Nasal Decolonization of Staphylococcus Aureus and the Risk of Surgical Site Infection After Surgery: A Meta-Analysis

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Research

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Abstract

Aim: To assess the effects of nasal decontamination on preventing surgical site infections (SSIs) in people who are S aureus carriers undergoing different types of surgeries.

Methods: Relevant randomized controlled trials (RCTs) were identified through systematic searches of the PubMed, Embase, Web of science, and the Cochrane Library databases. The risk ratios (RRs) and 95% confidence intervals (CIs) were calculated and the effects model was chosen according to the heterogeneity. Subgroup analyses were performed according to different types of surgeries that S aureus carriers were applied.

Results: Twenty RCTs published between 1996 and 2019 involving 10526 patients were included. Pooled results showed that the overall SSIs and pulmonary surgery SSIs presented with a statistical difference in measures of nasal decontamination (RR=0.59 and 0.47, respectively, both p<0.01). However, the associations between nasal decolonization and increased risks of SSIs in orthopedics surgery or cardiovascular surgery remained insignificant in studies.

Conclusion: It seems that nasal decolonization of Staphylococcus aureus may be associated with a reduction of SSI in these patients, especially in patients receiving pulmonary surgeries.

1. Introduction

Staphylococcus aureus, which is normally present in the flora of the human skin and is generally asymptomatic, remains one of the most common drug-resistant pathogens that cause infection in hospitalized patients1 2. Investments in infection reduction have been posed in intensive care units, which has been defined as an “epicenter” of nosocomial infections, by measurements of skin decolonization involving daily chlorhexidine bathing3. The practice was adopted because of evidence that universal decolonization reduces device-associated bacteremia, all-cause bacteremia, and multidrug-resistant organisms3 4. However, the nasal carriage is also unavoidable for endogenous infections and for transmission to other individuals, as the colonization of extra nasal sites often originates from the nasal reservoir5. S. aureus nasal carriage has been extensively studied by numerous studies, as it was reported the most common pathogen associated with a postoperative surgical site infections (SSIs), what remains unclear is the exact source of the pathogen6.

It has been shown that being a nasal carrier of S. aureus is a significant risk factor for developing a SSI7. In this regard, it seems that the number of SSIs acquired in hospitals may be reduced by decolonization of nasal S. aureus carriage on admission8. Special attention was paid to nasal decontamination for the prevention of SSIs in Staphylococcus aureus carriers. The results of several randomized trials in different hospitals or institutions limited by the population and surgery form are still mixed and inconclusive6 9.

The aim of the article is to evaluate the use of nasal decontamination in different types of surgery and give evidence that makes efforts to measure of infection control and prevention.

2. Methods

This study was performed in accordance with the guideline of Preferred Reporting Items for Systematic Reviews and Meta Analyses10 and Cochrane’s Handbook11 guidelines. A prospective protocol was created in advance and uploaded to the PROSPERO online platform.

2.1 Literature search

We searched English articles in PubMed, Embase, Web of science, and the Cochrane Library using combinations of the following terms: (1)Nasal or Nose; (2) Staphylococcus aureus; (3) Mupirocin or Chlorhexidine or Decontamination. We limited the search to human studies published in randomized trials. All databases were searched from the date of inception up to December 20, 2019. The search strategy used in PubMed is shown in Appendix 1.

2.2 Eligibility criteria

Studies were eligible for this review if they met the following criteria: (1) studies should use human originated samples and should be a randomized controlled trial; (2) had to describe the standard microbial isolation and identification; (3) included patients scheduled for surgery without infectious diseases. Reviews, letters, editorials, and studies without randomization were excluded.

2.3 Data extraction and quality evaluation

Data from appropriate studies were pulled out independently by authors and potted into a spreadsheet. Inconsistencies were resolved by unanimity. The data extracted included (1) first author, location, and study design characteristics; (2) procedure characteristics and number, mean age, and gender of patients; (3) methods for screening of nasal S. aureus colonization, and strategies for decolonization for nasal MRSA carriers; and (4) types of surgery and SSI; and (5) total numbers of S. aureus patients and non-colonized patients according to the results of nasal swab examination and the number of patients with SSI in each group after surgeries. Study quality evaluation was performed with the Cochrane risk of bias tool11 which

includes allocation concealment, blinding (patients, caregivers, investigators, data collectors, and outcome assessors), outcome assessment, loss to follow-up (attrition), and the extent of imbalance of the study arms at the beginning of the trial.

