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SUMMARY WITH CRITICAL APPRAISAL

Topical Antibiotics for Infection Prevention: A Review of the Clinical Effectiveness and Guidelines

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Authors: Srabani Banerjee, Charlene Argáez

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Context and Policy Issues

It is estimated that worldwide, 7% to 10% of hospitalized patients are affected by skin and soft tissue infections caused by microbial invasion of the skin and underlying soft tissues.[1] Surgical site infections (SSIs) occur in approximately 2% to 5% of patients undergoing clean extra-abdominal surgeries and in up to 20% of patients undergoing intra-abdominal surgeries.[2] Infections lead to delay in healing, increased morbidity, and prolonged hospital stay which will impact health care resources.[3] The bacteria, *Staphylococcus aureus* (*S. aureus*) is one of the most common causes of health care-associated infections such as SSIs, exit site infections (ESIs) in dialysis patients, and infections in patients in intensive care units (ICU).[4] It is estimated that 20% of healthy people are chronic carriers of *S. aureus*, 30% are intermittent carriers, and 50% are not susceptible.[5,6] The risk of infection is reported to be 2 to 12 times higher in *S. aureus* nasal carriers compared to non-carriers.[4] It has been reported that nasal decolonization of patients with *S. aureus* significantly reduces infections caused by *S. aureus*.[5] It has been reported that 18% to 25% of patients undergoing elective orthopedic surgery are nasal carriers of *S. aureus* and carriers are more likely to experience SSIs.[7] One systematic review[5] has reported that 26% of patients undergoing hemodialysis are nasal carriers of *S. aureus*. For patients with nasal *S. aureus* carriage, who were undergoing dialysis, colonization with the same bacteria was reported at the dialysis catheter exit site.[8] Patients with *S. aureus* colonization are at a greater risk of developing *S. aureus* infection in the ICU.[9] Topical antibiotics assist in preventing infections caused by bacteria. A variety of topical antibiotics are available such as bacitracin, mupirocin, gramicidin, fusidic acid and gentamycin. There is however some concern regarding the use of antibiotics because of the possible development of antibacterial resistance in the long term.[8]

The purpose of this report is to review the existing evidence on the clinical effectiveness of prevention of skin or wound infection with the topical antibiotics: polymyxin B sulfate-bacitracin (Polysporin ointment), polymyxin B sulfate-gramicidin (Polysporin cream), polymyxin B sulfate-bacitracin-gramicidin (Polysporin triple ointment), bacitracin (Bacitin ointment), mupirocin (Bactroban cream/ointment), silver sulfadiazine (Flamazine cream), fusidic acid/fusidate sodium (Fucidin cream/ointment), and fusidic acid 2% with hydrocortisone (Fucidin H). Additionally, this report aims to review evidence-based guidelines for the prevention of skin or wound infection using these topical antibiotics.

Research Questions

1. What is the clinical effectiveness of topical antibiotics for patients to prevent skin or wound infection?

2. What are the evidence-based guidelines regarding the use of topical antibiotics for the prevention of skin or wound infection?

Key Findings

Two systematic reviews and one non-randomized study showed that in non-surgical patients, exit site infection rates were statistically significantly reduced with mupirocin compared with placebo, no treatment, historic control or standard of care.

Two systematic reviews and one RCT showed that overall, in surgical patients, no statistically significant differences were observed in SSI rates with mupirocin compared with placebo, no intervention, no antibiotic, or historic control.

One systematic review showed that in patients undergoing peritoneal dialysis there was no statistically significant difference in ESI with fusidate compared with no treatment.

One systematic review showed that in surgical patients, there was a statistically significant reduction in SSI with bacitracin compared with no antibiotic

Findings need to be interpreted in the light of the limitations of the available data.

Relevant evidence regarding polysporin and silver sulfadiazine was not identified.

One guideline recommended the use of mupirocin for preventing surgical site infections for patients undergoing cardiothoracic or orthopedic surgery and one guideline recommended the use of mupirocin in adults undergoing intensive home hemodialysis. One guideline mentioned that the use of silver sulfadiazine in preventing burn wound infection has not been proven.

Methods

Literature Search Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2012 and March 2, 2017.

Rapid Response reports are organized so that the evidence for each research question is presented separately.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients of any age receiving topical antibiotics to prevent skin or wound infections
Intervention	Topical Antibiotics: Polymyxin B sulfate-bacitracin (Polysporin ointment) Polymyxin B sulfate-gramicidin (Polysporin cream) Poymyxin B sulfate-bacitracin-gramicidin (Polysporin triple ointment) Bacitracin (Bacitin ointment) Mupirocin (Bactroban cream/ointment) Silver sulfadiazine (Flamazine cream) Fusidic acid/fusidate sodium (Fucidin cream/ointment) Fusidic acid 2% plus hydrocortisone (Fucidin h)
Comparator	Placebo, topical antimicrobials compared to each other, oral antibiotics
Outcomes	Clinical effectiveness (infection prevention), safety and harms, antimicrobial resistance, evidence-based guidelines.
Study Designs	Health technology assessments (HTA), systematic reviews (SR), meta-analyses (MA), randomized controlled trials (RCT), non-randomized studies (NRS), and evidence-based guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2012. Studies on ear and eye infections were not of interest for this review and were excluded. Studies which were included in an included systematic review were excluded. Systematic reviews with studies which were included in a more comprehensive included systematic review were excluded.

Critical Appraisal of Individual Studies

The included systematic reviews were critically appraised using AMSTAR,[10] randomized studies and non-randomized studies were critically appraised using the Downs and Black checklist,[11] and guidelines were assessed with the AGREE II[12] instrument. Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 523 citations were identified in the literature search. Following screening of titles and abstracts, 501 citations were excluded and 22 potentially relevant reports from the electronic search were retrieved for full-text review. Three potentially relevant publications were retrieved from the grey literature search or hand searching. Of these potentially relevant articles, 16 publications were excluded for various reasons, while nine publications met the inclusion criteria and were included in this report. These nine publications comprised four systematic reviews,[3,4,6,13] one RCT,[14] one non-randomized study,[8] and three evidence-based guidelines.[15-17] Appendix 1 describes the PRISMA flowchart of the study selection.

Summary of Study Characteristics

Study characteristics are summarized below and details are provided in Appendix 2, Tables A1 and A4

Study Design

Four systematic reviews,[3,4,6,13] one RCT,[14] one non-randomized study,[8] and three evidence-based guidelines[15-17] were included. One systematic review by Levy et al.[6] searched multiple databases up to 2011, and included four systematic reviews and six individual studies comprising two RCTs and four non-randomized studies. One systematic review by Grothe et al.[13] searched multiple databases between January 1989 to January 2014 and included four RCTs relevant for this report. One systematic reviews by Heal et al.[3] had searched multiple databases between 1946 and May 2016, and included RCTs and non-randomized studies of which two RCTs were relevant for our report. One systematic review by Nair et al.[4] searched multiple databases from inception to August 2015, and included 23 studies (RCTs, quasi-experimental studies, and pre-post studies) which were relevant for our report.

