30] Study limitations were generally reported. Owen et al.[17] reported the proportion of missing data to be estimated at 50% in both study arms. Incomplete reporting of sample characteristics,[5] diagnostic groups and baseline comparison of group characteristics[17] was identified.

4.3. Oxygenation

Oxygenation saturation (SpO_2) measured by pulse oximeter was the primary outcome measure in two studies.[17,30] Owen et al.[17] defined oxygen desaturation as ≤90% or 5% below pre-suction SpO_2 baseline. In all studies patients' pre-suction baseline SpO_2 were compared with post ETS SpO_2. SpO_2 was measured at four time points immediately post ETS[17] and at 1, 2[30] and 10 min post ETS.[17,30] In comparison to the control (no NSI), NSI with ETS was associated with a statistically significant difference in SpO_2. Immediately post ETS (occurrence of desaturation event, 13.5% vs 26%, $p < 0.001$,[17]); 1 min post ETS (change from baseline, 1.5% vs 5.7%, $p = 0.013$[30]) and 2 min post ETS (change from baseline, 1.0% vs 4.8%, $p = 0.005$[30]). Persistent desaturation was not evident at the 10 min measurement in either study ($p = 0.52$,[30] $p = 0.27$[17]). Participant groups were comparable with regard to age and diagnosis in one study.[30] Control and experimental groups were not comparable in Owen's et al.[17] study due to the purposeful allocation of children with respiratory disease to the NSI intervention study arm.

4.4. Serious adverse events (SAE)

The definition of SAE as the primary[17] and secondary[5,30] outcome measure varied considerably, including VAP,[30] tube occlusion,[5,30] tube dislodgement[5] and a collective: haemodynamic instability, bronchospasm, oxygen desaturation and failure of saturation to return to baseline level.[17] Two studies compared the incidence of SAE in the ETS with NSI and ETS without NSI groups and found no statistically significant difference.[5,30] An association between NSI and incidence of SAE was reported in Owen et al.'s[17] study with an increased SAE odds ratios (OR, 2.78; 95% CI, 1.79–4.32). This study's definition of SAE did not align with the other two studies (see above definition). Incidence rates of VAP per 1000 ventilator days were not provided, in total three patients were diagnosed with VAP (diagnosis criteria not defined) and two ETT occlusion events. The significance of these findings were not discussed and incidence per treatment group not provided.[17] In general studies were not powered to detect statistical significance in this outcome measure.

5. Discussion

This integrative review is the first to synthesise research findings on the topic of NSI intervention with paediatric ETS. Despite only three studies meeting the review's inclusion criteria, the findings of the review capture the current state of knowledge and identifies gaps in the evidence. Oxygenation and SAE were the primary outcomes of included studies.

5.1. Oxygenation

Since the 1990s determining the efficacy of NSI as an intervention on outcomes such as oxygenation has proven challenging. A recognised complication of ETS is pulmonary decruitment, this phenomenon plays a key role in the post ETS hypoxemic event.[31] The application of negative pressure to retrieve respiratory secretions combined with the acute loss of positive end expiratory pressure (PEEP) disrupts normal alveolar mechanics and results in a loss of gas exchange surface area.[31] The contributing role NSI plays in the