2.4 Statistical analyses

We performed a meta-analysis to estimate pooled relative risks (RRs) and 95% confidence intervals (CIs) in STATA version 13.0 (StataCorp, College Station, TX, USA). Heterogeneity was assessed using the I2 statistic, for which an I2 > 50% suggested substantial heterogeneity and vice versa. The effects model was chosen according to the heterogeneity. If I2 was ≤ 50%, we applied the fixed effects model to pool the data. If no evidence on statistical heterogeneity was found, the random effects model was chosen. Furthermore, visual assessment of publication bias was shown using the funnel plot.

3. Results

3.1 Study selection

The study selection process is described in Fig. 1. The initial broad search identified 1271 studies. 681 studies were subjected to abstract review, excluding many reviews, letters, conference abstracts, editorials and laboratory studies. The remaining 30 studies were subjected to full-text review to exclude those with irrelevant subjects or those that did not fully meet the inclusion criteria. Ultimately, 20 randomized-controlled trials were included in the meta-analyses12-31.

3.2 Study characteristics and quality assessment

The characteristics of the included studies are presented in Table 1. The studies were published between 1996 and 2019 and performed in the United States14 17 18 21 24 26, Netherlands16 28–30, and Australia19 23 31. Besides, the quality of included articles according to Cochrane's Book was shown in Fig. 2.

Table 1

	First author	Year	Country	Study design	Types of surgery	Number	Age	Female:Male	Intervention
1	Akira Horiuchi	2006	Japan	RCT	endoscopic gastrostomy	48	73-74	27 vs 21	mupirocin, arbekacin inhalation, and oral sulfamethoxazole/trimethoprim vs untreated
2	Xavier Benoit	2018	Germany	RCT	lung cancer surgery	450	49-79	118 vs 269	chlorhexidine gluconate (CHG) vs placebo
3	Laura E.	2014	American	RCT	lung cancer surgery	365	55.5-77.9	177 vs 188	chlorhexidine vs untreated
4	Guy Shrem	2016	Israel	RCT	cesarean section	568	26.8-37.4	568 vs 0	Mupirocin vs control
5	Albertine J	1998	Netherlands	RCT	orthopedics	100	18 vs 10 ≥70 years)	55 vs 45	Mupirocin vs control
6	Michael Phillips	2014	American	RCT	arthroplasty or spine fusion	1697	19.1–93.2	1022 vs 675	Mupirocin vs iodine
7	Nalini Rao	2008	American	RCT	joint arthroplasty	1377	NA	NA	Mupirocin vs TJA
8	Helena Rosengren	2018	Australia	RCT	dermatological closures	142	55.2-77.4	65 vs 77	cephalexin vs placebo
9	Saleh, K.	2016	Sweden	RCT	dermatological closures	40	45-92	22 vs 18	PHMB-based solution vs sterile water
10	Shuman, A. G.	2012	American	RCT	head and neck surgery	84	57.5-58.14	36 vs 48	topical antimicrobial decolonization vs standard prophylaxis alone
11	Talesh, K. T.	2017	Iran	RCT	head and neck surgery	44	19.7-45.3	NA	Mupirocin vs untreated
12	Yee J Tai	2013	Australia.	RCT	Mohs micrographic surgery	738	64-67	492 vs 246	Mupirocin vs untreated
13	Berg, H. F.	2004	American	RCT	cardiac surgery	296	54.4-72.2	66 vs 230	clarithromycin vs placebo
14	A. Konvalinka	2006	Canada	RCT	cardiac surgery	257	51.7-73.3	37 vs 220	Mupirocin vs placebo
15	Zibari, G. B.	1997	American	RCT	thrombectomized grafts surgery	408	17-81	203 vs 205	vancomycin vs not vancomycin
16	Andenaes, K.	1996	Norway	RCT	orthopedics	339	24	NA	azithromycin vs placebo
17	Bode, L. G. M.	2016	Netherlands	RCT	cardiac surgery	793	NA	NA	Mupirocin vs placebo
18	Kalmeijer, M. D.	2002	Netherlands	RCT	orthopedics	614	48.1-77.3	407 vs 207	Mupirocin vs placebo
19	Kluytmans, J.	1998	Netherlands	RCT	lung cancer surgery	816	NA	NA	chlorhexidine vs placebo
20	Smith, H.	2019	Australia	RCT	Mohs micrographic surgery	1350	51-81	NA	Mupirocin vs untreated