The RCT by Shrem et al.[14] was conducted at a single center.

The non-randomized study by Davenport et al.[8] was a 36-month audit The audit was on the effect of different exit site treatments in routine clinical practice in a sample of peritoneal dialysis patients from 12 participating centers in the UK; information was recorded prospectively.

Three evidence-based guidelines[15-17] were included.

Country of Origin

Three systematic reviews were published in 2016, one each from USA,[4] Brazil,[13] and Australia.[3] One systematic[6] was published in 2013 from France. The RCT[14] was published in 2016 from Israel and the non-randomized study[8] was published in 2012 from the UK.

Of the three evidence-based guidelines, one guideline[16] was published in 2017 by the Joanna Briggs Institute (JBI), Australia; one guideline[17] was published by the World Health Organization (WHO) in 2016, and one guideline[15] was published by the Canadian Society of Nephrology (CSN) in 2013.

Patient Population

One systematic review[13] and one non-randomized study[8] were on patients undergoing dialysis. One systematic review[4] was on non-surgical patients (i.e. patients in intensive care units, in non-surgical wards, in long-term care facilities or undergoing dialysis). Two systematic reviews[3,6] and one RCT[14] were on patients undergoing surgery. One systematic review[6] was on patients undergoing orthopedic surgery. One systematic review[3] included two relevant RCTs, one of which was on clean surgery and one on contaminated surgery. The RCT[14] was on patients undergoing cesarean section.

One guideline[15] was for dialysis patients, one guideline[16] was on patients with burn wounds, and one guideline[17] was on surgical patients.

Interventions and Comparators

Mupirocin was compared with placebo, no treatment, or a historic control in four systematic reviews.[3,4,6,13] Historical controls were patients from a previous period without treatment. Mupirocin was compared with no mupirocin in one RCT.[14] A non-randomized study (an audit report)[8] examined outcomes in centers using no prophylaxis exit site antibiotics, a center switching from no prophylaxis to mupirocin and centers using mupirocin. Two different doses of mupirocin were compared in one systematic review.[13] Sodium fusidate was compared with no treatment in one systematic review.[13] Bacitracin was compared with no antibiotic in one systematic review.[3]

Two guidelines[15,17] reported on mupirocin use and one guideline[16] reported on silver sulfadiazine (SSD) use.

Outcomes

Two systematic reviews[4,13] and one non-randomized study[8] reported on exit site infection (ESI). Two systematic reviews[3,6] and one RCT[14] reported on surgical site infection (SSI).

All three guidelines[15-17] indicated the level of evidence and the strength of the recommendation.

Summary of Critical Appraisal

Critical appraisal of the studies is summarized below and details are provided in Appendix 3, Tables A5 and A6.

In all four systematic reviews,[3,4,6,13] the objective, inclusion and exclusion criteria, list of included studies, description of the study selection, and PRISMA flow chart were presented. All four systematic reviews conducted a comprehensive literature search. All four systematic reviews mentioned that there were no conflicts of interest. Selection of articles was done in duplicate in three systematic reviews[3,6,13] and was unclear in one systematic review.[4] Data extraction was done in duplicate in two systematic reviews[3,4] and was unclear in two systematic reviews.[6,13] The list of excluded studies was provided in one systematic review[3] but not in the remaining three systematic reviews. Quality assessment of studies were conducted in three systematic reviews[3,4,13] and was unclear in one systematic review.[6] In one systematic review,[13] most of the included studies were considered of good quality; in one systematic review[3] the qualities of the studies were variable (high to uncertain); and in one systematic review[4] it was reported that there was some likelihood of performance or detection bias due to inappropriate blinding. Publication bias was explored in one systematic review[4] and asymmetry in the Forest plot suggested possibility of bias. It was unclear if publication bias was explored in the other three systematic reviews.[3,6,13]

In the RCT[14] the objective, inclusion and exclusion criteria, patient characteristics, intervention and outcomes were described. A sample size calculation was described and the required sample was met. The method of randomization was not described. The number of patients lost to follow up was higher in the treated group compared to the control group and this could impact the findings. The authors mentioned there were no conflicts of interest.

In the non-randomized study[8] the objective, inclusion and exclusion criteria, patient characteristics, intervention and outcomes were described. As it was a non-randomized study, the potential for selection bias cannot be ruled out. It was unclear if a sample size determination was conducted, however the sample size was large (N = 2473). It was unclear if there were any patients lost to follow up. The authors mentioned there were no conflicts of interest.

Critical appraisals of the evidence-based guidelines are summarized below and details are provided in Appendix 3, Table A7.

In all three guidelines[15-17] the purpose was stated and recommendations were graded. For two guidelines,[15,17] the guideline development group was comprised of individuals from relevant areas and for one guideline,[16] details of the guideline development group was not presented. It was unclear from the guideline reports, if a systematic review had been conducted to identify evidence. There was limited information on the methodology for two guidelines[15,16] and for one guideline[17] it was mentioned that the methodology was as described in their methodology handbook, which appeared to be rigorous. All three guidelines presented the level of evidence and the strength of the recommendation. Two guidelines[15,17] were externally reviewed and for one guideline[16] it was unclear. For two guidelines[15,17] it was mentioned that there were no conflicts of interest and in one guideline there was no mention of conflict of interest.

Summary of Findings

What is the clinical effectiveness of topical antibiotics for patients to prevent skin or wound infection?

Findings are summarized below and details are provided in Appendix 4, Tables A8

Mupirocin

Two systematic reviews[4,13] showed that in non-surgical patients, ESI rates were statistically significantly reduced with mupirocin compared to placebo, no treatment , historic control, or standard of care (Table 2). Also, 3x/day mupirocin was more effective than 1x/day mupirocin as reported in one systematic review.[13] One non-randomized study[8] showed that in patients undergoing peritoneal dialysis mupirocin was statistically significantly more effective than in the control group with no antibiotic treatment, for preventing ESI (median rates per patient treatment year were 0.18 for mupirocin and 0.32 for control; P <0.01)

Two systematic reviews[3,6] showed that overall, in surgical patients, no statistically significant differences were observed in SSI rates with mupirocin compared to placebo, no intervention, no antibiotic, or historic control (Table 2). One RCT by Shrem et al.[14] showed that in the case of women undergoing cesarean section there was no statistically significant difference in SSI rates with nasal pretreatment with mupirocin compared to no pretreatment (SSI rates: 13.1% for mupirocin group, 12.1% for the untreated group, P = 0.78). Mupirocin was used for decolonization of nasal bacteria, mainly *S. aureus*. A subgroup analysis showed that SSI rates were not statistically significantly different between the three groups: carriers of *S. aureus* who were untreated, carriers of *S. aureus* who were treated, and non-carriers (P = 0.69).

One systematic review[4] on non-surgical patients, mentioned development of mupirocin resistance in five of the 14 studies that had reported such data. No further details were presented.

