UK Health Security Agency

Decolonisation of individuals to prevent recurrence of Staphylococcal infection

A rapid systematic review

Contents

Main messages

1. This rapid systematic review (search up to 26 June 2024) identified and summarised evidence on the effectiveness of decolonisation regimes to prevent recurrent Staphylococcal skin and soft tissue infection (SSTI) in those with a history of these infections, or to prevent the development of infections in close contacts of those with history of SSTI.

2. In total, 6,061 primary studies were screened at title and abstract and 154 studies were screened at full text. Four studies were included in this review: 3 randomised controlled trials (RCTs) (1 to 3) and one retrospective cohort study (4).

3. The 4 included studies evaluated the effect of the following decolonisation regimes on the prevention of recurrent infection in those with a history of SSTI infection: mupirocin compared to placebo (1), a combination of mupirocin and chlorohexidine compared against usual care with incision and drainage (2), mupirocin compared to a combination treatment of chlorohexidine and neomycin (3), and a combination of mupirocin and bleach baths compared to no decolonisation (4).

4. Evidence was conflicting on the effectiveness of the examined interventions, which may be explained by differences between studies in comparators used, duration of treatment, or study design. When mupirocin was applied 2 to 3 times a day for 14 days with bleach baths, no difference in recurrent infections was seen compared to no decolonisation (4). There were also no significant differences in rate of recurrence of infection in those treated with mupirocin applied 2 times a day for 5 days with daily chlorohexidine baths compared to usual care (2). However, when mupirocin was applied 5 days a month for one year, there were significantly fewer recurrent infections in individuals treated with mupirocin compared to placebo (1). When mupirocin applied twice daily for 5 days was compared against a combination treatment of chlorohexidine and neomycin, there was a small reduction in recurrent infection in the group that received mupirocin (3).

5. No evidence was identified that assessed the effect of decolonisation in preventing the development of SSTI in the close contacts of those who have a clinical history of recurrent SSTI.

6. An assessment of the certainty of the included evidence (how likely it is that the reported findings represent the true effect) was completed using a modified Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach for each outcome (5). The certainty of evidence for rate of recurrent infection was assessed as moderate (the true effect is probably close to the estimated effect) (1, 3), to very low (the true effect is probably different from the estimated effect) (2, 4). These were downgraded due to methodological limitations identified in the risk of bias assessment,

and concerns that the measurement of the outcome was not directly relevant to this review question for one outcome (4).

7. In summary, 4 studies were identified for inclusion that examined the effectiveness of different decolonisation regimes to prevent recurrent infection in those with a history of SSTI infection (1 to 4). Different interventions, comparators, and duration of treatment were evaluated in each study: mupirocin compared to placebo (1), a combination of mupirocin and chlorohexidine compared against usual care with incision and drainage (2), mupirocin compared to a combination treatment of chlorohexidine and neomycin (3), and a combination of mupirocin and bleach baths compared to no decolonisation (4). Evidence was conflicting, and differences in the interventions and comparators evaluated meant that evidence could not be synthesised or compared, and the most effective intervention could not be determined. All studies included in this review had methodological limitations identified in the risk of bias assessment that may introduce bias into the results. Using a modified GRADE approach, the certainty of evidence was rated between very low and moderate for the 4 included studies (1 to 4). The limitations of the evidence should be considered when interpreting the results from this review.

Purpose

The purpose of this rapid systematic review was to identify and summarise the available evidence for regimes to decolonise individuals who have a clinical history of Staphylococcal skin and soft tissue infections (SSTI) to prevent recurrence, or to prevent secondary infections in their close contacts.

The review questions were:

1. Is decolonisation an effective method for preventing recurrent infections in individuals affected by Staphylococcal skin and soft tissue infection, or secondary infections in their close contacts?

2. If so, what is the most effective decolonisation regimen for preventing recurring infections and secondary infections in close contacts?

Methods

A rapid systematic review was conducted, following streamlined systematic methods to accelerate the review process. A literature search was undertaken to look for relevant interventional or observational studies, published or available as preprint, up to 26 June 2024. The reference lists of relevant reviews were checked to identify any additional primary studies.

A protocol was produced before the literature search was conducted, including the review question, the eligibility criteria, and all other methods. To answer the review questions, the following population, intervention, and outcome was applied:

1. Population: Individuals who have a history of recurrent SSTI (cutaneous abscesses, boils, furuncles, or carbuncles), or those who have had confirmed contact with those diagnosed with a history of recurrent SSTI.

2. Intervention: Any of the following decolonisation regimes: prontoderm, octenisan, chlorhexidine, mupirocin, clindamycin, rifampicin, linezolid, naseptin, flucloxacillin, tetracycline (including doxycycline and minocycline), trimethoprim, or hypochlorous acid compared to each other or no decolonisation (for review question one), or against each other (for review question 2).

3. Outcome: Recurrence of SSTI in those with a history of recurrent SSTI, or development of SSTI in those who have come in to contact with those diagnosed with a history of recurrent SSTI.

Full details of the methodology are provided in the protocol in Annexe A.

Screening on title and abstract was undertaken in duplicate by 2 reviewers for 20% of the eligible studies, with the remainder completed by one reviewer. Screening on full text was undertaken by one reviewer and checked by a second. Data extraction was performed by one reviewer and checked by a second.

Risk of bias assessment was conducted in duplicate by 2 reviewers using the appropriate JBI checklist for the study design (6). The certainty of evidence identified in this review was assessed using a modified version of the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework (5). This process is described in detail in Annexe A. In brief, the certainty of evidence at the outcome level was assessed across 4 domains (inconsistency, imprecision, risk of bias, indirectness) and given one of 4 ratings:

- very low (the true effect is probably different from the estimated effect)
- low (the true effect might be different from the estimated effect)
- moderate (the true effect is probably close to the estimated effect)
- high (the authors are confident that the true effect is similar to the estimated effect)

There was one clarification to the review protocol:

- evidence was included where an intervention or comparator of interest was combined with another intervention

There was one deviation from the review protocol:

- a study was included that reported that the majority (more than 90%) rather than all included participants had a history of previous SSTI

Evidence

In total, 6,061 studies were screened at title and abstract, with 155 studies sought for retrieval. One record could not be retrieved, and so 154 studies were screened at full text. Of these, 4 studies met the inclusion criteria (1 to 4).

A PRISMA diagram showing the flow of studies through the review is shown in Annexe B, and studies excluded on full text screening are available with the reasons why in Annexe C. Study characteristics are available in Annexe D, risk of bias assessments are available in Annexe E, and GRADE certainty of evidence assessments are available in Annexe F and Annexe G.

There were 3 randomised controlled trials (RCTs) (1 to 3), and one retrospective cohort study (4). Two studies were conducted in the United States (2, 4), one in England (3) and one in Israel (1).

All studies evaluated the effectiveness of mupirocin for preventing recurring infection in those with a history of SSTIs: one evaluated mupirocin compared to placebo (1), one evaluated a combination of mupirocin and chlorohexidine compared to usual care which was described as incision and drainage (2), one evaluated mupirocin compared to a combination treatment of chlorohexidine and neomycin (3), and one evaluated a combination of mupirocin and bleach baths compared to no decolonisation (4). Details for all included studies are presented in Table D.1.

The effectiveness of mupirocin compared to placebo was evaluated in one RCT in Israel (1). Thirty-four participants (whole group demographics not reported) who were carriers of staphylococcus with a clinical history of 3 or more staphylococcal skin infections were enrolled into the study. Participants were only included if their culture was negative for *Staphylococcus aureus* after applying mupirocin 2% ointment topically to the nostrils twice daily for 5 days. Seventeen participants (mean age 25.5 years [standard deviation (SD): 17.4 years, age range: 8 to 52 years], 71% male, average of 4.03 (SD: 5.5) skin infections in the past year) were randomised to receive mupirocin 2% ointment applied topically to the nostrils twice daily for 5 days a month for one year, and 17 were randomised to placebo ointment following the same regime (mean age 24.9 years [SD: 12.5 years, age range: 8 to 46 years], 71% male, average of 4.38 (SD: 5.7) skin infections in the past year). There were statistically significantly fewer recurrent skin infections reported by people who received mupirocin compared to those who received placebo (26 infections compared to 52 infections respectively, $p<0.002$), although adherence to the protocol was not measured in participants. Nine of the 17 participants in the mupirocin group experienced recurrence of infection, while 16 of the 17 participants in the

placebo group experienced recurrence of infection (p<0.02). This evidence was rated as moderate certainty evidence using the modified GRADE approach described in Annexe A (assessment summarised in Section: Certainty of Evidence).