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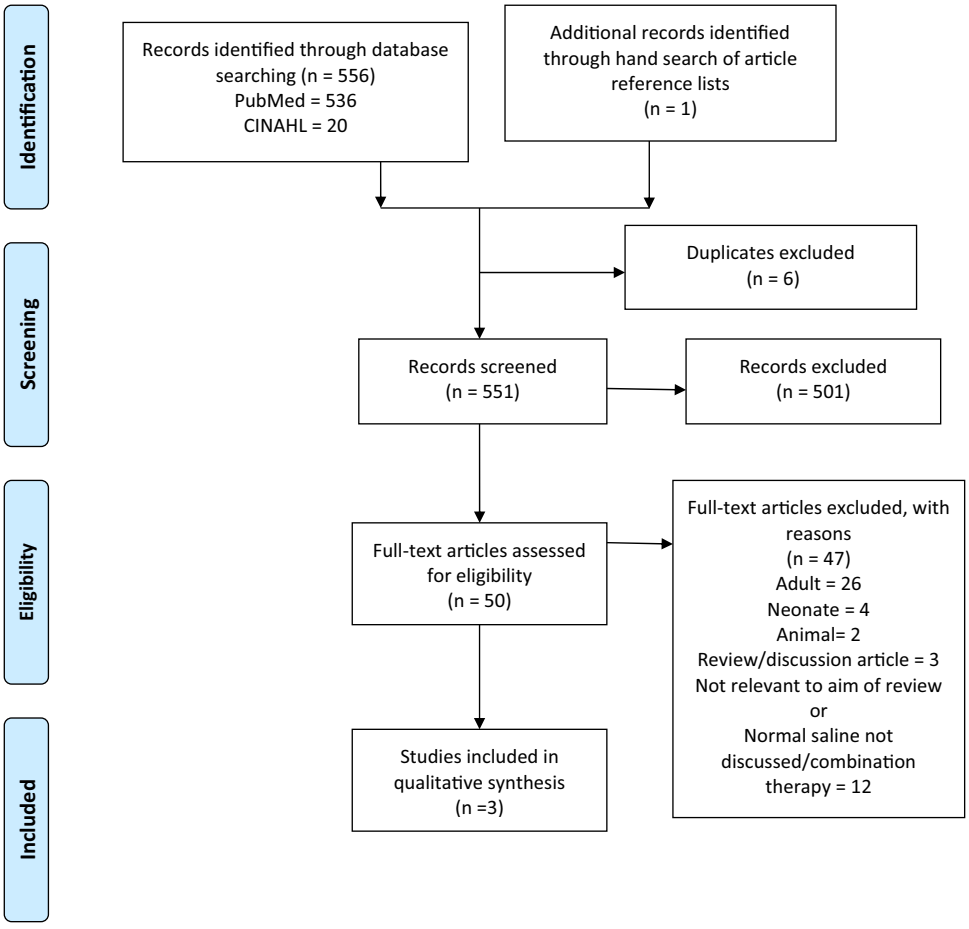

Fig. 1. PRISMA flow chart of study selection.

post suction desaturation has been poorly investigated. Two of the studies included in the review found NSI and ETS to have a transient, negative effect on oxygenation in the short term, however this was not persistent and the clinical significance of the result was not discussed.[17,30]

Few researchers have investigated the inclusion of ETS mitigation strategies with the use of a NSI intervention. Those that do concentrate on preventing or reversing the hypoxemia post ETS.[32,33] Earlier authors suggest transient desaturation events are preventable with pre and post ETS hyperoxygenation,[33] however more recent evidence suggests sustained hyperoxia increases the risk of absorption atelectasis and the formation of free radicals, both of which contribute to the development of an acute lung injury.[34] Consequently, researchers are now considering the role lung recruitment manoeuvrers (LRM) play in reducing suction induced hypoxemia. Ventilation research undertaken by Australian authors in 60 mechanically ventilated children, found the application of a LRM significantly improved end expiratory lung volume in children with 'healthy lungs' and acute lung injury (ALI).[35] Jauncey-Cooke et al.[35] found that by doubling the PEEP for two minutes post ETS in children with an ALI and a p/f ratio >200 (ratio of arterial oxygen partial pressure (PaO_2) to fractional inspired oxygen), oxygenation significantly improved (PaO_2 221.42(46.47)–239.94(63.84) p = 0.014). These findings suggest that the inclusion of a LRM post ETS may minimise the post ETS hypoxemic event, however, further research is needed to determine the optimal management and timing of pre and post-suction manoeuvres in mechanically ventilated children.

5.2. SAE

VAP is a significant adverse patient outcome in mechanically ventilated children. Poor oral hygiene and ETS practices increase a child's risk of retained respiratory secretions being colonised by bacteria.[36] In a recent Australian review researchers Chang and Schibler[37] suggest the prevalence of VAP is as high as 12% of mechanically ventilated children, however local, national and international incidence data and health economy evaluation is lacking. VAP is the second most common type of health care associated infection and is associated with increased prolonged mechanical ventilator days and PICU length of stay.[38,39] In adult populations NSI as an intervention has been shown to reduce the risk of developing microbiologically proven VAP by 54% (95% CI 18%–74%).[40] However, in paediatrics, small underpowered paediatric studies have been unable to detect a significant association between NSI and the incidence of VAP.[5,17,30]

In mechanically ventilated children with impaired mucociliary clearance, mucous plugs can occlude the narrow diameter ETTs. Partial ETT occlusion can result in hypoventilation and atelectasis; total ETT occlusion can lead to cardiopulmonary arrest.[41] In neonatal cohort studies, NSI with ETS has been shown to increase ETT patency by up to 64 h (p = <0.05), however the increase was only significant in ETT size 2.5 mm, with no difference found in paediatric ETT sizes 3.0 mm or 3.5 mm.[15] Interestingly, no study included in the review evaluated secretion clearance as an outcome measure. This could be attributed to the difficultly in accurately measuring respiratory secretions and the variability of PICU admission char-

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Table 1
Included study summaries.