Sodium fusidate

One systematic review[13] showed that in patients undergoing peritoneal dialysis there was no statistically significant difference in ESI with fusidate compared to no treatment (Table 2).

Bacitracin

One systematic review[3] showed that in surgical patients, there was a statistically significant reduction in SSI with bacitracin compared with no antibiotic (Table 2).

Table 2: Effect of mupirocin, fusidate or bacitracin on infection rates

Study	No. of relevant included studies in SR	Population	Comparison	Findings
Grothe,[13] 2016	2 RCT	Peritoneal dialysis	Mup vs plb or no treatment	ESI: 0.26 (0.14 to 0.46)[a]
	1 RCT		Mup (3x/day) vs mup (1x/day)	ESI: 0.10 (0.01 to 0.83)[a]
Nair,[4] 2016	10	Non-surgical (in ICU, non-surgical wards, in LTCF, or undergoing dialysis)	Mup vs placebo, no intervention, historic control, or SOC	ESI: 0.43 (0.34 to 0.55)[b]
Heal,[3] 2016	1 RCT	Surgical wounds	Mup vs no antibiotic	SSI: 1.51 (0.75 to 3.03)[b]
Levy,[6] 2013	4 SRs (RCTs and NRSs)	Surgical	Mup vs placebo, no intervention, historic control	SSI: Overall with mup there was no significant decrease in SSI in surgical patients. However one SR reported a significant effect of mup in cardiothoracic and orthopedic surgery whereas one SR reported no reduction in SSI in orthopedic, digestive, or cardiac surgery
	6 studies (2 RCTs and 4 NRS)	Surgical: orthopedic	Mup vs no preventive treatment	SSI: 0.06 (0.34 to 1.06)[a]
Grothe,[13] 2016	1 RCT	Peritoneal dialysis	Fusidate vs no treatment	ESI: 0.86 (0.20 to 3.72)[a]
Heal,[3] 2016	1 RCT	Surgical wounds	Bacitracin vs no antibiotic	SSI: 0.29 (0.14 to 0.58)[b]

CI = confidence interval; ESI = exit site infection; ICU = intensive care unit; LTCF = long term care facility; mup = mupirocin; NRS = non-randomized study; OR = odds ratio;RCT = randomized controlled trial; RR = relarive risk; SR = systematic review; SSI = surgical site infection

[a]Result expressed as OR (95% CI)

[b]Result expressed as RR (95% CI)

What are the evidence-based guidelines regarding the use of topical antibiotics for the prevention of skin or wound infection?

The included guidelines are summarized below and details are provided in Appendix 4, Tables A9.

The WHO guideline[17] recommended perioperative intranasal applications of mupirocin 2% ointment with or without a combination of chlorhexidine gluconate body wash for patients with known nasal carriage of *S. aureus,* undergoing cardiothoracic or orthopedic surgery (strong recommendation, moderate quality evidence). In the case of patients undergoing other types of surgery, the recommendation was considered to be conditional.

The CSN guideline[15] suggested the use of mupirocin cream to reduce the risk of infection in adults with end-stage renal disease undergoing intensive home hemodialysis using button hole cannulation (conditional recommendation; very low-quality evidence). This recommendation related specifically to home intensive dialysis and not to in-center intensive hemodialysis. It was mentioned that mupirocin resistance rates and institutional policy need to be considered before deciding on use of mupirocin cream.

The best practice recommendations[16] from the Joanna Briggs Institute were that the clinical effectiveness of SSD in either preventing or treating burn wound infection has not been proven and that clinical judgement needs to be used (Grade B).

Limitations

The included systematic reviews had broad objectives, hence summary findings from the meta-analyses could not be used; instead, only the findings from studies that had relevant interventions and outcomes were extracted. In some systematic reviews, only one or two relevant studies were available.

In the systematic reviews, the specifics of the comparator group were not always clear; sometimes historical controls were used, and sometimes the comparator was described as no treatment. It was not always clear if additional procedures were undertaken and if they were equivalent in both the treatment and control arms. The audit study by Davenport,[8] presented results of effectiveness of mupirocin compared to no antibiotic use. The practices at different centers varied in that additional procedures such as washing the exit site with soap and water; normal saline and chlorhexidine; sterile alcohol swab; or iodine were used. It was however unclear if the additional procedures were used for both the groups.

In the light of limitations, the findings need to be interpreted with caution.

Information on antibiotic resistance for the antibiotics relevant for our report was sparse.

It was unclear in the systematic reviews, if any of the included studies were conducted in Canada. Also the RCT and non-randomized study were not conducted in Canada. Hence generalizability to the Canadian setting is difficult.

Conclusions and Implications for Decision or Policy Making

Four systematic reviews,[3,4,6,13] one RCT,[14], one non-randomized study,[8] and three evidence-based guidelines[15-17] were identified.

Two systematic reviews[4,13] and one non-randomized study[8] showed that in non-surgical patients, ESI rates were statistically significantly reduced with mupirocin compared to placebo, no treatment , historic control or standard of care.

Two systematic reviews[3,6] and one RCT[14]showed that overall, in surgical patients, no statistically significant differences were observed in SSI rates with mupirocin compared to placebo, no intervention, no antibiotic, or historic control.

One systematic review[13]showed that in patients undergoing peritoneal dialysis there was no statistically significant difference in ESI with fusidate compared to no treatment.

One systematic review[3] showed that in surgical patients, there was a statistically significant reduction in SSI with bacitracin compared with no antibiotic

Findings need to be interpreted in the light of the limitations mentioned.

Relevant evidence regarding polysporin and silver sulfadiazine was not identified.

Information on resistance to the antibiotics of relevance in our report was scarce.

The WHO guideline[17] recommended perioperative intranasal applications of mupirocin 2% ointment for patients with known nasal carriage of *S. aureus,* undergoing cardiothoracic and orthopedic surgery.

The CSN guideline[15] suggested that use of mupirocin cream to reduce the risk of infection in adults undergoing intensive home hemodialysis

The best practice recommendations[16] from the Joanna Briggs Institute was that the clinical effectiveness of SSD in preventing burn wound infection has not been proven.