The effectiveness of a combination treatment of mupirocin and chlorohexidine compared to usual care (incision and drainage plus selective oral antibiotics only) was evaluated in one RCT in the USA (2). Participants (n=119, mean age 38.1 years [SD: 14.9 years], 60.5% male, 64.9% Hispanic or Latino, 90.8% with abscess or boil) were recruited after presenting with symptoms of an SSTI infection (laboratory confirmed for either methicillin-resistant *Staphylococcus aureus* [MRSA] or methicillin-susceptible *Staphylococcus aureus* [MSSA]). Of these, 90.7% had a documented pre-study SSTI in their electronic health record (30.5% self-reported a previous SSTI). On enrolment, participants were randomised to receive either:

- usual care (incision and drainage plus oral antibiotics as per the U.S Centre for Disease Control and Infectious Disease Society of America guidelines (7, 8)) plus mupirocin applied to nostrils twice daily for 5 days, a once daily wash with 4% chlorhexidine gluconate solution and household decontamination measures that included proper handwashing, regular laundering, and disinfection of high touch surfaces (n=63, mean age 39.5 years [SD: 15.4 years], 65.1% male, 62.7% Hispanic or Latino, 90.5% presenting with a boil or abscess at baseline)
- usual care only (n=56, mean age 36.5 years [SD: 14.4 years], 55.4% male, 67.3% Hispanic or Latino, 91.1% presenting with a boil or abscess at baseline)

Infection recurrence rates were presented by method of reporting (from electronic health record, by participant self-report, or both).

When recurrence rate was taken from participants electronic health record it was similar between groups with 7 out of 63 (11.1%) who received mupirocin having a documented recurrence at 6 month follow-up, compared with 6 out of 56 (10.7%) of those who received usual care (odds ratio [OR]: 1.14, 95% Confidence Interval [CI]: 0.35 to 3.6, p=0.82). However, when recurrence rate was based on self-reported SSTI recurrence, 10 out of 63 (22.2%) in the treatment group reported SSTI recurrence at 6 month follow-up, compared to 3 out of 56 (7.5%) participants in the usual care group (OR: 3.5, 95% CI: 0.89 to 13.8, p value=0.07). Regardless of how rate of recurrence was reported, there were no statistically significant differences between the intervention and usual care group. Only 15.4% of participants who self-reported an SSTI recurrence also had a documented clinical SSTI recurrence. Nether participants or those delivering treatment in this study were blinded to intervention assignment, which may have introduced bias into the reporting of recurrence of infection. This was rated as very low certainty evidence using the modified GRADE approach described in Annexe A (assessment summarised in Section: Certainty of Evidence)

The effectiveness of mupirocin compared to a combination treatment of chlorohexidine and neomycin was evaluated in one RCT in England (3). Thirty-two index participants with recurrent staphylococcal infections and their families (67 family members, n=99 total [age, sex and ethnicity not reported]) underwent household decolonisation. The participants were assigned to one of the following 3 treatment groups:

- mupirocin nasal ointment containing 2% mupirocin to nostrils twice daily for 7 days (n=32; 9 index patients and 23 family members)
- 0.1% chlorhexidine and 0.5% neomycin cream to nostrils twice daily for 7 days (n=34; 11 index patients and 23 family members)
- mupirocin nasal ointment containing 2% mupirocin to nostrils twice daily for 7 days after unsuccessful treatment (definition not reported) with chlorohexidine and neomycin (n=33; 12 index patients and 21 family members)

All patients (index patients and their families) were also given 4% chlorhexidine gluconate for washing, and 1% chlorhexidine as a powder twice daily for 7 days, and were followed for up to 91 days after starting treatment. At baseline, 72% of the index cases and 64% of family members were found to have positive nasal carriage of *Staphylococcus aureus*.

In the group who were treated with mupirocin, 4 out of the 9 (44.4%) index patients experienced recurrence of infection (3 patients experienced recurrence after one month, and one patient experienced recurrence at 3 months), compared to 8 out of 11 (72.7%) index patients in the chlorohexidine and neomycin group (7 patients experienced recurrence at one month, and one patient experienced recurrence at 2 months) and 8 out of 12 (66.7%) index patients in the mupirocin after unsuccessful treatment with chlorohexidine and neomycin group (7 patients experienced recurrence after one month, and one patient experienced recurrence at 3 months). Statistical differences between the groups were not calculated. Two families were included in the results of this study twice, after receiving unsuccessful treatment with chlorhexidine and neomycin before being treated with mupirocin, and all groups had some patients with active infection at baseline (described in Table D.1). For the outcome of recurrence of infection, this study was rated as moderate certainty evidence using the modified GRADE approach described in Annexe A (assessment summarised in the Certainty of Evidence section).

Following treatment, eradication rate of all carrier sites in index patients and their families (nostrils, groin, perianal and armpit) at 8-days after treatment was 95% in mupirocin group, 85% in the mupirocin after unsuccessful treatment with chlorohexidine and neomycin group, and 61% in the neomycin group. At 91 days after treatment this was 57% in mupirocin group, 48% in the mupirocin after unsuccessful treatment with chlorohexidine and neomycin group, and 11% in the neomycin group.

The effectiveness of mupirocin combined with bleach baths compared to no decolonisation was evaluated in one retrospective cohort study in the USA (4). From a cohort of 399 paediatric patients (mean age 3.4 years [SD: 4.4 years], 45% male, 79% African American or Hispanic,

3.5% immunocompromised) who underwent incision and drainage for an SSTI with a positive MRSA culture, 230 were identified as having either:

1. A personal history of either abscess or cellulitis (n=85), or of MRSA (n=34).

Or:

2. A familial history of abscess or cellulitis (n=81), or of MRSA (n=30).

Of these 230 children, 120 were prescribed decolonisation of both the index case and their household and caregivers with mupirocin applied to the nostril 2 to 3 times a day for 14 days, as well as bleach baths with Clorox, chlorhexidine solution or chlorhexidine gluconate wipes (full decolonisation procedure detailed in Table D.1). 110 children and their household and caregivers were not prescribed any decolonisation. Recurrence of infection was only measured if the patient returned to the same hospital, meaning the recurrence rate is out of those who did not report infection as opposed to those who didn't have recurrence of infection.

Recurrence rates were reported as follows:

- in those who had a personal history of either abscess or cellulitis: 7 out of 38 (18.4%) children who were prescribed decolonisation experienced recurrence of infection, compared to 16 out of 47 (34.0%) who were not prescribed decolonisation (p=0.1)
- in those who had personal history of MRSA: 6 out of 21 (28.6%) children who were prescribed decolonisation experienced recurrence of infection, compared to 4 out of 13 (30.8%) children who were not prescribed decolonisation (p=0.89)
- in those who had familial history of either abscess or cellulitis: 12 out of 41 (29.3%) children who were prescribed decolonisation experienced recurrence of infection, compared to 9 out of 40 (22.5%) who were not prescribed decolonisation (p=0.49)
- in those who had familial history of MRSA: 8 out of 20 (40.0%) children who were prescribed decolonisation experienced recurrence of infection, compared to 3 out of 10 (30.0%) who were not prescribed decolonisation (p=0.59)

There were no statistically significant differences in infection recurrence rate between those who were prescribed decolonisation with mupirocin and bleach baths, and those who were not. However, compliance with decolonisation regime was not measured, and recurrence of infection was only recorded if the patient returned to the same hospital for further treatment. This was rated as very low certainty of evidence using the modified GRADE approach described in Annexe A (assessment summarised in the Certainty of Evidence section).

Certainty of evidence

In this review, evidence could not be combined at the outcome level due to differences in the interventions, comparators, and study designs. Risk of bias and indirectness were assessed for each study per outcome. Imprecision was assessed in one study only (2), as the outcomes of

interest were presented as a percentage, without confidence intervals (and these could not be calculated using the available data). Inconsistency was not assessed as data could not be pooled.

Risk of bias was assessed using the JBI checklists for RCTs and cohort studies (6). For the RCTs, the most frequently reported methodological limitations were lack of blinding of those delivering treatment, or the blinding of outcome assessors (not clearly reported in any RCT). A lack of blinding may introduce bias into the results. For the retrospective cohort study, methodological limitations included not reporting whether the groups were similar at baseline, unreliable measurement of the intervention (adherence and compliance were not measured) and outcome (recurrence only recorded if patient returned to same hospital for further treatment), and incomplete follow-up of participants. These limitations may introduce measurement bias (where study variables and outcomes are inaccurately measured). A summary of the risk of bias assessment for RCTs is presented in Table E.1, and for the cohort study is presented in Table E.2.

Indirectness, where elements of the study differ from the intended elements in the review question, was assessed for each study for the outcome of recurrence of SSTI after decolonisation for population, intervention, comparator, and outcome. Only one study was rated as having concerns relating to indirectness. For the retrospective cohort study, the measurement of the intervention was assessed as probably not being sufficiently direct, as adherence to the treatment regime was not reported. A summary of the assessment of indirectness is presented in Table G.1.

Only one study provided information to evaluate imprecision (2). The results for the outcome of this study were rated as very imprecise, due to wide confidence intervals that crossed of the line of no effect.

After assessment of risk of bias, indirectness and imprecision, the certainty of evidence from the RCTs was rated as moderate in 2 RCTs (1) (3), and as very low in one RCT (2). This is due to methodological limitations identified in the risk of bias assessment, including the lack of blinding (or lack of reporting of blinding) of those delivering the intervention and those assessing outcomes, and where measured imprecision was rated as very imprecise. Evidence from the retrospective cohort study was downgraded to very low, due to methodological limitations including a lack of valid and reliable measurement of both the intervention and the outcome (4). A GRADE summary of findings table is presented in Annexe F.