Reference Country	Study design	Population + sample	Intervention	Outcomes	Measure of effect Results	MMAT score
Evans et al.[5]	Prospective cohort	PICU	Open suction ± NSI or closed suction ± NSI[a]	Normal saline usage	• NSI usage more common in open suction compared to closed (1397 vs 572, $p < 0.001$) • No significant difference in comparative adverse events ($p = 0.23$)	75%
Australia		229 patients 6691 ETS episodes		Adverse events[b]		
Owen et al.[17]	Prospective cohort	PICU	1–2 mL NSI	Adverse event:	Hemodynamic instability (1.2% vs 0.3% of ETS, $p = 0.04$); bronchospasm (17.6% vs 7.1% of episodes, $p < 0.001$); oxygen desaturation (26% vs 13.5% of episodes, $p < 0.001$). No significant difference in oxygen saturation recovery 10 min post ETS	75%
USA		62 patients 1986 ETS episodes		Haemodynamic instability Bronchospasm Oxygen desaturation Persistent desaturation		
Ridling et al.[30]	RCT	PICU	NSI	Oxygen saturation	Change in baseline SaO_2 at 1,2,10 min	75%
USA		24 patients	Age adjusted dosing	Tube occlusion	• 1 min: NSI (5.7), no NSI (1.5, $p = 0.013$) • 2 min: NSI (4.8), no NSI (1.0, $p = 0.005$) • 10 min: NSI (0.7), no NSI (0.2, $p = 0.52$)	
		104 ETS episodes		VAP	Nil comparative adverse events	

ETS, endotracheal suction; SaO_2, oxygen saturation; PICU, paediatric intensive care unit; NSI, normal saline instillation; RCT, randomised control trial; VAP, ventilator associated pneumonia.
[a] NSI dose not reported.
[b] This study examined additional outcome measures not reported here specific to open and closed suction.

Table 2
Risk of bias summary.

Clinical trial and observational studies	Adequate sequence generation	Allocation concealment	Blinding (clinician)	Blinding (outcome assessor)	Incomplete outcome data	Predefined outcome measures	Intention to treat analysis
Evans et al.[5]	–	–	–	U	U	+	+
Owen et al.[17]	–	–	–	U	–	+	U
Ridling et al.[30]	+	+	–	U	+	+	+

+ = decrease risk of bias, – = increase risk of bias, U = uncertain.

acteristics which makes the comparison of patients with 'healthy lung' versus respiratory patients problematic.

The lack of standardised ETS technique for mechanically ventilated children reported in the reviewed studies is concerning. In the absence of NSI and ETS clinical practice guidelines, clinicians are forced to rely on subjective assessments and clinical experience to inform their use of NSI in practice. The development of evidence-based clinical practice guidelines is therefore an important clinical objective to guide practice.

5.3. Limitations of the review

Whilst there is no gold standard for 'true' methodological quality of clinical trials or observational studies, the validated MMAT was used to provide an indication of overall study quality. The MMAT is limited to reporting methodological quality.[26] Grey literature was not included in the search strategy which may have introduced a publication bias. Further, the English language limiter may have introduced selection bias.

6. Implications for clinical practice and future research

Our findings can be examined through an evidence based practice lens. In the PICU, nurses base clinical decisions on knowledge, experience and evidence.[42] However, the current lack of evidence has contributed to PICU nurses making NSI and ETS decisions in a vacuum of evidence. To date, researchers investigating paediatric ETS and NSI have predominately applied prospective observational or descriptive methods due to the challenges associated with the design and execution of a RCT within the PICU.[43] However these approaches have disadvantages including inadequate or unreported sample estimates and likely inadequately powered

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studies; poor methods for sequence generation, narrowly defined study populations that are not representative of the population, no evaluation of intervention fidelity and incomplete reporting of outcome data. To overcome these issues future clinical trials need to be conducted with a key focus on a rigorous and high quality research protocol, following a feasibility study. The inclusion of innovative lung recruitment strategies would also provide evidence for clinical practice. The data generated from a quality clinical trial could then be used to inform an ETS and NSI clinical practice guideline. The first step in this process would be to conduct feasibility work to determine sample calculations, identify outcome measures and test research processes including intervention fidelity and research protocols.[44]

7. Conclusion

Research findings regarding the efficacy and safety of NSI during ETS in the PICU were synthesised. We found that NSI as an intervention was associated with a transient desaturation event. However evidence concerning the efficacy of NSI is inconsistent and limited by age or methodological problem. To progress knowledge regarding the benefits and risks of NSI with paediatric ETS, we propose an adequately powered RCT needs to be undertaken to provide definitive information on the safety and efficacy of NSI.

Authors' contributions

Review design: JO, MM, MC; data collection and analysis: JO, MM and manuscript preparation: JO, MM, MC, AS.

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