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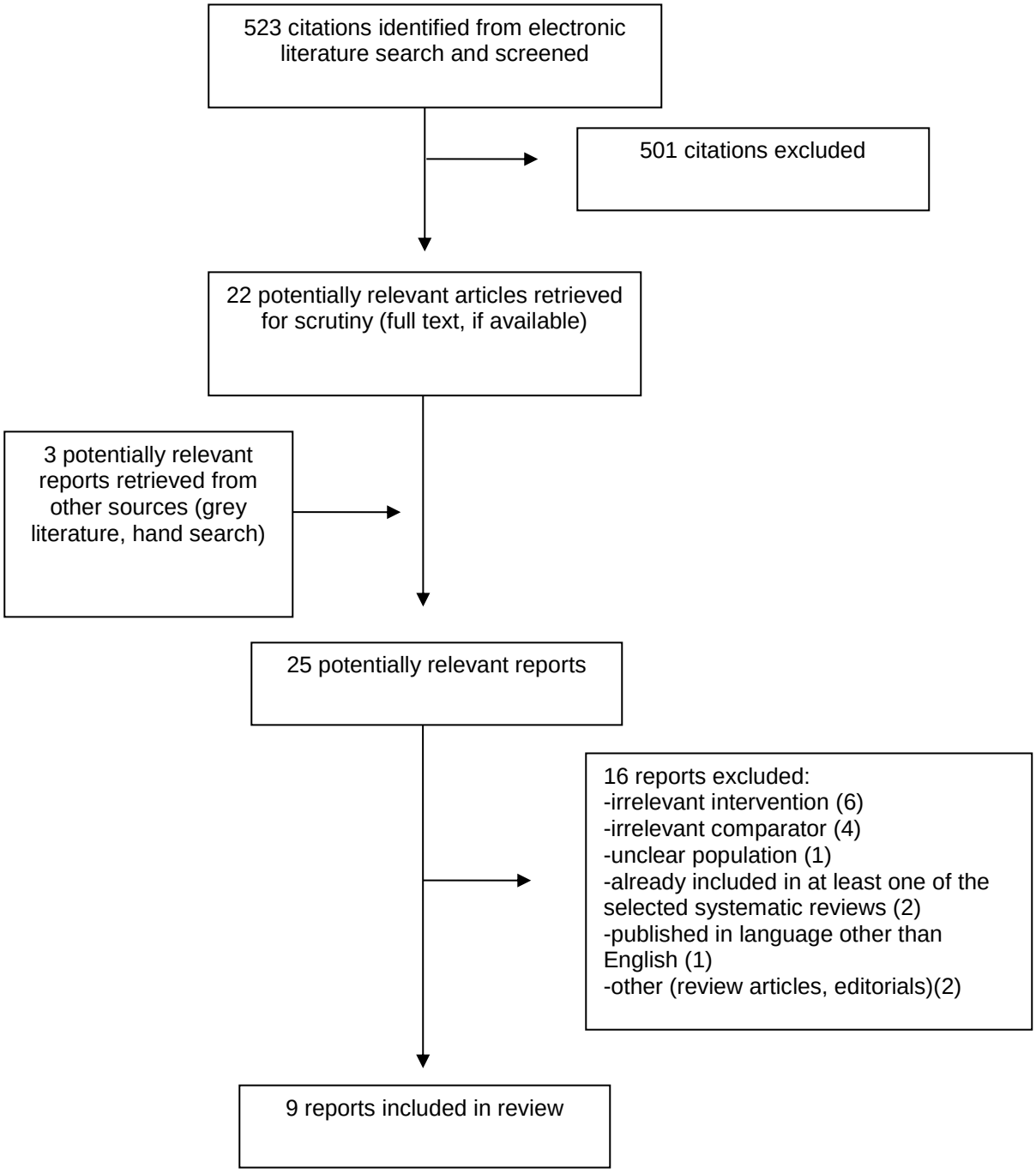
Abbreviations

CESS	catheter exit site skin
CH (or CHX)	chlorhexidine
CHG	chlorhexidine gluconate
CI	confidence interval
CS	caesarean section
CSN	Canadian Society of Nephrology
DM	diabetes mellitus
ESRD	end stage renal disease
GDG	guideline development group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
ICU	intensive care unit
JBI	Joanna Briggs Institute
LTCF	long-term care facility
MSG	mupirocin study group
MRSA	methicillin-resistance Staphylococcus aureus
MSSA	methicillin-sensitive Staphylococcus aureus
mup	mupirocin
NRS	non-randomized study
OR	odds ratio
PD	peritoneal dialysis
RCT	randomized controlled trial
RR	relative risk
S. aureas	Staphylococcus aureus
SE	standard error
SOC	standard of care
SR	systematic review
SSD	silver sulfadiazine
SSI	surgical site infection
STROBE	strength of reporting of observational studies in epidemiology
UTI	urinary tract infection
vs	versus
WHO	World Health Organization

Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table A1: Characteristics of Included Systematic Reviews

Author, Year, Country	Type and Number of Primary Studies Included	Population characteristics	Comparison	Outcome
Grothe,[13] 2016, Brazil	The SR included 9 RCTs of which 4 RCTs were relevant for this report and are included here (the remaining 5 RCTs were on comparisons not relevant for our report) The 4 RCTs were published between 1996 and 2004 Aim: to determine the clinical effectiveness of various strategies for the prevention and treatment of patients undergoing peritoneal dialysis and colonized by S. aureus	Patients with chronic renal disease undergoing peritoneal dialysis (PD) N = 479 (in the 4 relevant RCTs)	Mup 2x/day for 5 days) vs placebo (1 RCT); CESS mup 1x/day vs no treatment (1 RCT); mup 3x/day vs mup 1x/day; and Nasal and CESS sodium fusidate vs no treatment (1 RCT)	Infection at PD catheter exit site; peritonitis
Heal,[3] 2016, Australia	The SR included 10 RCTs and 4 quasi-RCTs of which 2 RCTs with relevant outcomes reported were relevant for our report and are included here. Aim: to evaluate topical antibiotics for preventing surgical site infection in wounds healing by primary intention.	Individuals with surgical wounds that are healing by primary intention. N = 3128 (in the 2 relevant RCTs)	Bacitracin zinc vs no antibiotic vs other (1RCT); mup ointment (20mg/g) vs no antibiotic vs other;	SSI; allergic contact dermatitis; wounds healed in 5 to 14 days
Levy,[6] 2013, France	The SR included 4 systematic reviews (which included RCTs and NRSs) and 6 studies (2 RCTs and 4 NRSs) Aim: to address if there is a correlation between nasal *S. aureus* carriage and osteo-articular infection and to examine the efficacy of existing decolonization methods	Surgical patients N = 5972 (in 4 studies, NR in two studies)	Mup vs placebo, no treatment or historical control (unclear if additional agents were used)	SSI
Nair,[4] 2016, USA	The SR included 37 studies (RCTs, quasi-experimental studies, pre-post studies, retrospective study). Of these 37 studies, 23 studies assessed mupirocin as the only decolonizing agent compared with a control group and are included in our report. The remaining 14 studies assessed mupirocin in combination with other agents and are not relevant interventions for our report.	Patients in non-surgical settings (in ICU, non-surgical wards, in LTCF, or undergoing dialysis) N = 8010 (in 22 studies, in one study patient number was not reported)	Mup vs placebo; mup vs historic control or no intervention; mup vs SOC; mup vs hand hygiene, feedback and PICC bundle	Infection rate, mup resistance

Table A1: Characteristics of Included Systematic Reviews

Author, Year, Country	Type and Number of Primary Studies Included	Population characteristics	Comparison	Outcome
	Aim: to determine the effectiveness of mupirocin for decolonization to prevent *S. aureus* infections in non-surgical settings			