Summary

All of the included studies provide some information for review question one relating to the effectiveness of decontamination regimes, all considering mupirocin as treatment but as part of differing regimes, or with different comparators. Results differed between studies. Compared to a placebo, those who were prescribed mupirocin reported statistically significantly fewer

infections (1), but in the cohort study, there were no statistically significant differences in recurrence between those treated with mupirocin and bleach baths compared to those who had no decolonisation (4). This difference may be explained in part by differences between the studies: there were differences in follow-up (compliance was not measured in the respective cohort, and recurrence was only measured if the participant returned to the same hospital for further treatment), intervention length (participants in the study by Raz and others applied mupirocin 5 days a month for one year (1), rather than the 5 to 14 days prescribed in the other studies), sample size (the RCT by Raz and others (1) had 34 participants, whereas the retrospective cohort had 399 participants (4)), and study design.

When compared to usual care (incision and drainage plus antibiotics), there were no statistically significant differences in rate of recurrent infection in those treated with a combination usual care with mupirocin and chlorohexidine compared to usual care only (2). Compared to a combination treatment with chlorohexidine and neomycin, mupirocin had slightly lower rates of recurrence, however statistical differences were not reported and participant numbers in each group were small (3). Conflicting evidence, differences in interventions, and methodological limitations in the included studies limit definitive conclusions for this review question.

Only one of the 4 included studies provides information relevant to review question 2 about which regime is most effective. This study compared the effectiveness of mupirocin against chlorohexidine and neomycin (3). Rates of recurrence in the group that received mupirocin were slightly lower than either the group that received chlorohexidine and neomycin, or those that received mupirocin after unsuccessful treatment with chlorohexidine and neomycin group (statistical differences not reported). However, the study did not present demographics or any assessment of the groups at baseline, so it is unclear if there were differences between groups. The evidence for review question 2 is too limited to draw any conclusions on which is the most effective treatment for people with a history of SSTI to prevent recurrence.

Health inequalities

Community settings more likely to experience health inequalities, including closed accommodation settings such as prisons and group accommodation settings, were explicitly defined within the inclusion criteria in the review protocol.

For all included studies, there were limited data on which to assess health inequalities in the population of interest (individuals with history of SSTI infection). However, the RCT by Tobin and others represented a population in which health inequalities may be present (2). Study participants were recruited from community health centres in New York, USA. The population was predominantly Hispanic and Latino (64.9% of participants), with over half (56.9%) claiming Medicare or Medicaid (federal or state health insurance) and 22% with no health insurance. While this may indicate that participants were likely to be on lower incomes, we were unable to make direct comparisons of the results in this study and therefore cannot draw conclusions on whether the effectiveness of treatment differed between groups.

The retrospective cohort study by Papastefan and others highlighted potential health inequalities in all patients (those with or without history of recurrence) (4). There were statistically significant differences in the races of those patients (who were all children) who were prescribed decolonisation compared to those who were not (p=0.04), with African-American patients statistically significantly less likely to be prescribed decolonisation than other races (p=0.012). Race was statistically significantly associated with recurrence of infection (p=0.04), with recurrence statistically significantly more likely to occur in Hispanic participants (p=0.02), and statistically significantly less likely to occur in African-American patients (p=0.02). Of the 399 children in this study 230 had a personal or familial history of either abscess or cellulitis, but data was not available for those who had a clinical history of recurrence only.

Limitations

This rapid systematic review used streamlined systematic methods to accelerate the review process. Sources of evidence searched included databases of peer-reviewed and preprint research, but an extensive search of other sources was not conducted and most article screening was completed without duplication, so it is possible relevant evidence may have been missed.

The interventions and comparators differed between the included studies (for example, one study compares mupirocin plus chlorohexidine to usual care, while another compares mupirocin against chlorohexidine combined with neomycin). Duration of intervention and follow up of outcomes also differed between studies. For example, Raz and others (1) gave the intervention for 5 days a month for one year, whereas participants in the study by Leigh and others (3) received the intervention for 7 days only. These differences mean that evidence within this review cannot be synthesised, and comparison of the effectiveness of interventions between the included studies is challenging. While all included studies are relevant for review question one, it is not possible to make a conclusion on the effectiveness of decolonisation for preventing recurrent infections in individuals with a history of SSTI due to these methodological differences, and conflicting findings.

Only one study was identified that answered review question 2 on which treatment regime was most effective (3). Methodological limitations in this study included unclear reporting of blinding of participants, outcome assessors and those delivering treatment, no comparison of the groups at baseline and no statistical analysis of outcomes. These limitations, and the limited evidence available, mean that no definitive conclusions on the effectiveness of different treatment regimens can be made.

All studies included in this review had methodological limitations identified in the risk of bias assessment that may introduce bias into the results. For example, the RCTs in this review did not (or did not clearly report) whether those delivering treatment or assessing outcomes were blinded to the treatment group assigned. These limitations may introduce bias into the results of

these studies and should be considered as part of the interpretation as they may affect the findings. These limitations make it difficult to determine the true impact of decolonisation on recurrent infection in those with a history of SSTI.

One study highlighted differences in the reporting of recurrence of SSTI infection (2). Tobin and others reported that when rate of recurrent infection was measured by electronic health record, there was no statistically significant difference between the intervention and comparator group. However, when rate of recurrent infection was self-reported by the participants, those who received the intervention reported statistically significantly more infections than the comparator group. This study did not blind participants to the intervention that they were receiving, which may explain this difference, but it highlights the risk of potential differences in reporting depending on how the outcome is assessed.

This review used a modified version of GRADE (5) to assess the certainty of the evidence. When using GRADE to assess the certainty of evidence, the expectation is that the evidence will be assessed at the outcome level across all domains. Publication bias (selective publishing, or the failure to publish study findings based on the strength or direction of results) was not assessed as part of the modified approach used in this review. Inconsistency was not assessed as differences in study design and intervention and comparators prescribed could not reasonably be pooled, and imprecision was assessed in one study only as outcome data in other studies was presented without confidence intervals. This means that the assessment of certainty was incomplete and not comprehensive. The limitations of this approach, and the limited data available to assess certainty, should be considered when interpreting the rating of the certainty of evidence in this review.

Evidence gaps

This review resulted in very little evidence, meaning we have not been able to answer the review question definitively. No evidence was identified that assessed the effect of decolonisation in preventing the development of SSTI in the close contacts of those who have a history of recurrent SSTI.

No evidence was identified in neonates (aged 0 to 4 weeks).

No evidence was identified for most treatments considered as part of this review protocol, including prontoderm, octenisan, clindamycin, rifampicin, linezolid, naseptin, flucloxacillin, tetracycline (including doxycycline and minocycline), trimethoprim, or hypochlorous acid.

Conclusion

The aim of this review was to identify and assess available that evaluated the effectiveness of decolonisation regimes in those who had a history of recurrent SSTI infection to prevent further recurrence, or to prevent the development of secondary infection of close contacts of those who have a history of recurrent SSTI infection. Four studies were identified for inclusion with the following decolonisation regime comparisons: mupirocin against placebo (1), mupirocin and chlorohexidine against usual care (2), mupirocin against a combination treatment of chlorohexidine and neomycin (3), and mupirocin and bleach baths against no decolonisation (4).

In summary, there was limited evidence for the effectiveness of decolonisation regimes for the prevention of recurrent infection. Evidence was conflicting, with one study showing no statistically significant effect when mupirocin was compared to no decolonisation (4), one showing no statistically significant effect when mupirocin and chlorohexidine were compared to usual care with incision and drainage (2), and one reporting statistically significant fewer recurrent infections when individuals were treated with mupirocin compared to placebo (1) (though the certainty of evidence for the outcome of recurrence of infection in this study was rated as moderate, compared to the evidence from studies discussed above of which were rated as very low certainty evidence). These differences may be due to differences in the duration of treatment, as the study which reported a potentially beneficial effect of mupirocin compared to placebo administered 5 days a month for one year, whereas the studies that found no effect administered the intervention for between 5 and 7 days only.

The certainty of evidence was assessed as moderate in 2 RCTs (1, 3), as very low in one RCT (2), and as very low for the retrospective cohort study (4). The potential risks of bias and limitations of included studies, as well as differences in the interventions administered and measurement of outcomes, should be considered when interpreting the results from this review.

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Annexe A. Protocol

Review question

There are 2 review questions:

1. Is decolonisation an effective method for preventing recurrent infections in individuals affected by Staphylococcal skin and soft tissue infection, or secondary infections in their close contacts?
2. If so, what is the most effective decolonisation regimen for preventing recurring infections and secondary infections in close contacts?

A search for primary evidence to answer these review questions will be conducted up to 26 June 2024.