3.3 Nasal decolonization and the risk of overall SSI after surgery

The pooled results from 20 studies12-31 accounting of 10526 patients showed that nasal decolonization may be associated with a significantly decreased risk of overall SSI in patients after surgery (RR = 0.59, 95% CI: 0.38 − 0.90; Fig. 3). Random effects model was chosen to balance the statistical heterogeneity (p for Cochrane's Q test = 0.000, I2 = 75.8%).Thus, further subgroups analyses were posed to illustrate specific relationships.

3.4 Nasal decolonization and the risk of SSI after orthopedics surgery

Three included articles16-18 with 3174 patients reported the SSIs and orthopedics surgery, showing that there was no statistical difference (RR = 0.68, 95% CI: 0.16 − 2.82; Fig. 4). The substantial heterogeneity (p for Cochrane's Q test = 0.009, I2 = 78.8%) was demonstrated with analysis of random

model.

3.5 Nasal decolonization and the risk of SSI after cardiovascular surgery

Four documents24-26 28 enrolled 1754 patients comparing the decolonization in cardiovascular surgeries. No statistical difference was detected in the meta-analysis (RR = 0.33, 95% CI: 0.08 − 1.35; Fig. 5). Statistical heterogeneity (p for Cochrane's Q test = 0.000, I2 = 86.0%) was handled in random model.

3.6 Nasal decolonization and the risk of SSI after pulmonary surgery

Pooled estimates from three studies13 14 30 presented that nasal decolonization related to a significantly decreased risk of SSI in patients after pulmonary surgery (RR = 0.47, 95% CI: 0.30 − 0.73; Fig. 6). Moreover, no significant heterogeneity was detected (p for Cochrane's Q test = 0.20, I2 = 37.9%).

3.7 Publication bias

Funnel plots for the associations between nasal S. aureus decolonization and overall SSI risk are shown in Appendix 2. The funnel plots were symmetric on visual inspection.

4. Discussion

Our systematic review has identified important gaps in the literature on targeted decolonization strategies in Staphylococcus aureus carriers with different types of surgery. The overall SSIs and pulmonary surgery SSIs presented with a statistical difference in measures of nasal decontamination.

In an early meta-analysis of two randomized trials in cardiac surgery patients, limited by the number of studies, the results showed that no clear difference in SSI risk following the use of mupirocin compared with placebo (RR 1.60, 95%CI 0.79 to 3.25)9 25. Moreover, a recent meta-analysis32 reported that nasal MRSA colonization may be associated with increased risks of overall SSI and MRSA-SSI after spine surgeries through seven studies (RR = 2.52 and 6.21, respectively, both p < .001). Furthermore, a prospective, randomized, single-blinded trial, mentioned about SSIs after elective orthopedic surgery, found that no difference in the risk of SSI between the decolonization and control groups in 1318 patients, both in S. aureus carriers and non-carriers33. In light of this, more high-quality trials are needed to help to articulate the relationships among them.

Trojan Horse 34claimed a hypothesis trying to explain SSI pathogenesis, showing that pathogens remote from the SSI area—such as within the teeth, noses, or gastrointestinal tract—can be taken up by immune cells (macrophages or neutrophils) and travel to the wound site where they cause wound infections. This mechanism could be verified in a mice model, which can also explain why some infections occur latently following surgery and are due to organisms not found in the wound at the end of the operation6 35.

Several limitations derived from this systematic review must be acknowledged. First, the number of included randomized studies was small, which prevented us from evaluating the potential influences of strains of S. aureus (e.g hospital-associated MRSA/MSSA, community-associated MRSA/MSSA) or procedure characteristics (different types of eradicating measures) on the association between nasal S. aureus colonization and SSI events. Second, the adverse effects of decolonization (e.g increased risk of drug resistance) had been merely mentioned, which is significant for an appliance.