CESS = catheter exit site skin; ICU = intensive care unit; LTCF = long-term care facility; MRSA = methicillin-resistant Staphylococcus aureus; NRS = non-randomized study; PD = peritoneal dialysis; RCT = randomized controlled trial; S. aureus = Staphylococcus aureus; SOC = standard of care

Table A2: Characteristics of Included Clinical Studies

Author, Year, Country	Study Design	Population Characteristics	Intervention	Comparator	Outcome
Randomized controlled trial					
Shrem,[14] 2016, Israel	RCT conducted Obstetrics and Gynecology Department of the Hillel-Yaffe Medical Center, Israel. Study period: September 2010 to January 2013 Aim: to examine if screening for nasal colonization of S. aureus and treating carriers prior to a Cesarean section (CS) decreases the likelihood of SSI.	Women undergoing elective or urgent CS. N = 568 (284 in mupirocin [mup] group and 284 in control group) Age (mean) (years): 32. 11% of the women had gestational or pre-gestational DM. Both groups were comparable except for smoking status (19.8% in mup and 11.1% in control; P = 0.008) and previous CS (73% in mup and 61% in control; P = 0.002)	Mupirocin ointment was provided to individuals with positive nose culture for S. aureus. Dosage: 2 times daily for 5 days in each nostril. Abdominal prep protocol included use of CHX gluconate 4% (Septal Scrub) followed by CHX gluconate 0.5%, Alcohol 70% (Alcosept).	Control: No mupirocin Abdominal prep protocol included use of CHX gluconate 4% (Septal Scrub) followed by CHX gluconate 0.5%, Alcohol 70% (Alcosept).	SSI rate, eradication rate of nasal colonization, and other infections (such as UTI, pneumonia)
Non-randomized study					
Davenport,[8] 2012, UK	An audit (of the effect of different exit site practices for peritoneal dialysis patients) was conducted. 36-month audit Aim: to determine the effectiveness of	Patients undergoing peritoneal dialysis in the expanded Thames area and South eastern England. N = 1203 (no toipical antibiotic)	During the audit period, 4 centers continued using no prophylaxis exit site antibiotics, 5 centers used topical mup, I center switched from no prophylaxis to mup, I center from mup to gentamicin, and 1 center from no prophylaxis to gentamycin Additionally, practices at different centers varied from washing to exit site with soap		ESI, peritonitis

Table A2: Characteristics of Included Clinical Studies

Author, Year, Country	Study Design	Population Characteristics	Intervention	Comparator	Outcome
	topical antibiotic preparations on ESI and peritonitis rates	and 1270 (topical mupirocin) Age (years) (mean ± SE): 59.4 for no antibiotics group, and 56.0 for mup group. (Number of patients of age >75 years was statistically significantly higher in the no antibiotic group compared to the mup group (P < 0.05) Female (%): 44 for for no antibiotics group, and 42 for mup group.	and water to using normal saline and chlorhexidine, alcohol wipes or iodine. (As gentamycin is not relevant for our report, it is not discussed further)		

CHX = chlorhexidine; CS = Cesarean section; DM = diabetes mellitus; mup = mupirocin; RCT = randomized controlled trial; S. aureas = Staphylococcus aureus; SE = standard error; SSI = surgical site infection; UTI = urinary tract infection

Table A3: Characteristics of Included Guidelines

First Author/ Group, Year, Country	Objective	Guideline Development group (GDG), Target users	Methodology
Ong/ The Joanne Briggs Institute,[16] 2017	To find the best available evidence for silver sulfadiazine for burn wounds and provide best practice recommendations	The GDG was not specified. Target users were not specified.	The guideline was developed according to JBI methods[18,19] which includes a systematic review of evidence. Levels of evidence and grading of recommendations were provided
WHO – Global Guidelines,[17] 2016	To provide evidence-based recommendations for the prevention of SSI during the pre-, intra, and post-operative periods	The GDG comprised of individuals from relevant areas (surgery, microbiology and methodology) The primary target audience was the surgical team. Other audiences included pharmacists, sterilization unit staff, policy-makers, senior managers and infection prevention and control professionals.	Methodology used for identifying evidence was rigorous (details in WHO handbook for guideline development[20]) Levels of evidence and grading of recommendations were provided. The GRADE methodology was used

Table A3: Characteristics of Included Guidelines

First Author/ Group, Year, Country	Objective	Guideline Development group (GDG), Target users	Methodology
Nesrallah/ CSN,[15] 2013, Canada[15]	To provide guidelines for the management of patients with end-stage renal disease who are undergoing intensive hemodialysis	The GDG comprised of physicians with clinical interest in intensive hemodialysis and with a background in clinical investigation, research methodology, guideline development and knowledge translation. The guideline was for physicians and allied health care practitioners in the management of patients with end-stage renal disease who are undergoing intensive hemodialysis	Systematic reviews were conducted but details of the methodology used was not presented Levels of evidence and grading of recommendations were provided. The GRADE methodology was used.

CSN = Canadian Society of Nephrology; GDG = Guideline development group; **GRADE = Grading of Recommendations Assessment, Development and Evaluation** JBI = Joanna Briggs Institute; RCT = randomized controlled trial; WHO = World Health Organization;

Table A4: Grade of Recommendations and Level of Evidence

First Author/ Group, Year,	*Grade of Recommendation*	*Level of Evidence*
Ong/ The Joanne Briggs Institute,[16] 2017	***Grade A**: Strong Recommendation:* *-Desirable benefits clearly outweigh undesirable effects* *-Evidence of adequate quality support recommendation* *-Benefit or no impact on resource use* *-Values, preferences, and patient experience have been considered* ***Grade B**: Weak Recommendation:* *-Desirable effects appear to outweigh undesirable effects, although this is not clear* *-Evidence supports use but may not be of high quality* *-Benefit, no impact, or minimal impact on resource use* *-Values preferences, and patient experience may not have been considered*	***Level 1**: Experimental designs (1a: SR of RCT, 1b: SR of RCT and other study designs, 1c: RCTs, 1d: pseudo-RCTs)* ***Level 2**: Quasi-experimental design (2a: SR of quasi-experimental studies, 2b: SR of quasi-experimental studies and other lower study designs, 2c: quasi-experimental prospectively controlled study, 2d: pre-test/ post-test or historic/ retrospective control group study)* ***Level 3**: Observational – analytical designs (3a: SR of comparable cohort studies; 3b: SR of comparable cohort and other lower study designs; 3c: cohort study with control group; 3d: case-controlled study; 3e: observational study without a control group)* ***Level 4**: Observational – descriptive studies (4a: SR of descriptive studies; 4b: cross-sectional study; 4c: case-series; 4d: case study)* ***Level 5**: Expert opinion and bench research (5a: SR of expert opinion, 5b: expert consensus; 5c: bench research or single expert*
WHO – Global Guidelines,[17] 2016	*(From page 129 of WHO Handbook of guideline development[20])* ***Strong recommendation** (interpretation for different audiences)* *For patients: "Most individuals in this situation would want the recommended course of action; only a small proportion would not.* *Formal decision aides are not likely to be needed to*	*Quality based on GRADE* ***"High** We are very confident that the true effect lies close to that of the estimate of the effect.* ***Moderate** We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.*