Eligibility criteria

Table A.1 Inclusion and exclusion criteria

	Included	Excluded
Population	• adults (over 18 years), children (under 18 years) or neonates (0 to 4 weeks of age) who have a history of recurrent staphylococcal purulent skin and soft tissue infection (cutaneous abscesses, boils, furuncles, or carbuncles) • adults (over 18 years), children (under 18 years) or neonates (0 to 4 weeks of age) with confirmed contact with those diagnosed with history of recurrent staphylococcal skin and soft tissue infection (cutaneous abscesses, boils, furuncles, or carbuncles)	• non-human studies • any other skin or soft tissue infection
Settings	• household and shared spaces (for example, university accommodation) • community settings (for example, sports clubs)	• laboratory settings • hospitals

	Included	Excluded
	• educational settings (for example, schools or nurseries) • group accommodation settings (for example, homeless accommodations, adult social care settings) • other closed accommodation settings (for example, prisons, military bases) • healthcare settings (for example, nursing homes)	
Context	• all contexts	
Intervention or exposure	For question one, treatment with the following decolonisation regimes compared to each other or with no decolonisation: • Prontoderm • Octenisan • Chlorhexidine • Mupirocin • Clindamycin • Rifampicin • Linezolid • Naseptin • Flucloxacillin • Tetracycline (including doxycycline and minocycline) • Trimethoprim • Hypochlorous acid For question 2, treatment with any of the following decolonisation regimes compared to each other: • Prontoderm • Octenisan • Chlorhexidine • Mupirocin	Any other treatment of staphylococcal skin or soft tissue infection

	Included	Excluded
	• Clindamycin • Rifampicin • Linezolid • Naseptin • Flucloxacillin • Tetracycline (including doxycycline and minocycline) • Trimethoprim • Hypochlorous acid	
Outcomes	• recurrence of staphylococcal skin and soft tissue infection (cutaneous abscesses, boils, furuncles, or carbuncles) • development of staphylococcal skin and soft tissue infection (cutaneous abscess, boils, furuncles, or carbuncle) after coming into contact with an infected person	
Language	English	Non-English language studies
Date of publication	Up to 26 June 2024	
Study design	• interventional studies (randomised controlled trials, non-randomised controlled trials) • cohort studies • case-control studies • cross-sectional studies	• systematic or narrative reviews • modelling studies • laboratory studies • case reports • case series • single-arm trials
Publication type	• published (peer-reviewed) • pre-print	• guidelines • opinion pieces • letters • conference abstracts • editorials • news articles

Identification of studies

We will search OVID Medline, OVID Embase, Cochrane Central, Web of Science Core Collection and Web of Science Preprint Citation Index for studies published before 26 June 2024. The search strategy will be checked by another information specialist.

Additional studies may be identified through other methods such as grey literature searching or through consultation with topic experts within UKHSA.

Screening

Screening on title and abstract will be undertaken in duplicate by 2 reviewers for at least 20% of the eligible studies, with the remainder completed by one reviewer. Disagreement will be resolved by discussion.

Screening on full text will be undertaken by one reviewer and checked by a second.

Data extraction

Summary information for each study will be extracted and reported in tabular form. Information will include study date, decontamination method used, results, and any relevant contextual data. This will be undertaken by one reviewer and checked by a second.

Risk of bias assessment

We will perform risk of bias assessment at the primary study level using the relevant JBI checklist (6). Risk of bias will be assessed by 2 reviewers independently with disagreements resolved through discussion or with a third reviewer.

Quality of evidence

The quality of evidence identified within this review will be assessed using a modified version of the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework (5). Quality of evidence will be assessed at the outcome level, and be rated as one of 4 levels:

- very low (the true effect is probably different from the estimated effect)
- low (the true effect might be different from the estimated effect)
- moderate (the true effect is probably close to the estimated effect)
- high (the authors are confident that the true effect is similar to the estimated effect)

The quality of evidence will be assessed for each outcome across 4 domains:

1. Risk of bias: where results may not represent the true effect because of limitations in the design or conduct of the study. This will be measures as described under Risk of bias assessment.

2. Inconsistency: where studies show different effects for the same outcome of interest. This will be assessed where there are 2 or more studies measuring the same outcome. Inconsistency will be rated down if the point estimates are not similar, or the confidence intervals do not overlap. If there is only one study for the outcome of interest, then inconsistency will not be assessed. Inconsistency will be assessed by one reviewer and checked by a second.

3. Indirectness: where elements of the study differ from the intended elements in the review question (for example, the outcome of interest has not been directly measured). This will be rated down if the population, intervention, comparator, or outcome of interest have not been directly measured. Indirectness will be assessed by one reviewer and checked by a second.

4. Imprecision: a measure of how uncertain the estimate is. Imprecision will be rated down if the confidence intervals cross the line of no effect, or if the reviewer judges that the confidence intervals are overly wide and so the true effect is likely to be different at the upper versus the lower end of the confidence interval. Imprecision will be assessed by one reviewer and checked by a second.

Publication bias will not be used to assess the quality of the evidence in this review.

Because the JBI checklist will be used to assess risk of bias, evidence from randomised controlled trials will start at high quality, and evidence from observational studies will start at low quality. Evidence may be downgraded one or two levels following the assessment of quality, or upgraded if there is a large magnitude of effect or clear dose-response gradient.

Synthesis

If data is presented in a consistent format between studies, a narrative synthesis will be produced to describe the results from this review. The number of studies, the number of participants in each study, effect size and variance and a summary of the quality assessment across the outcomes will be presented. Alternatively, if studies present methodological differences that would make synthesis inappropriate, a narrative summary of each study will be provided.

Search strategy

Ovid MEDLINE(R) ALL (1946 to 3 July 2024)

1. exp *Staphylococcus aureus/ (54,731)
2. exp *Staphylococcal Infections/ (53,583)
3. S* aureus.tw,kf. (144,294)
4. MRSA.tw,kf. (30,805)
5. MSSA.tw,kf. (4,494)
6. staphylococc*.tw,kf. (186,802)
7. or/1-6 (211975)
8. (decoloni* or de-coloni*).tw,kf. (2,837)
9. (re-coloni* or recoloni*).tw,kf. (3,083)
10. (coloni#ing or colony or colonies).tw,kf. (198,371)
11. (coloni#e* or coloni#ation).ab. /freq=3 or (coloni#e* or coloni#ation).ti,kf. (32380)
12. Carrier State/ (22,594)
13. carrier*.tw,kf. (271,709)
14. carriage.tw,kf. (18,720)
15. clearance.tw,kf. (194,178)
16. exp Infection Control/ (71,935)
17. exp Communicable Diseases/pc (93,794)
18. (infect* adj3 (prevent* or control*)).tw,kf. (126,688)
19. (disease* adj3 (prevent* or control*)).tw,kf. (210,807)
20. (bacteri* adj3 (prevent* or control*)).tw,kf. (18,417)
21. (spread* adj3 (prevent* or control*)).tw,kf. (19,143)
22. (prevent* adj3 transmi*).tw,kf. (17,998)
23. or/8-22 (1,191,746)
24. exp Anti-Infective Agents/ (1,870,785)
25. Octenisan.tw,kf. (4)
26. Chlorhexidine*.tw,kf. (13,501)
27. mupirocin.tw,kf. (2,166)
28. clindamycin.tw,kf. (12,784)
29. rifampicin.tw,kf. (20,185)
30. rifampin.tw,kf. (9,532)
31. linezolid.tw,kf. (8,154)
32. naseptin.tw,kf. (16)
33. chloramphenicol.tw,kf. (31,752)
34. erythromycin.tw,kf. (24,239)
35. fluoroquinolone.tw,kf. (11,337)
36. levofloxacin.tw,kf. (10,601)
37. methicillin.tw,kf. (42,988)
38. minocycline.tw,kf. (8,390)
39. mupirocin.tw,kf. (2,166)
40. oxacillin.tw,kf. (5,558)

41. penicillin.tw,kf. (59,867)
42. tetracycline.tw,kf. (42,705)
43. doxycycline.tw,kf. (17,592)
44. trimethoprim.tw,kf. (20,702)
45. fusidic acid*.tw,kf. (2,094)
46. retapamulin.tw,kf. (142)
47. Bacitracin.tw,kf. (3,873)
48. povidone iodine.tw,kf. (4,064)
49. triclosan.tw,kf. (4,480)
50. prontoderm.tw,kf. (5)
51. (flucloxacillin or floxacillin).tw,kf. (1,083)
52. (anti microb* or antimicrob*).tw,kf. (252,399)
53. (anti infective* or antiinfective*).tw,kf. (8,122)
54. (anti bacterial* or antibacterial*).tw,kf. (123,739)
55. (antiseptic* or anti septic*).tw,kf. (11,538)
56. (antibiotic* or anti biotic*).tw,kf. (452,590)
57. Hypochlorous Acid/ (3,099)
58. (hypochlorite or hypochlorous acid*).tw,kf. (12,752)
59. (chloric* acid or chloranol or hydroxidochlorine).tw,kf. (53)
60. (hypochlorite or Chlorine hydroxide or Hypochloric acid or Chlorooxidane).tw,kf. (10,140)
61. or/24-60 (2,240,408)
62. exp Recurrence/ (204,650)
63. Chronic Disease/ (286,148)
64. recurr*.tw,kf. (738,565)
65. (boil or boils).tw,kf. (1,275)
66. Furunculosis/ or Carbuncle/ (1,588)
67. (furuncle* or furunculo*).tw,kf. (1,508)
68. carbuncle*.tw,kf. (651)
69. abscess*.tw,kf. (91,889)
70. exp Abscess/ (60,525)
71. persist*.tw,kf. (606,403)
72. (reinfect* or re-infect*).tw,kf. (15,830)
73. (repeat* adj3 (infect* or disease*)).tw,kf. (7,502)
74. or/62-73 (1,774,023)
75. 7 and 23 and 61 and 74 (2,356)

Embase (1974 to 3 July 2024)

1. exp Staphylococcus aureus/ (227,216)
2. exp Staphylococcus aureus infection/ (19,112)
3. S* aureus.tw,kf. (182,199)
4. MRSA.tw,kf. (445,00)
5. MSSA.tw,kf. (7,473)
6. staphylococc*.tw,kf. (217,861)