To conclude, the main pillars of from available evidence, it seems that nasal decontamination may be associated with a reduction of overall SSI and patients with pulmonary surgery. Further studies are needed to validate and propose the specific relationships between host and infection.

Abbreviations

SSIs
surgical site infections,RCTs:randomized controlled trials
RRs
risk ratios, CIs:95% confidence intervals, S. Aureus:Staphylococcus aureus
MRSA
Methicillin-resistant Staphylococcus aureus
MSSA
Methicillin Sensitive Staphylococcus Aureus

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Jia Tang and Jiangjin Hui : Design the research direction, acquisition and interpretation of data, technical procedures, analyzed and interpreted the patient data , drafted the initial manuscript, approved the final manuscript, supervised all phases of the study.

Jing Ma : Acquisition and interpretation of data, technical procedures, drafted the initial manuscript, and approved the final manuscript.

Chen Mingquan : Design the research direction, approved the final manuscript, supervised all phases of the study.

All authors read and approved the final manuscript.

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Figures

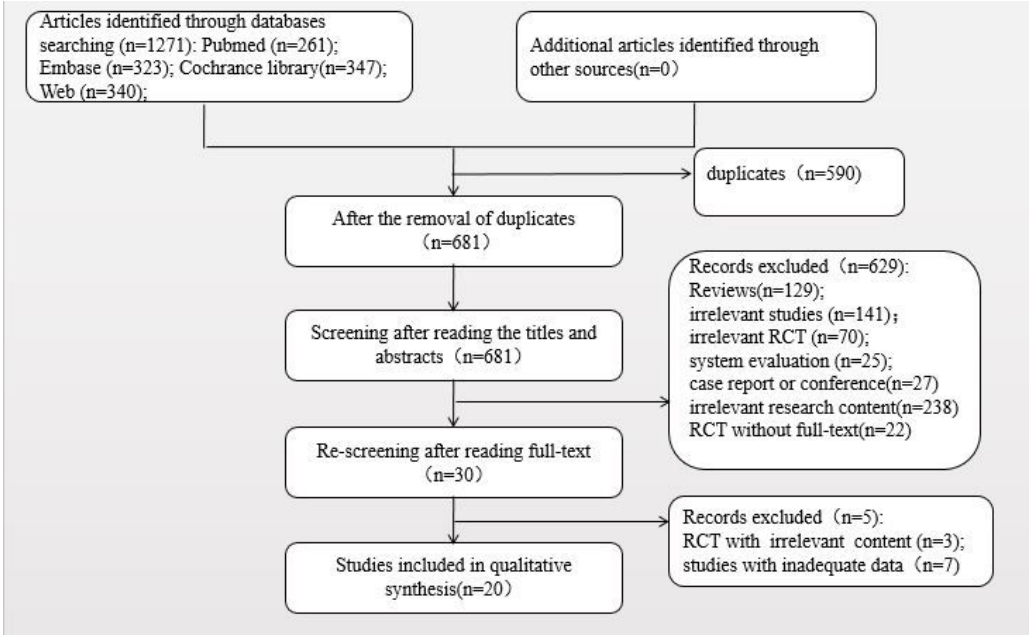

Figure 1

Figure 1

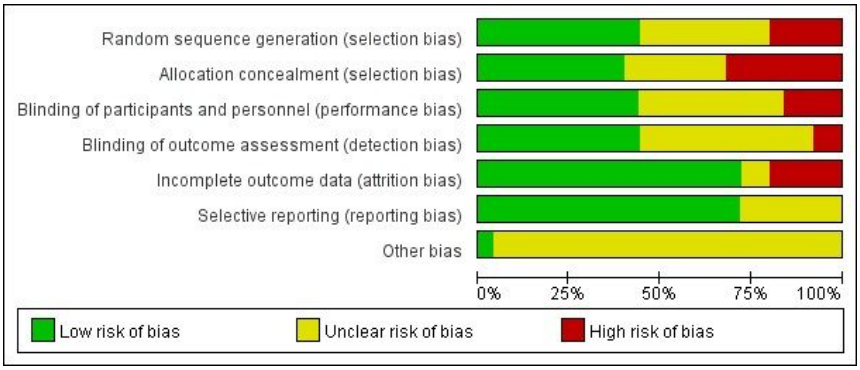

Figure 2

Figure 2

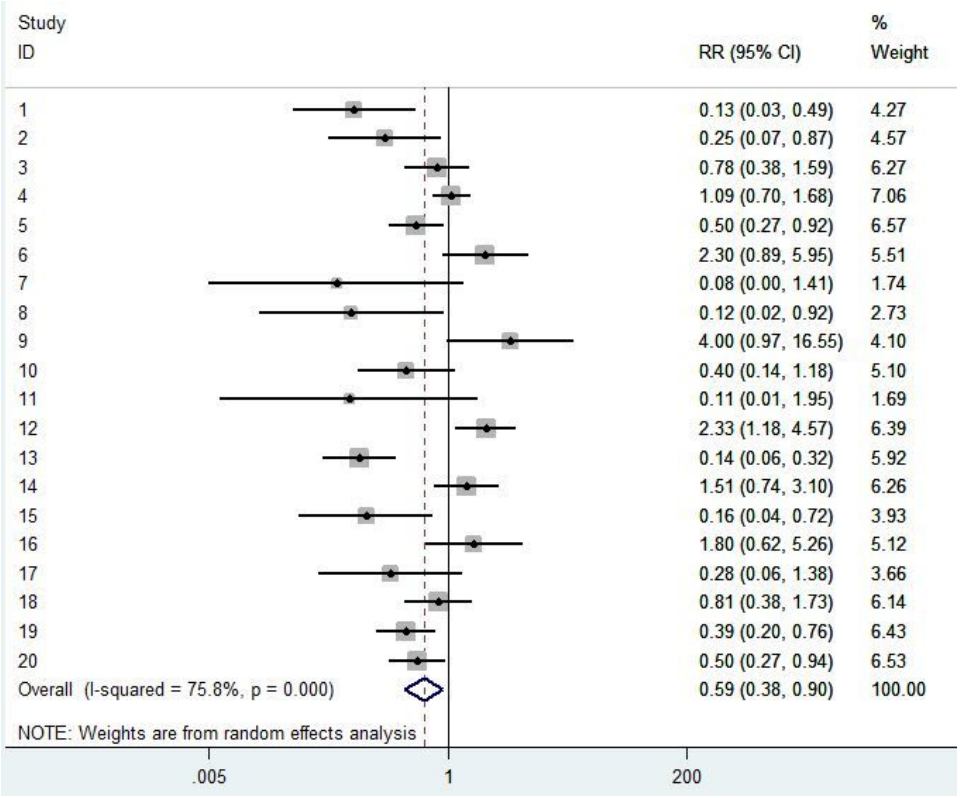

Figure 3

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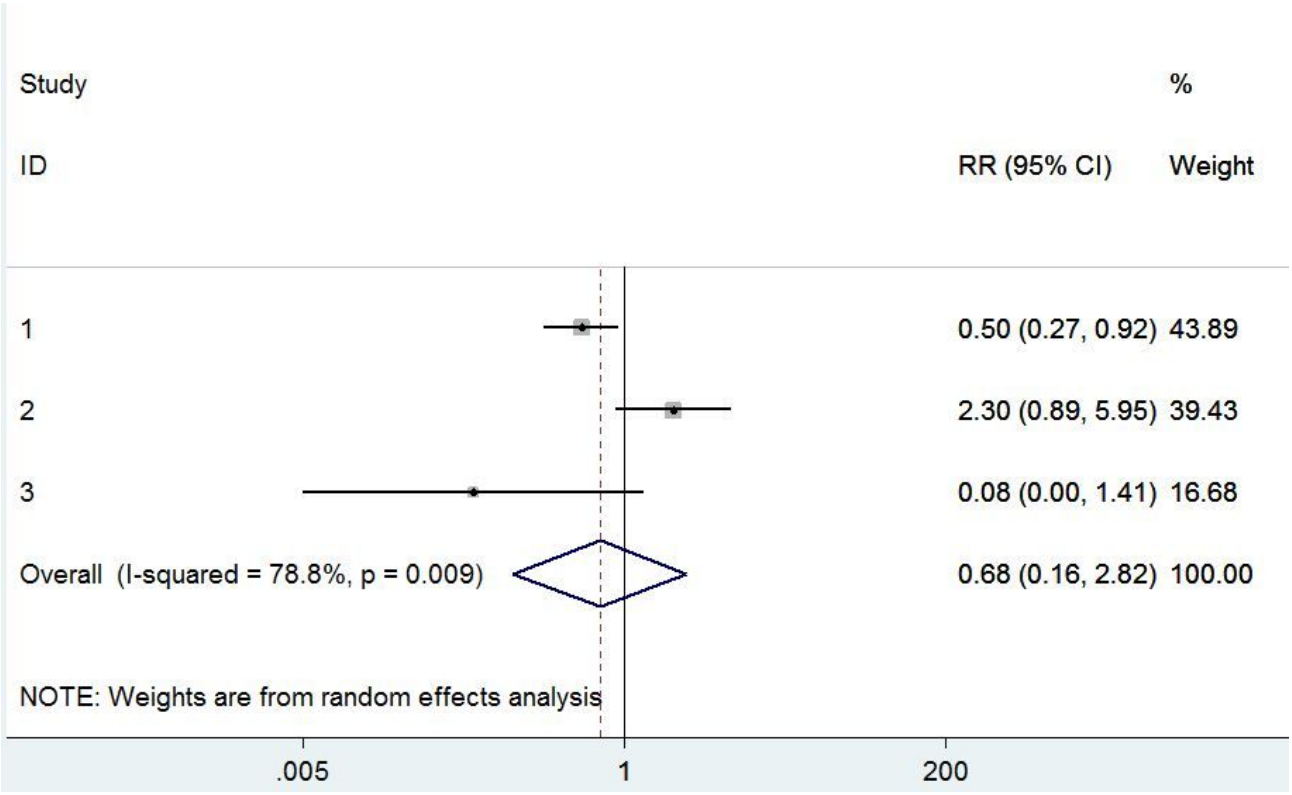

Figure 4

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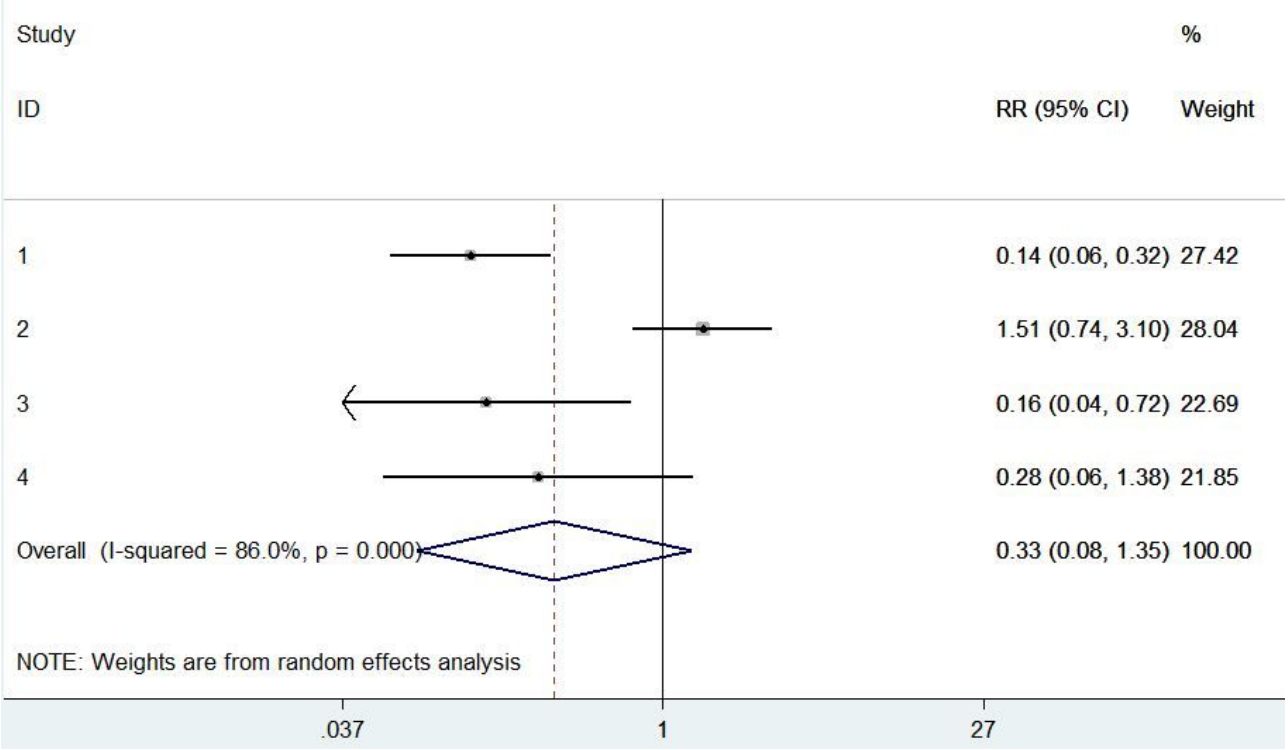