Table A4: Grade of Recommendations and Level of Evidence

First Author/ Group, Year,	Grade of Recommendation	Level of Evidence
	help individuals make decisions consistent with their values and preferences." *For clinicians: "Most individuals should receive the intervention.* *Adherence to the recommendation could be used as a quality criterion or performance indicator."* *For Policy-makers: "The recommendation can be adopted as policy in most situations."* ***Conditional recommendation*** *(interpretation for different audiences)* *For patients: "Most individuals in this situation would want the suggested course of action, but many would not."* *For clinicians: "Different choices will be appropriate for individual patients, who will require assistance in arriving at a management decision consistent with his or her values and preferences. Decision aides may be useful in helping individuals make decisions consistent with their values and preferences."* *For Policy-makers: "Policy-making will require substantial debate and involvement of various stakeholders."*	***Low*** *Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.* ***Very low*** *We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect." Page 113 of WHO Handbook of guideline development*[20]
Nesrallah/ CSN,[15] 2013, Canada	*GRADE approach was used*	*GRADE approach was used*

GRADE = Grading of Recommendations Assessment, Development and Evaluation; SR = systematic review;

Appendix 3: Critical Appraisal of Included Publications

Table A5: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR[10]

Strengths	Limitations
Grothe,[13] 2016, Brazil	
• The objective was clearly stated. • The inclusion and exclusion criteria were stated. • Multiple databases (Embase, LILACS, SciELO, CINAHL, and Medline/PubMed)) were searched from January 1989 to January 2014. Also, Cochrane library, Cochrane Controlled Trials register was searched. • Study selection was described and a flow chart for study selection was presented • List of included studies was provided • Article selection was done in duplicate • Quality assessment was done in duplicate using the Cochrane framework and the STROBE statement. Majority of the studies (8 out of 9 studies included in the SR) were assessed to be of good quality (category A: >80% compliance with the STROBE criteria) • Characteristics of the individual studies were provided • Meta-analyses were conducted • The authors stated that there was no conflict of interest.	• List of excluded studies was not provided • Unclear if data extraction was done in duplicate. • Publication bias does not appear to have been explored
Heal,[3] 2016, Australia	
• The objective was clearly stated. • The inclusion and exclusion criteria were stated. • Multiple databases (Medline [1946 to May 2016], Embase [1974 to May 2016], EBSCO CINAHL [1982 to May 2016], clinical trials registries) were searched. In addition bibliographies of relevant publications were searched and manufacturers and pharmaceutical companies were contacted for studies. • Study selection was described a flow chart for study selection was presented • Lists of included and excluded studies were provided • Article selection was done in duplicate • Data extraction was done in duplicate • Quality assessment was done in duplicate using the Cochrane risk of bias tool. Of the two RCTs relevant for our report, the risk of bias was high for one RCT and uncertain for one RCT • Characteristics of the individual studies were provided • Meta-analyses were conducted • The authors stated that there was no conflict of interest.	• Publication bias does not appear to have been explored
Levy,[6] 2013	
• The objective was clearly stated. • The inclusion and exclusion criteria were stated. • Multiple databases (Cochrane Central register of Controlled	• List of excluded studies was not provided • Unclear if data extraction was done in duplicate • Details of the individual studies were lacking

Table A5: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR[10]

Strengths	Limitations
Trials [latest version] Medline, and Embase [up to 2011], were searched. • Study selection was described a flow chart for study selection was presented • List of included studies was provided • Article selection was done in duplicate • Meta-analyses were conducted • The authors stated that there was no conflict of interest.	• Unclear if quality assessment of included studies was conducted • Publication bias does not appear to have been explored
Nair,[4] 2016	
• The objective was clearly stated. • The inclusion and exclusion criteria were stated. • Multiple databases (PubMed, Scopus which includes Embase], clinical trial registries) were searched. Databases were searched from inception to August 2015. In addition conference proceedings and bibliographies of relevant publications were searched. • Study selection was described a flow chart for study selection was presented • List of included studies was provided • Data extraction was done in duplicate • Quality assessment was done using the Cochrane risk of bias tool and modified Downs and Black tool. There was some likelihood of performance and detection bias due to inappropriate blinding methodology. • Characteristics of the individual studies were provided • Meta-analyses were conducted • Publication bias was explored using the Funnel plot. The asymmetry in the plot suggests there may be publication bias • The authors stated that there was no conflict of interest.	• List of excluded studies was not provided • Unclear if article selection was done in duplicate • Some discrepancies in reporting (such as some times the number of studies and the number of references cited did not match or the study and citation referred to did not match)

GRADE = Grading of Recommendations Assessment, Development and Evaluation; SR = systematic review; STROBE = Strength of reporting of observational studies in epidemiology

Table A6: Strengths and Limitations of Randomized Controlled Trials using Downs and Black checklist11

Strengths	Limitations
Shrem,[14] 2016, Israel	
• The objective was clearly stated • The inclusion and exclusion criteria were stated • Patient characteristics, intervention and outcomes were described • Block randomization was used in which every three months women were allocated to one of the two study arms. Method of randomization was not described. • Sample size determination was undertaken and met. • Number lost to follow-up was reported. It was lower in the control (no treatment) group (27 [9.5%]) than in the treated group and (55 [19.4%]. • *P*-values were reported • The authors mentioned that there was no conflict of interest	• It appears that ITT analysis was not conducted; calculations of SSI rates were based on the number of patients who were not lost to follow up. However, as SSI is an adverse outcome this analysis would not under-estimate it, and is acceptable.
Davenport,[8] 2012, UK	
• The objective was clearly stated • The inclusion criteria were stated • Patient characteristics, intervention and outcomes were described • *P*-values were reported • The authors mentioned that there was no conflict of interest	• Non-randomized study • The exclusion criteria were not explicitly stated • Unclear if a sample size determination was conducted. However, the sample size was relatively large (N = 2473 considering the mup and no antibiotic groups) • Unclear if any patients were lost to follow-up

ITT = intention-to-treat; SSI = surgical site infection

Table A7: Strengths and Limitations of Guidelines using AGREE II[12]

Strengths	Limitations
Ong/ The Joanne Briggs Institute,[16] 2017	
• The purpose was clearly stated. • Recommendations were graded.	• No information regarding the guideline development group or if patient input was sought. According to the Reviewer's manual, [19] the review panel should consist of methodology experts, content experts, and lay/ consumer representatives • No information on the literature search methodology • Very limited methodology reported. However, the JBI Reviewer's manual [19] indicates a systematic approach to identifying evidence. • Unclear if cost implications and implementation barriers were considered • Unclear if the guideline document was internally or externally reviewed • Unclear if there was any policy regarding updating the guideline • No information on conflicts of interest