7. or/1-6 (316,166)
8. (de-coloni* or decoloni*).tw,kf. (3,435)
9. (recoloni* or re-coloni*).tw,kf. (3,245)
10. (coloni#e* or coloni#ation).ab. /freq=3 or (coloni#e* or coloni#ation).ti,kf. (39,300)
11. (coloni#ing or colony or colonies).tw,kf. (235,908)
12. disease carrier/ or asymptomatic carrier/ (34,791)
13. carrier*.tw,kf. (325,907)
14. carriage.tw,kf. (23,406)
15. clearance.tw,kf. (271,622)
16. skin decontamination/ (2,006)
17. exp bacterial colonization/ (65,532)
18. infection control/ (103,425)
19. communicable disease control/ (5,215)
20. (infect* adj3 (prevent* or control*)).tw,kf. (159,155)
21. (disease* adj3 (prevent* or control*)).tw,kf. (282,825)
22. (bacteri* adj3 (prevent* or control*)).tw,kf. (21,225)
23. (spread* adj3 (prevent* or control*)).tw,kf. (21,429)
24. (prevent* adj3 transmi*).tw,kf. (21,489)
25. or/8-24 (1,457,069)
26. exp *antiinfective agent/ (1,857,129)
27. Octenisan.tw,kf. (26)
28. Chlorhexidine*.tw,kf. (16,111)
29. mupirocin.tw,kf. (3,169)
30. clindamycin.tw,kf. (17,583)
31. rifampicin.tw,kf. (25,936)
32. rifampin.tw,kf. (12,762)
33. linezolid.tw,kf. (12,202)
34. naseptin.tw,kf. (61),
35. chloramphenicol.tw,kf. (28,213)
36. erythromycin.tw,kf. (27,888)
37. fluoroquinolone.tw,kf. (14,984)
38. levofloxacin.tw,kf. (17,207)
39. methicillin.tw,kf. (54,447)
40. minocycline.tw,kf. (11,385)
41. oxacillin.tw,kf. (6,931)
42. penicillin.tw,kf. (54,537)
43. tetracycline.tw,kf. (45,312)
44. doxycycline.tw,kf. (26,596)
45. trimethoprim.tw,kf. (26,293)
46. fusidic acid*.tw,kf. (2,525)
47. retapamulin.tw,kf. (198)
48. Bacitracin.tw,kf. (3,770)
49. povidone iodine.tw,kf. (5,166)
50. triclosan.tw,kf. (4,970)

51. prontoderm.tw,kf. (11)
52. (flucloxacillin or floxacillin).tw,kf. (1,836)
53. (anti microb* or antimicrob*).tw,kf. (324,114)
54. (anti-infective* or antiinfective*).tw,kf. (10,946)
55. (anti-bacterial* or antibacterial*).tw,kf. (155,497)
56. (antiseptic* or anti septic*).tw,kf. (12,591)
57. (antibiotic* or anti biotic*).tw,kf. (590,034)
58. hypochlorous acid/ (4,013)
59. (hypochlorite or hypochlorous acid*).tw,kf. (13,531)
60. (chloric* acid or chloranol or hydroxidochlorine).tw,kf. (50)
61. (hypochlorite or Chlorine hydroxide or Hypochloric acid or Chlorooxidane).tw,kf. (10,445)
62. or/26-61 (2,525,133)
63. recurrent disease/ (227,311)
64. chronic disease/ (210,476)
65. recurr*.tw,kf. (1,105,245)
66. (boil or boils).tw,kf. (1,668)
67. exp furunculosis/ (2,457)
68. carbuncle/ (650)
69. (furuncle* or furunculo*).tw,kf. (1,472)
70. carbuncle*.tw,kf. (536)
71. abscess*.tw,kf. (117,202)
72. exp abscess/ (129,870)
73. persist*.tw,kf. (832,666)
74. (reinfect* or re-infect*).tw,kf. (19,723)
75. (repeat* adj3 (infect* or disease*)).tw,kf. (10,811)
76. or/63-75 (2,303,518)
77. 7 and 25 and 62 and 76 (4,053)

Cochrane Central Register of Controlled Trials

Date of search: 4 July 2024

ID	Search	Hits
#1	MeSH descriptor: [Staphylococcus aureus] explode all trees	1,182
#2	MeSH descriptor: [Staphylococcal Infections] explode all trees	1,550
#3	(S* aureus):ti,ab,kw (Word variations have been searched)	4,457
#4	(MRSA):ti,ab,kw (Word variations have been searched)	1,135
#5	(MSSA):ti,ab,kw (Word variations have been searched)	151
#6	(staphylococc*):ti,ab,kw (Word variations have been searched)	6,203
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	6,745
#8	((decoloni* OR de-coloni*)):ti,ab,kw (Word variations have been searched)	361

ID	Search	Hits
#9	((re-coloni* OR recoloni*)):ti,ab,kw (Word variations have been searched)	213
#10	((coloni#e* or coloni#ation or coloni#ing OR colony OR colonies)):ti,ab,kw (Word variations have been searched)	10,082
#11	MeSH descriptor: [Carrier State] explode all trees	574
#12	carrier*:ti,ab,kw	7,502
#13	carriage:ti,ab,kw	1,475
#14	clearance:ti,ab,kw	31,147
#15	MeSH descriptor: [Infection Control] explode all trees	1,669
#16	MeSH descriptor: [Communicable Diseases] explode all trees	30,757
#17	(infect* NEAR/3 (prevent* or control*)):ti,ab,kw	25,626
#18	(disease* NEAR/3 (prevent* or control*)):ti,ab,kw	95,457
#19	(bacteri* NEAR/3 (prevent* or control*)):ti,ab,kw	3,541
#20	(spread* NEAR/3 (prevent* or control*)):ti,ab,kw	450
#21	(prevent* NEAR/3 transmi*):ti,ab,kw	3,335
#22	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21	186,772
#23	MeSH descriptor: [Anti-Infective Agents] explode all trees	40,752
#24	(Octenisan):ti,ab,kw (Word variations have been searched)	3
#25	(Chlorhexidine*):ti,ab,kw (Word variations have been searched)	6,298
#26	(mupirocin):ti,ab,kw (Word variations have been searched)	549
#27	(clindamycin):ti,ab,kw (Word variations have been searched)	2,086
#28	(rifampicin):ti,ab,kw (Word variations have been searched)	1,962
#29	(rifampin):ti,ab,kw (Word variations have been searched)	1,935
#30	(linezolid):ti,ab,kw (Word variations have been searched)	645
#31	(naseptin):ti,ab,kw (Word variations have been searched)	7
#32	(chloramphenicol):ti,ab,kw	651
#33	(erythromycin):ti,ab,kw	2,138
#34	(fluoroquinolone):ti,ab,kw	719
#35	(levofloxacin):ti,ab,kw	1,889
#36	(methicillin):ti,ab,kw	1,657
#37	(oxacillin):ti,ab,kw	160
#38	(penicillin):ti,ab,kw	2,901
#39	(tetracycline):ti,ab,kw	2,265

ID	Search	Hits
#40	(doxycycline):ti,ab,kw	2,564
#41	(minocycline):ti,ab,kw	1,319
#42	(trimethoprim):ti,ab,kw	2,209
#43	(fusidic acid*):ti,ab,kw	254
#44	(retapamulin):ti,ab,kw	36
#45	(Bacitracin):ti,ab,kw	267
#46	(povidone iodine):ti,ab,kw	1,962
#47	(triclosan):ti,ab,kw	748
#48	(prontoderm):ti,ab,kw	4
#49	(flucloxacillin or floxacillin):ti,ab,kw	238
#50	(anti microb* or antimicrob*):ti,ab,kw	18,216
#51	(anti infective* or antiinfective*):ti,ab,kw	7,390
#52	(anti bacterial* or antibacterial*):ti,ab,kw	21,976
#53	(antiseptic* or anti septic*):ti,ab,kw	2,866
#54	(antibiotic* or anti biotic*):ti,ab,kw	39,137
#55	MeSH descriptor: [Hypochlorous Acid] explode all trees	669
#56	(hypochlorite or hypochlorous acid*):ti,ab,kw	1,296
#57	(chloric* acid or chloranol or hydroxidochlorine):ti,ab,kw	3
#58	(hypochlorite or Chlorine hydroxide or Hypochloric acid or Chlorooxidane):ti,ab,kw	1,232
#59	{OR #23 - #58}	2182,697
#60	MeSH descriptor: [Recurrence] explode all trees	16,596
#61	MeSH descriptor: [Chronic Disease] explode all trees	43,508
#62	recurr*:ti,ab,kw	94,942
#63	(boil OR boils):ti,ab,kw	83
#64	MeSH descriptor: [Furunculosis] explode all trees	17
#65	MeSH descriptor: [Carbuncle] explode all trees	4
#66	(furuncle* OR furunculo*):ti,ab,kw	109
#67	carbuncle*:ti,ab,kw	50
#68	abscess*:ti,ab,kw	4,636
#69	MeSH descriptor: [Abscess] explode all trees	836
#70	persist*:ti,ab,kw	49,903
#71	(reinfect* OR re-infect*):ti,ab,kw	1,439

ID	Search	Hits
#72	(repeat* NEAR/3 (infect* OR disease*)):ti,ab,kw	505
#73	#60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72	184,491
#74	#7 AND #22 AND #59 AND #73	417

Filtered to records from CENTRAL only: 414 results.