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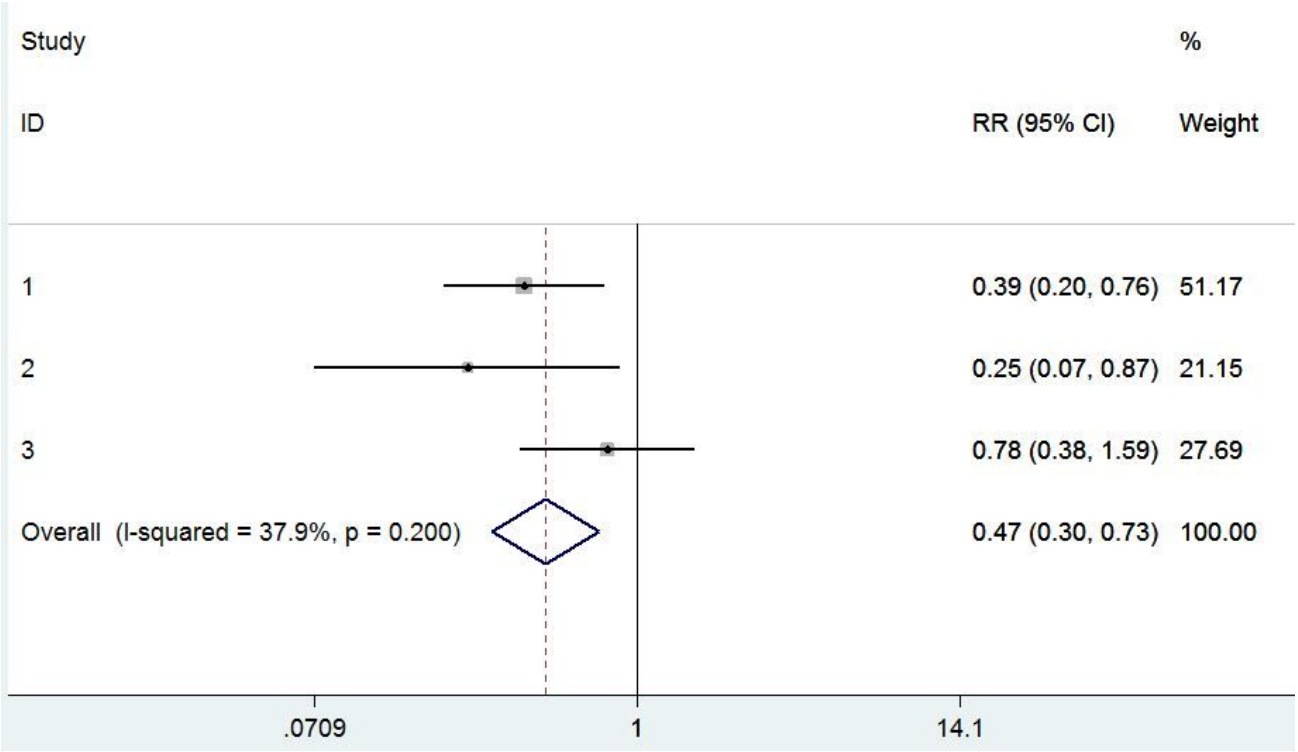

Figure 6

Figure 6

Supplementary Files

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- Appendix2.Funnelplot.JPG
- Appendix1.SearchStrategy.doc