Table A7: Strengths and Limitations of Guidelines using AGREE II[12]

Strengths	Limitations
WHO – Global Guidelines,[17] 2016	
• The scope and purpose were clearly stated. • The guideline development group (GDG) comprised of individuals from relevant areas (surgery, microbiology and methodology) • Methodology used for identifying evidence was rigorous (described in WHO handbook for guideline development[20] • Values and preferences of stakeholders were considered • Resource implications of the interventions were considered • The scientific evidence was synthesized using the GRADE approach • Recommendations were graded. • The guideline was externally reviewed • The recommendations will be reviewed and updated following identification of new evidence, at least every five years • Conflicts of interest were declared and in all cases were considered irrelevant and did not warrant any exclusion from GDG	• Appears to have no major limitations
CSN guideline,[15] 2013, Canada	
• The scope and purpose were clearly stated. • The GDG comprised of individuals from relevant areas (physicians with clinical interest in intensive hemodialysis and with a background in clinical investigation, research methodology, guideline development and knowledge translation) • The scientific evidence was synthesized using the GRADE approach • Recommendations were graded. • The guideline was externally reviewed • The authors mentioned that they had no relevant financial interests	• Details of the systematic review conducted was not presented • Appears to have placed a relatively low value on patient convenience and cost implications • Unclear if there was any policy regarding updating the guideline

Appendix 4: Main Study Findings and Author's Conclusions

Table A8: Summary of Findings of Included Studies

<table>
<tr><th>Main Study Findings</th><th>Author's Conclusion</th></tr>
<tr><td colspan="2">Systematic Reviews</td></tr>
<tr><td colspan="2">Grothe,[13] 2016, Brazil</td></tr>
<tr><td>
Probability of skin infection at the PD catheter exit site caused by S. aureus
<table>
<tr><th>Comparison</th><th>No. of studies included</th><th>Odds ratio (95% CI)</th></tr>
<tr><td>Mup vs placebo or no treatment</td><td>2</td><td>0.26 (0.14 to 0.46)</td></tr>
<tr><td>Mup (3x/day) vs mup (1x/day)</td><td>1</td><td>0.10 (0.01 to 0.83)</td></tr>
<tr><td>Fusidate vs no treatment</td><td>1</td><td>0.86 (0.20 to 3.72)</td></tr>
</table>
Probability of peritonitis caused by S. aureus
<table>
<tr><th>Comparison</th><th>No. of studies included</th><th>OR (95% CI)</th></tr>
<tr><td>Mup vs placebo or no treatment</td><td>2</td><td>0.68 (0.37 to 1.24)</td></tr>
<tr><td>Fusidate vs no treatment</td><td>1</td><td>0.23 (0.03 to 1.95)</td></tr>
</table>
</td><td>"Mupirocin and topical antibiotics were effective for reduction of S. aureus catheter site infection in patients undergoing peritoneal dialysis when compared with no treatment or placebo. However, evidence was insufficient to identify the optimal agent, route, or duration of antibiotics to treat peritonitis." (pp. 1)

"This meta-analysis supports the use of local antibiotics at the catheter exit site in patients undergoing PD. However, the available data are very limited, and more studies are needed to examine the clinical importance of antibiotics at the catheter exit site in patients undergoing PD." (pp. 9)</td></tr>
<tr><td colspan="2">Heal,[3] 2016, Australia</td></tr>
<tr><td>
SSI with topical antibiotics compared with no antibiotics
<table>
<tr><th>Comparison</th><th>No. of studies included</th><th>Risk ratio (95% CI)</th></tr>
<tr><td>Bacitracin zinc vs no antibiotic vs placebo or no treatment</td><td>1</td><td>0.29 (0.14 to 0.58), favours antibiotic</td></tr>
<tr><td>Mup vs no antibiotic</td><td>1</td><td>1.51 (0.75 to 3.03)</td></tr>
</table>
</td><td>" Topical antibiotics applied to surgical wounds healing by primary intention probably reduce the risk of SSI relative to no antibiotic [….]" (pp. 2)</td></tr>
<tr><td colspan="2">Levy,[6] 2013, France</td></tr>
<tr><td>
Findings from included systematic reviews in the systematic review[6]
<table>
<tr><td>Systematic review</td><td>Included studies</td><td>Findings</td></tr>
<tr><td>Kallen et al., 2005</td><td>3RCTs, 4 cohort studies</td><td>No decrease in SSI in general surgery, but a significant effect of mup in cardiothoracic and orthopedic surgery (in RCTs)</td></tr>
</table>
</td><td>"there is established scientific evidence (grade A recommendation) that mupirocin is more effective than other agents in eradicating nasal S. aureus carriage […]" (pp.650)

"there is no established scientific evidence that mupirocin alone reduces the risk of orthopedic S. aureus SSI […]" (pp.650)</td></tr>
</table>

Table A8: Summary of Findings of Included Studies

Main Study Findings	Author's Conclusion

Trautman et al., 2008	4 RCTs and in 7 cohort studies	No reduction in SSI with mup in orthopedic, digestive, or cardiac surgery
Van Rijen et al., 2008 - a	4 RCTs	Mupirocin decreased the rate of nosocomial *S. aureus* infection but there was no significant difference in SSI
Van Rijen et al., 2008 - b	9 RCTs (of which 4 RCTs were on surgical patients)	The surgery subgroup demonstrated a significant decrease in nosocomial *S. aureus* infection with mup but there was no significant difference in SSI

Findings from included studies in the systematic review[6]
The authors conducted a meta-analysis with 6 studies (2 RCTs and 4 NRS; with full or partial data) focusing on osteo-articular infection and showed with mup, there appeared to be a numerical decrease in *S. aureus* SSI but the difference was not statistically significant (OR, 0.60; 95% CI [0.34 to 1.06]; *P* = 0.08)

Nair,[4] 2016, USA

Overall, mupirocin was observed to have a protective effect in preventing *S. aureus* infections.

Effectiveness of mupirocin in preventing S. aureus infection (subgroups by study design)

Subgroup	No. of studies	RR (95% CI)	Heterogeneity I^2 (%)
Clinical trials	5	0.54 (0.46 to 0.63)	0
Non-equivalent control group	12	0.46 (0.38 to 0.56)	80
Pre-post	5	0.44 (0.29 to 0.67)	89

Effectiveness of mupirocin in preventing *S. aureus* infection (subgroups by healthcare setting)

Subgroup	No. of studies	RR (95% CI)	Heterogeneity I^2 (%)
Non-dialysis	6	0.64 (0.37 to 1.10)	87
Dialysis	15	0.42 (0.35 to 0.50)	78

"Mupirocin decolonization was protective against *S. aureus* infections among both dialysis and adult intensive care patients. Future studies are needed in other settings such as long-term care and pediatrics." (pp.618)

Table A8: Summary of Findings of Included Studies

Main Study Findings	Author's Conclusion
Effectiveness of mupirocin in preventing *S. aureus* infection (subgroups by type of *S. aureus* infection)	

Subgroup	No. of studies	RR (95% CI)	Heterogeneity I^2 (%)
ESI	10	0.43 (0.34 to 0.55)	84
Bacteremia	5	0.44 (0.34 to 0.58)	60
Other infections	1	0.76 (0.22 to 2.62)	NA

Mupirocin resistance: The authors mentioned that they noted development of resistance in five of the 14 studies that had reported such data. No further details were presented.