Web of Science Core Collection

Date of search: 4 July 2024

TS=(“S* aureus” OR MRSA OR MSSA OR staphylococc*)

AND

TS=(decoloni* or “de-coloni*” OR “re-coloni*” or recoloni* OR coloni?ing or colony or colonies OR coloni?e* or coloni?ation OR carrier* OR carriage OR clearance) OR TS=(infect* NEAR/3 (prevent* or control*)) OR TS=(disease* NEAR/3 (prevent* or control*)) OR TS=(bacteri* NEAR/3 (prevent* or control*)) OR TS=(spread* NEAR/3 (prevent* or control*)) OR TS=(prevent* NEAR/3 transmi*)

AND

TS=(Octenisan OR Chlorhexidine* OR mupirocin OR clindamycin OR rifampicin OR rifampin OR linezolid OR naseptin OR chloramphenicol OR erythromycin OR fluoroquinolone OR levofloxacin OR methicillin OR minocycline OR mupirocin OR oxacillin OR penicillin OR tetracycline OR doxycycline OR trimethoprim OR “fusidic acid*” OR retapamulin OR Bacitracin OR “povidone iodine” OR triclosan OR prontoderm OR flucloxacillin or floxacillin OR “anti microb*” or antimicrob* OR “anti infective*” or antiinfective* OR “anti bacterial*” or antibacterial* OR antiseptic* or “anti septic*” OR antibiotic* or “anti biotic*” OR hypochlorite or “hypochlorous acid*” OR “chloric* acid” or chloranol or hydroxidochlorine OR hypochlorite or “Chlorine hydroxide” or Hypochloric acid or Chlorooxidane)

AND

TS=(recurr* OR boil or boils OR furuncle* or furunculo* OR carbuncle* OR abscess* OR persist* OR reinfect* or “re-infect*”) OR TS=(repeat* NEAR/3 (infect* or disease*))

3.105 results.

Web of Science Preprint Citation Index (1990 to current)

Date of search: 4 July 2024

TS=(“S* aureus” OR MRSA OR MSSA OR staphylococc*)

AND

TS=(decoloni* or “de-coloni*” OR “re-coloni*” or recoloni* OR coloni?ing or colony or colonies OR coloni?e* or coloni?ation OR carrier* OR carriage OR clearance) OR TS=(infect* NEAR/3 (prevent* or control*)) OR TS=(disease* NEAR/3 (prevent* or control*)) OR TS=(bacteri* NEAR/3 (prevent* or control*)) OR TS=(spread* NEAR/3 (prevent* or control*)) OR TS=(prevent* NEAR/3 transmi*)

AND

TS=(Octenisan OR Chlorhexidine* OR mupirocin OR clindamycin OR rifampicin OR rifampin OR linezolid OR naseptin OR chloramphenicol OR erythromycin OR fluoroquinolone OR levofloxacin OR methicillin OR minocycline OR mupirocin OR oxacillin OR penicillin OR tetracycline OR doxycycline OR trimethoprim OR “fusidic acid*” OR retapamulin OR Bacitracin OR “povidone iodine” OR triclosan OR prontoderm OR flucloxacillin or floxacillin OR “anti microb*” or antimicrob* OR “anti infective*” or antiinfective* OR “anti bacterial*” or antibacterial* OR antiseptic* or “anti septic*” OR antibiotic* or “anti biotic*” OR hypochlorite or “hypochlorous acid*” OR “chloric* acid” or chloranol or hydroxidochlorine OR hypochlorite or “Chlorine hydroxide” or Hypochloric acid or Chlorooxidane)

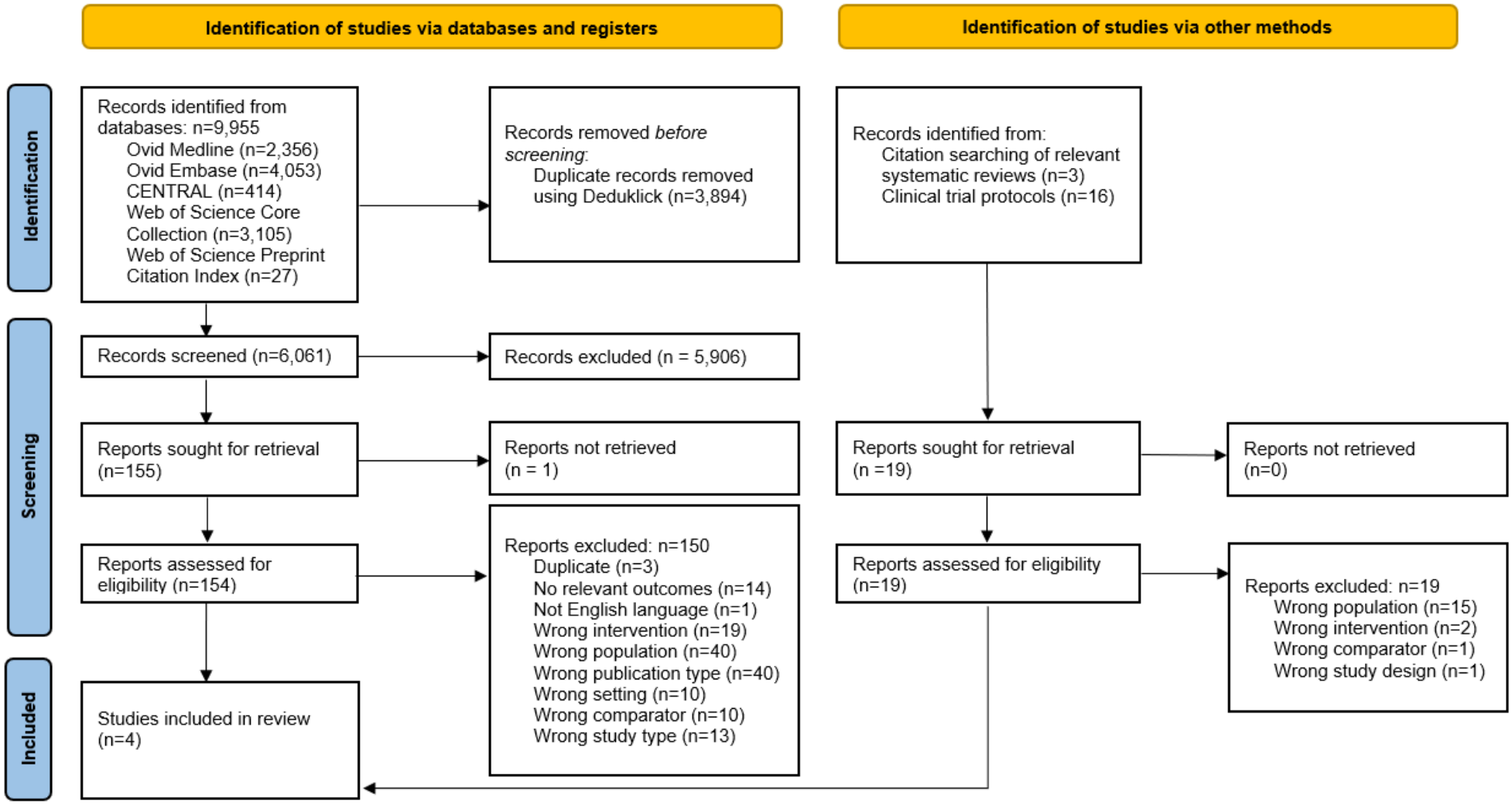
AND

TS=(recurr* OR boil or boils OR furuncle* or furunculo* OR carbuncle* OR abscess* OR persist* OR reinfect* or “re-infect*”) OR TS=(repeat* NEAR/3 (infect* or disease*))

27 results.

Annexe B. Study selection flowchart

Figure B.1. PRISMA diagram



Text version of Figure B.1. PRISMA diagram

A PRISMA diagram showing the flow of studies through this review, ultimately including 4 studies.

From identification of studies via databases and registers, n=9,955 records identified from databases:

- Ovid Medline (n=2,356)
- Ovid Embase (n=4,053)
- CENTRAL (n=414)
- Web of Science Core Collection (n=3,105)
- Web of Science Preprint citation index (n=27)

From these, records removed before screening:

- duplicate records removed using Deduklick (n=3,894)
- duplicate records removed manually (n=0)
- records marked as ineligible by automation tools (n=0)
- records removed for other reasons (n=0)

n=6,061 records screened, of which n=5,906 were excluded, leaving n=155 records sought for retrieval, of which n=1 was not retrieved. n=3 additional studies were identified from citation searching of relevant systematic reviews and n=16 additional studies were identified from protocols of clinical trials.

Of the n=173 studies assessed for eligibility, n=169 reports were excluded:

- duplicate (n=3)
- no relevant outcomes (n=14)
- not English language (n=1)
- wrong intervention (n=21)
- wrong population (n=55)
- wrong publication type (n=40)
- wrong setting (n=10)
- wrong comparator (n=11)
- wrong study type (n=14)

n=4 studies included in the review.