Randomized Controlled Trial (RCT)

Shrem,[14] 2016, Israel

Comparison of outcomes in women treated with mupirocin pre-CS with those untreated (control)

Outcome variable	Mupirocin group, N = 284	Untreated control group, N = 284	*P* value
SSI rate	30 (13.1%)	30 (12.1%)	0.78
SSI rate during initial hospitalization, with respect to all SSIs in the group	5/30 (16.6%)	4/30 (13.3%)	1.00

SSI rates in carriers and non-carriers of S. aureus

Outcome variable	Subgroup[a]	Outcome, n (%)	*P* value[b]
SSI rate	Non-carriers	52 (13.1%)	0.69
	Carriers not treated	6 (13.0%)	
	Carriers treated	2 (7.4%)	
Other infection (UTI or pneumonia)	Non-carriers	11 (2.4%)	0.61
	Carriers not treated	1 (1.7%)	
	Carriers treated	0	

[a]Number of participants were 466, 59, and 38 respectively in non-carriers, carriers not treated and carriers treated groups. The total number for the three subgroups is less than the total number of the study participants, because of missing data.
[b]*P* values were calculated by Pearson chi-square test.

SSI rates were numerically lower in the treated carriers compared to untreated carriers but the difference was not statistically significant. The authors mentioned that a post-hoc analysis revealed that for this comparison the study was underpowered (390 would be needed in each group to detect a statistically significant difference).

"Pre-cesarean screening for nasal *S. aureus* carriage and decolonization does not appear to be an effective intervention in reducing SSI rates." (pp3906)

"We feel that efforts of reducing post-cesarean SSI rates should be directed in exploring other alternatives. Additional larger prospective studies are required in order to better define useful policies for lowering postoperative maternal infectious morbidity in general and SSIs in particular." (pp.3910)

Table A8: Summary of Findings of Included Studies

<table>
<tr><th>Main Study Findings</th><th>Author's Conclusion</th></tr>
<tr><td colspan="2">Non-randomized study</td></tr>
<tr><td colspan="2">Davenport,[8] 2012, UK</td></tr>
<tr><td>Effectiveness of mupirocin in preventing exit site infection and peritonitis
<table>
<tr><th rowspan="2">Outcome</th><th colspan="2">Rate (per patient treatment year), median (interquartile range)</th><th rowspan="2">P value</th></tr>
<tr><th>Mupirocin</th><th>No antibiotic</th></tr>
<tr><td>ESI</td><td>0.18 (0.13 to 0.23)</td><td>0.32 (0.24 to 0.69)</td><td><0.01</td></tr>
<tr><td>Peritonitis</td><td>0.55 (0.53 to 0.75)</td><td>0.56 (0.50 to 0.65)</td><td>NR</td></tr>
</table></td><td>"[…] in this audit of routine clinical practice, topical mupirocin did reduce overall ESI rates […]" (pp.819)</td></tr>
</table>

CI = confidence interval; CS = caesarean section; ESI = exit site infection; MRSA = methicillin resistant *S. aureus*; MSSA = methicillin sensitive mup = mupirocin; NA = not applicable; NR = not reported; OR = odds ratio; PD = peritoneal dialysis; RR = relative risk; S. aureas = Staphylococcus aureus; SR = systematic review; SSI = surgical site infection; UTI = urinary tract infection; vs = versus

Table A9: Summary of Findings of Included Evidence-based Guidelines

Main Study Findings	Recommendations
Ong/JBI, [16] 2017 (citation)	
Based on one systematic review it was stated that there was no evidence to support SSD use for prevention of wound infection in partial thickness wounds. (Level 1) Based on one systematic review it was stated that compared with dressings or skin substitutes, prophylaxis with topical SSD was associated with significant increase in rates of burn wound infection and increased length of hospital stay, however the evidence is unclear or at high risk of bias. (Level 1) Based on one systematic review it was stated that honey had more antibacterial properties and was more efficacious than silver for wound healing.(Level 1)	"• The prophylactic use of topical antibiotics in burn wounds needs to be reconsidered, and specifically the use of SSD, since the available evidence suggests that patients treated with SSD have a higher risk of burn wound infection and longer length of hospital stay than those treated with dressings. (Grade A) • Although silver sulfadiazine has proven antimicrobial properties, its clinical effectiveness in either preventing or treating infected burns wounds has not been proven. Clinician judgment is required. (Grade B) • Honey may be considered in place of silver sulfadiazine for burns. (Grade B)" (pp.3)
WHO - Global Guidelines,[17] 2016	
From the systematic review conducted by the systematic review team it was determined that there was moderate quality evidence showing significant benefit of mupirocin 2% ointment with or without chlorhexidine gluconate body wash in surgical patients with *S. aureus* nasal carriage when compared to placebo or no treatment in reducing the *S. aureus* SSI rate, as well as the overall *S. aureus* health-care associated infection. Additionally, sub-group analysis showed that the evidence was most solid for the cardiothoracic and orthopaedic patient population	"1. The panel recommends that patients undergoing cardiothoracic and orthopaedic surgery with known nasal carriage of *S. aureus* should receive perioperative intranasal applications of mupirocin 2% ointment with or without a combination of CHG body wash. *(Strong recommendation, moderate quality of evidence)* 2. The panel suggests considering to treat also patients with known nasal carriage of *S. aureus* undergoing other types of surgery with perioperative intranasal applications of mupirocin 2% ointment with or without a combination of CHG body wash. *(Conditional recommendation, moderate quality of evidence)*" (pp.63)

Table A9: Summary of Findings of Included Evidence-based Guidelines

Main Study Findings	Recommendations
CSN guideline,[15] 2013, Canada	
One study of limited quality showed that for hemodialysis patients, application of mupirocin cream to the buttonhole cannulation site reduced the risk of infection associated with this technique. This study was a pre-post retrospective comparison of periods before and after the implementation of antimicrobial cream application procedure	"For adult ESRD patients using buttonhole cannulation for intensive home hemodialysis, we suggest the use of mupirocin antibacterial cream to reduce the risk of infection. (Conditional recommendation; very low-quality evidence)" (pp. 191)

CHG = chlorhexidine gluconate; CSN = Canadian Society of Nephrology; ESRD = end-stage renal disease; JBI = Joanna Briggs Institute; SSD = silver sulfadiazine; WHO = World health organization