Annexe C. Excluded full texts

Duplicate (3 studies)

D'Orazio BM and others. 'Implementing and evaluating an evidence-based intervention from the intensive care unit (ICU) setting into primary care using promotoras to reduce CA-MRSA recurrence and household transmission' Journal of Clinical and Translational Science 2018: volume 2, page 71

Eum LY and others. 'Randomized controlled trial of chlorhexidine gluconate, intranasal mupirocin, rifampin, and doxycycline versus chlorhexidine gluconate and intranasal mupirocin alone for the eradication of methicillin-resistant Staphylococcus aureus (MRSA) colonization' Canadian Journal of Infection Control 2022: volume 37, pages 77 to 86

Tobin JN and others. 'Comparative Effectiveness Study of Home-Based Interventions to Prevent CA-MRSA Infection Recurrence' medRxiv 2020

No relevant outcomes (14 studies)

Archibald K and others. 'Methicillin-resistant *Staphylococcus aureus* infection in a college football team: risk factors outside the locker room and playing field' Infection Control and Hospital Epidemiology 2008: volume 29, issue 5, pages 450 to 453

Banjar H and others. 'The first report of Methicillin-resistant *Staphylococcus aureus* (MRSA) in cystic fibrosis (CF) patients in Saudi Arabia' International Journal of Pediatrics and Adolescent Medicine 2020: volume 7, issue 4, pages 186 to 190

Blok HEM and others. 'Role of healthcare workers in outbreaks of methicillin-resistant *Staphylococcus aureus*: a 10-year evaluation from a Dutch university hospital' Infection Control and Hospital Epidemiology 2003: volume 24, issue 9, pages 679 to 685

Cederna JE and others. '*Staphylococcus aureus* nasal colonization in a nursing home: eradication with mupirocin' Infection Control and Hospital Epidemiology 1990: volume 11, issue 1, pages 13 to 16

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Annexe D. Data extraction tables

Abbreviations: CI: Confidence Interval, GP: General Practitioner, OR: odds ratio, MRSA: methicillin-resistant S*taphylococcus aureus*, MSSA: methicillin-susceptible *Staphylococcus aureus*, RCT: Randomised controlled trial, SD: standard deviation, SSTI: skin and soft tissue infection, USA: United States of America

Study, study design	Country, time period	Population	Treatment groups (Intervention, comparator)	Outcomes
Leigh and Joy, 1993 RCT (3)	England, not reported	n=26 families (99 individuals; n=32 index patients referred by their GP for recurrent staphylococcal infections, and 67 family members [demographics not reported]) Recruited from Microbiological outpatients at Wycombe General Hospital. Patients whose family members were not staphylococcal carriers were excluded. Two families were included in the results twice, after receiving unsuccessful treatment with chlorhexidine and neomycin before being treated with mupirocin. The interval between treatments was over 3 months with different phage types of infecting staphylococci. When first recruited as outpatients, 3 of the 9 index patients in the mupirocin group had active infections from which *Staphylococcus aureus* was isolated. Five did not have current infection, and one in the culture from lesions was negative. Six of the 11 index patients in the chlorhexidine/neomycin group had active infection, one had no current infection, and 4 were culture negative (as identified from lesions). In the group treated with mupirocin after unsuccessful treatment with chlorhexidine and neomycin, 5 of the 12 index patients had current infection, one did not have current infection and 6 were culture negative from lesions.	Mupirocin group: applied mupirocin nasal ointment containing 2% mupirocin using a cotton bud to anterior nares (nostrils) twice a day for 7 days (n=32; 9 index patients and 23 family members [demographics not reported]). Chlorohexidine and neomycin group: applied 0.1% chlorhexidine and 0.5% neomycin cream using a cotton bud to anterior nares twice a day for 7 days (n=34; 11 index patients and 23 family members [demographics not reported]) Mupirocin after failure with chlorhexidine and neomycin (n=33; 12 index patients and 21 family members [demographics not reported). All patients used 4% chlorhexidine gluconate for washing, and 1% chlorhexidine as a powder twice daily for 7 days. Follow up at 8,14, 28 and 91 days after starting treatment.	Mupirocin group: • 5 out of 9 index patients (55.6%) experienced no further infection after treatment • 4 out of 9 index patients (44.4%) experienced recurrence (3 experienced recurrence at one month, one experienced recurrence at 3 months) Chlorhexidine and neomycin group: • 3 out of 11 patients (27.3%) experienced no further infection after treatment • 8 out of 11 patients (72.7%) experienced recurrence (7 experience recurrence at one month, one experienced recurrence at 2 months) Mupirocin after failure with chlorhexidine and neomycin: • 4 out of 12 patients (33.3%) experienced no further infection after treatment • 8 out of 12 patients (66.7%) experienced recurrence (7 experienced recurrence at one month, one experienced recurrence at 3 months) Statistical differences between groups not reported.
Papastefan and others, 2019 Retrospective cohort study (4)	USA, January 2007 to December 2017	n=399 paediatric patients (under 18 years) underwent surgical incision and drainage for a SSTI with a positive MRSA culture at a tertiary care children's hospital (45% male, mean age 3.4 years	Decolonisation group: For all family members, Mupirocin was to be applied to anterior nares 2 to 3 times a day for 14 days, as well as Clorox bleach baths (which could be substituted with	Recurrence rate for patients with personal history of abscess or cellulitis: Prescribed decolonisation: 7 out of 38 (18.4%) paediatric patients

Study, study design	Country, time period	Population	Treatment groups (Intervention, comparator)	Outcomes
		[SD: 4.4 years], 79% African American or Hispanic, 3.5% immunocompromised) Of these, n=230 had either a personal or familial history of MRSA or abscess or cellulitis: n=119 personal history of MRSA or abscess or cellulitis (MRSA: n=34, abscess or cellulitis: n=85) n=111 familial history of MRSA or abscess or cellulitis (MRSA: n=30, abscess or cellulitis: n=81)	chlorhexidine solution or Hibiclens [chlorhexidine gluconate wipes]). Clorox bleach baths procedure: 1 to 3 years of age: one-fourth cup Clorox bleach in full tub of water 4 years and older: Half cup of Clorox bleach in a full tub of water Patients were asked to soak in water for 10 to 15 minutes, neck to feet, then scalp for 2 to 3 times a week for 2 weeks. (n=120, [demographics not reported]) No decolonisation group: no prescription decolonisation (n=110, [demographics not reported]).	Not prescribed decolonisation: 16 out of 47 (34.0%) paediatric patients (p=0.1) Recurrence rate for patients with personal history of MRSA: Prescribed decolonisation: 6 out of 21 (28.6%) paediatric patients Not prescribed decolonisation: 4 out of 13 (30.8%) paediatric patients (p=0.89) Recurrence rate for patients with family history of abscess or cellulitis: Prescribed Decolonisation: 12 out of 41 (29.3%) paediatric patients Not Prescribed Decolonisation: 9 out of 40 (22.5%) paediatric patients (p=0.49) Recurrence rate for patients with familial history of MRSA: Prescribed decolonisation: 8 out of 20 (40.0%) paediatric patients Not prescribed decolonisation: 3 out of 10 (30.0%) paediatric patients (p=0.59) For all patients (with or without clinical history of recurrence), patient race was significantly different between decolonised and non-decolonised patients (p=0.04), with African-American patients less likely to be prescribed decolonisation than other races (p=0.012). Race was significantly associated with recurrence (p=0.04), with Hispanic patients statistically significantly more likely to recur (p=0.02), and African American patients statistically significantly less likely to recur (p=0.02). Data was not available in those who had clinical history of recurrence only.

Study, study design	Country, time period	Population	Treatment groups (Intervention, comparator)	Outcomes
Raz and others, 1996 RCT (1)	Israel, not reported	n=34 patients with clinical history of 3 or more staphylococcal skin infections within the last year who were identified as carriers of staphylococcus (whole group demographics not reported).	All patients applied mupirocin 2% ointment in a polyethylene glycol base (Bactroban) topically to the anterior nares twice daily for 5 days before being randomised. After a negative culture, patients were randomly divided under double-blind conditions into 2 groups. Mupirocin group: applied nasal mupirocin twice daily for 5 days a month for one year (n=17 [20 originally recruited, but 3 patients were poorly compliant and did not complete the study], mean age 25.5 years [SD: 17.4 years, age range 8 to 52 years], 71% male, average of 4.03 [SD: 5.5] skin infections in the past year). Placebo group: applied a placebo ointment twice daily, 5 days a month for one year (n=17 [20 originally recruited, but 3 patients were poorly compliant and did not complete the study], mean age 24.9 years [SD: 12.5 years, age range: 8 to 46 years], 71% male, average of 4.38 [SD: 5.7] skin infections in the past year).	26 skin infections were reported in the follow up period in the mupirocin group, compared to 52 in the placebo group ($p<0.002$) Mupirocin group: 8 out of 17 patients did not experience recurrence Placebo group: 1[a] out of 17 did not experience recurrence ($p<0.02$).
Tobin and others, 2021 RCT (2)	USA, November 2015 to November 2017	n=119 recruited from community health centres or hospitals after presenting with symptoms of an SSTI infection with a laboratory-confirmed baseline wound positive for either MRSA or MSSA (mean age 38.1 years [SD: 14.9 years], 60.5% male, 64.9% Hispanic or Latino, 90.8% with abscess or boil). 90.7% had documented pre-study SSTIs in their electronic health records (but only 30.5% of participants self-reported a previous SSTI) Type of insurance: 47.5% Medicaid, 22.0% No insurance, 12.8% other insurance, 9.4% Medicare, 8.5% private insurance	Participants were randomised to either a usual care or experimental group. Experimental group: received usual care plus detailed verbal, written, and demonstrated instructions of a 5 day protocol for application of nasal mupirocin twice daily to anterior nares, once daily wash with chlorohexidine gluconate solution 4% and household decontamination instructions (proper handwashing technique, laundering bed linens in warm water every other day, disinfection of high touch surfaces with disinfecting wipes) (n=63, mean age 39.5 years [SD: 15.4 years], 65.1% male, 62.7% Hispanic or Latino, 90.5% presenting with a boil or abscess at baseline).	The outcome of rate of recurrent infection was measured by instance of recurrent infection recorded in electronic health record during 6-month follow-up, or by participant reported recurrence of infection during 6-month follow-up When recurrence was measured using electronic health records, 7 out of 63 patients (11.1%) in the experimental group compared to 6 out of 56 patients (10.7%) in the usual care group had a documented SSTI recurrence at 6 month follow-up in their electronic health record (OR=1.14, 95% CI=0.35 to 3.6, p=0.82) When recurrence was measured using participant reported recurrence of infection, 10 out of 63 patients (22.2%) of the experimental group compared to 3 out of 56 patients (7.5%) of the usual care group self-reported SSTI recurrence at 6 month follow-up (OR=3.5, 95% CI=0.89 to 13.8, p value=0.07)

Study, study design	Country, time period	Population	Treatment groups (Intervention, comparator)	Outcomes
			Usual care group: received incision and drainage plus selective oral antibiotics only (n=56, mean age 36.5 years [SD: 14.4 years], 55.4% male, 67.3% Hispanic or Latino, 91.1% presenting with a boil or abscess at baseline).	When recurrence was measured using either the participant electronic health record or participant reported recurrence, 15 out of 63 patients (24.2%) of the experimental group compared to 9 out of 56 patients (16.1%) of the usual care group had a documented SSTI recurrence at 6 month follow-up in either their electronic health record or by self-report (OR=1.7, 95% CI=0.66 to 4.2, p value=0.27) Only 15.4% of participants who self-reported an SSTI recurrence also had a documented clinical SSTI recurrence

a = There is a lack of clarity in the text of this study regarding the number of participants in the placebo group who did not experience recurrence.

Annexe E. Risk of bias assessment

Table E.1 Risk of bias assessment for randomised controlled trials

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Comments
Leigh and Joy, 1993 (3)	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	No	Yes	Q2: Concealment of allocation to treatment groups not reported Q3: Unclear if treatment groups similar at baseline as only carriage reported Q4: Blinding of participants to treatment assignment not reported Q5: Blinding of those delivering the treatment not reported Q7: Blinding of outcome assessor not reported Q12: No statistical analysis between groups
Raz and others, 1996 (1)	Yes	Unclear	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Q2: Concealment of allocation to treatment groups not reported Q5: Not clear if those delivering treatment blinded to intervention assigned Q7: Not clear if outcome assessor was blind to treatment assessment
Tobin and others, 2021 (2)	Yes	Yes	Yes	No	No	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Q4: Participants not blinded to intervention assigned Q5: Those delivering treatment not blinded to intervention assigned Q7: Not clear if outcome assessor was blind to treatment assessment

Critical appraisal was done using the JBI checklist for randomised controlled trials (6)..

List of questions:

Question 1: Was true randomization used for assignment of participants to treatment groups?
Question 2: Was allocation to treatment groups concealed?
Question 3: Were treatment groups similar at the baseline?
Question 4: Were participants blind to treatment assignment?
Question 5: Were those delivering the treatment blind to treatment assignment?
Question 6: Were treatment groups treated identically other than the intervention of interest?
Question 7: For each outcome, were outcome assessor blind to treatment assignment?
Question 8: For each outcome, were outcomes measured in the same way for treatment groups?
Question 9: For each outcome, were outcomes measured in a reliable way?
Question 10: For each outcome, was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?
Question 11: For each outcome, were participants analysed in the groups to which they were randomised?
Question 12: For each outcome, was appropriate statistical analysis used?
Question 13: Was the trial design appropriate and any deviations from the standard RCT design (individual randomisation, parallel groups) accounted for in the conduct and analysis of the trial?

Table E.2 Risk of bias assessment for cohort studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Comments
Papastefan and others, 2019 (4)	No	Yes	No	Yes	Yes	Not Assessed	No	Yes	No	No	Yes	Q1: Significant difference of race and personal or familial history of skin and soft tissue infection between groups Q3: Adherence and compliance not measured as prescription of decolonisation measured retrospectively from medical chart review Q6: Not assessed as study was measuring treatment to prevent recurrence Q7: Outcome only measured if participant returned to one specific hospital Q9: One participant lost to follow up and not discussed Q10: Follow up not adequately complete

Critical appraisal was done using the JBI checklist for cohort studies (6).

Question 1: Were the 2 groups similar and recruited from the same population?
Question 2: Were the exposures measured similarly to assign people to both exposed and unexposed groups?
Question 3: Was the exposure measured in a valid and reliable way?
Question 4: Were confounding factors identified?
Question 5: Were strategies to deal with confounding factors stated?
Question 6: Were the groups or participants free of the outcome at the start of the study (or at the moment of exposure)?
Question 7: Were the outcomes measured in a valid and reliable way?
Question 8: Was the follow up time reported and sufficient to be long enough for outcomes to occur?
Question 9: Was follow up complete, and if not, were the reasons to loss to follow up described and explored?
Question 10: Were strategies to address incomplete follow up utilised?
Question 11: Was appropriate statistical analysis used?

Annexe F. GRADE Summary of findings

Table F.1. GRADE summary of findings table for rate of recurrent infection

Quality assessment							Quality	Importance
Study	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**		
Leigh and Joy, 1993 (3)	Randomised trial	Serious [note 1]	Not assessed	Not serious	Not assessed	None	⊕⊕⊕◯ Moderate	IMPORTANT
Raz and others, 1996 (1)	Randomised trial	Serious [note 2]	Not assessed	Not serious	Not assessed	None	⊕⊕⊕◯ Moderate	IMPORTANT
Tobin and others, 2021 (2)	Randomised trial	Serious [note 3]	Not assessed	Not serious	Very serious [note 4]	None	⊕◯◯◯ Very low	IMPORTANT
Papastefan and others, 2019 (4)	Cohort study	Very serious [note 5]	Not assessed	Serious [note 6]	Not assessed	None	⊕◯◯◯ Very low	IMPORTANT

Notes

Note 1: Concealment of allocation to treatment groups not reported, unclear if treatment groups similar at baseline as only carriage reported, blinding of participants to treatment assignment not reported, blinding of those delivering the treatment not reported, blinding of outcome assessor not reported, no statistical analysis between groups.

Note 2: Concealment of allocation to treatment groups not reported, not clear if those delivering treatment blinded to intervention assigned, not clear if outcome assessor was blind to treatment assessment.

Note 3: Participants not blinded, those administering intervention not blinded, unclear if outcome assessors blinded.

Note 4: Wide confidence intervals, line of no effect crossed.

Note 5: Significant difference of race and personal or familial history of skin and soft tissue infection between groups, adherence and compliance of intervention not available, outcome only measured if participant returned to one specific hospital, one participant lost to follow up and not discussed, follow up not adequately complete.

Note 6: Adherence and compliance to intervention not measured, take retrospectively from medical record, not clear if patients adhered to no treatment, outcome only measured if participant returned to same hospital (see Table G.1)

Annexe G. Assessment of indirectness

Table G.1. Summary of assessment of indirectness for each study for the outcome of rate of recurrent infection

Outcome	Study	Q1	Q2	Q3	Q4	Q5	Comments
Recurrence of skin and soft tissue infection after decolonisation	Leigh and Joy, 1993	Yes	Probably yes	Probably yes	Yes	Yes	Q2: Adherence of index patient and family to intervention not measured. Q3: Adherence of index patient and family to comparator not measured.
Recurrence of skin and soft tissue infection after decolonisation	Raz and others, 1996	Yes	Yes	Yes	Yes	Probably yes	Q5: All episodes of skin infection were recorded, but number of episodes in total not per person. Was a secondary outcome of the study, and so outcome of interest often combined with number of positive nasal cultures
Recurrence of skin and soft tissue infection after decolonisation	Tobin and others, 2021	Probably yes	Yes	Yes	Yes	Probably yes	Q1: Did not explicitly recruit those experiencing skin and soft tissue infection; 90.7% of participants had documented history of SSTI infection on their electronic health record. Q5: Differences in outcome depending on whether self-reported or from electronic health record.
Recurrence of skin and soft tissue infection after decolonisation	Papastefan and others, 2019	Yes	Probably no	Probably yes	Yes	Probably yes	Q2: Adherence and compliance not measured. Prescription of decolonisation taken retrospectively from medical record, unclear if prescription followed through with. Q3: Comparator was no prescription of decolonisation. Not clear if patients adhered to no treatment, could have sought treatment elsewhere. Q5: Outcome only measured if participant returned to same hospital.

Q1: Is the evidence for the population assessed sufficiently direct?
Q2: Is the evidence for the intervention assessed sufficiently direct?
Q3: Is the evidence for the comparator assessed sufficiently direct?
Q4: Is the evidence for the direct comparison assessed sufficiently direct?
Q5: Is the evidence for the outcome assessed sufficiently direct?

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